A RANDOMIZED, CONTROLLED, SIX-WAY CROSSOVER CLINICAL STUDY TO CHARACTERIZE THE NICOTINE PHARMACOKINETICS AND SUBJECTIVE EFFECTS OF FOUR HEATED TOBACCO PRODUCTS IN ADULT MENTHOL AND NON- MENTHOL CIGARETTE SMOKERS

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STATISTICAL ANALYSIS PLAN

A RANDOMIZED, CONTROLLED, SIX-WAY CROSSOVER CLINICAL STUDY TO CHARACTERIZE THE NICOTINE PHARMACOKINETICS AND SUBJECTIVE EFFECTS OF FOUR HEATED TOBACCO PRODUCTS IN ADULT MENTHOL AND NON-MENTHOL CIGARETTE SMOKERS

Altria Client Services LLC Study No. ALCS-REG-23-08-HT (Ploom® PK)
Final Protocol Date: 19 October 2023
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[redacted]
Final Version 1.0
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Sponsor:
Altria Client Services LLC
601 E. Jackson Street
Richmond, Virginia 23219, USA

STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

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Issue Date: 14 May 2024

Signature: DocuSigned by: [redacted] 3D6AF47F39BD44F0872CA6D388D93769 Date: _____

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Signature: [redacted] C78FAC5F913745B6B7514D09F8A8CA64 Date: _____

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[redacted]

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1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the analysis and presentation of the data from this study. Any changes made from the planned analysis described in the protocol or after finalization of this SAP will be documented in the Clinical Study Report (CSR). The section referred to as "Table, Figure, and Listing Shells" within this SAP describes the Clinical Data Interchange Standards Consortium (CDISC) input in order to provide traceability to the corresponding tables, figures, and listings (TFLs). Analysis data model (ADaM) is the source for tables and figures (as well as listings that may contain derived data) and study data tabulation model (SDTM) is the source for the data listings.

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

2. OBJECTIVES AND ENDPOINTS

2.1 Objectives

The main objectives of the study are:

- Characterize pharmacokinetic (PK) parameters of nicotine in plasma during and after a single *ad libitum* use of heated tobacco products (HTP; two menthol and two tobacco flavor varieties) relative to usual brand combustible cigarette (UBCC) and the nicotine gum (nicotine replacement therapy [NRT]).

- Characterize Product Liking of HTP (two menthol and two tobacco flavor varieties) during and after a single *ad libitum* use relative to UBCC and the nicotine gum.

- Characterize additional subjective measures of HTP (two menthol and two tobacco flavor varieties) during and after a single *ad libitum* use relative to UBCC and the nicotine gum.

- Assess heart rate following the use of HTP (two menthol and two tobacco flavor varieties) relative to UBCC and the nicotine gum.

- Characterize product use of HTP during a single *ad libitum* use.

- Assess safety profiles of HTP (two menthol and two tobacco flavor varieties) compared to UBCC and nicotine gum with monitoring of adverse experiences, symptom-driven physical examinations, and relevant clinical laboratories as needed.

The exploratory objectives of the study are:

- Characterize N-nitrosonornicotine (NNN) uptake during HTP use relative to UBCC use.
- Assess additional Product Liking parameters during each morning *ad libitum* product use.

2.2 Endpoints

The main endpoints are:

- Baseline-adjusted plasma nicotine PK parameters following a single *ad libitum* HTP, UBCC, or nicotine gum use:
  - C_{max}: Maximum measured plasma concentration.
  - $AUC_{(0\text{-}180)}$: Area under the nicotine concentration-time curve calculated using linear trapezoidal summation from time zero (defined as the start of product use) to 180 minutes.
  - T_{max}: Time of the maximum measured plasma concentration.
- Assessment of Product Liking during and following the morning *ad libitum* product use PK test session:
  - Original VAS scores for responses to Product Liking questionnaire
  - $E_{max\text{-}PL}$: Maximum product liking in visual analogue scale (VAS) score during each morning *ad libitum* product use.
- Subjective Effects (questionnaires scores during and following the morning *ad libitum* product use PK test session):
  - Tobacco/Nicotine Withdrawal Questionnaire
    - Original VAS scores for responses to Tobacco/Nicotine Withdrawal questionnaire
    - $E_{max\text{-}TNW}$: Maximum reduction in VAS score from baseline pre-use to post-use (i.e., VASpre-use – VASpost-use) for each morning *ad libitum* product use.
  - Direct Effects of Product Questionnaire
    - Original VAS scores for responses to Direct Effects of Product questionnaire

- $E_{max\text{-}DEP}$: The largest VAS score recorded for each morning *ad libitum* product use.

- Use the Product Again Questionnaire
  - Original VAS scores for responses to Use the Product Again Questionnaire
  - Bipolar scores (-50 to < 0, 0, > 0 to 50), calculated by subtracting 50 from the original VAS score (0 to 100)
- Modified Cigarette Evaluation Questionnaire (mCEQ)
  - Original scores for individual item responses to mCEQ (12 items rated on a 7-point Likert-type scale)
  - Factor scores with responses grouped into 5 factors (Product use satisfaction, Psychological reward, Aversion. Enjoyment of the sensation, and Craving reduction)

- Physiological heart rate measurements prior to and for up to 180 minutes following the start of morning *ad libitum* product use PK test session
- Product Use
  - Number of HTP, UBCC, and nicotine gum used in the afternoon product use session
  - Puff count during the morning *ad libitum* product use PK test sessions for HTP and UBCC products
- Safety
  - Physical examination (symptom driven) findings
  - Results of adverse experience (AE) monitoring
  - Clinical laboratory findings, as applicable

Exploratory endpoints are:

- Maximum change from baseline ($C_{max\text{-}NNN}$) for plasma NNN levels following HTP and UBCC use
- Area under the effect curve (AUEC-PL) for product liking assessment during each morning ad libitum product use
- Physiological Heart Rate Assessment:

- $E_{max\text{-}HR}$: Maximum heart rate change from baseline
- $TE_{max\text{-}HR}$: Time of maximum heart rate change from baseline

3. STUDY DESIGN

This is a randomized, controlled, six-way crossover clinical study to characterize the nicotine PK and subjective effects of HTPs (2 menthol varieties, Products A and B; 2 tobacco flavor varieties, Products C and D) in adult menthol and non-menthol combustible cigarette smokers. The study will include participants' UBCC (Product F) and a nicotine gum (Product E) as high and low abuse liability reference products, respectively, to the HTP. Results of this study will help in determining abuse liability of HTP products in current smokers.

The study will include generally healthy adult males and females who smoke factory manufactured combustible cigarettes. This study will recruit approximately 60 participants (composed of approximately 30 menthol and 30 non-menthol adult smokers) in an attempt to obtain approximately 48 study completed participants (approximately 24 menthol and 24 non-menthol smokers). Every attempt will be made to enroll no less than 40% of either sex for menthol and non-menthol smokers, respectively. Enrolled participants will be randomized based on sex and their UBCC (menthol or non-menthol) to one of six product use sequences.

Adult participants will be between 22 and 65 years of age at screening, inclusive. Participants must have a history of smoking ≥ 10 to ≤ 30 menthol or non-menthol factory manufactured combustible cigarettes daily for at least 12 months prior to screening. Screening will occur within 28 days prior to Day 1.

Enrollment visit (Day -6) will occur 5 days prior to Check-in (Day -1). Participants will receive the Ploom® HTP products for at-home product acclimation to become familiar with the product during the next 5 days.

Participants will check-in on the morning of Day -1, when product use sequence randomization and assignment to one of six product use sequences.

Starting on Day -1 through Day 5, participants will use their assigned product (HTP, UBCC, or nicotine gum) during an afternoon product use session. Participants will use the same assigned product to be tested during the next day's morning *ad libitum* product use PK test session. Participants will be required to abstain from any tobacco- or nicotine-containing products for at least 12 hours prior to the start of the following morning's *ad libitum* product use PK test session.

Morning *ad libitum* product use PK test sessions will occur on the mornings of Days 1, 2, 3, 4, 5, and 6 (for a total of 6 morning *ad libitum* product use PK test sessions).

Participants will use a single UBCC or HTP for 5 minutes *ad libitum* or use the nicotine gum for 30 minutes. Blood samples for PK will be collected prior to and for 3 hours following the start of each morning *ad libitum* product use PK test session. Heart rate measurements will be taken at specified time points during each morning *ad libitum* product use PK test session.

In addition, participants will complete subjective effects questionnaires (Product Liking, Tobacco/Nicotine Withdrawal, Direct Effects of Product, Use Product Again, and mCEQ) at designated time points during each morning *ad libitum* product use PK test session.

Participants will remain in confinement until after all study activities are completed on Day 6.

4. SAMPLE SIZE ESTIMATION

The purpose of this study is to characterize the nicotine PK and subjective effects of four Ploom® HTPs in healthy adult menthol and non-menthol combustible cigarette smokers. Assuming an intra-subject variability of 60% for plasma nicotine C_{max} and AUC (Picavet et al., 2016) as well as a true geometric mean ratio (GMR) of 100%, a sample size of 48 participants would result in a 90% confidence interval (CI) of (83%, 121%). If true GMR of 105% is assumed, a sample size of 48 participants would result in a 90% CI of (87%, 127%). Based on previously published literature, typical sample sizes range from 10 to 32 participants for studies examining the PK and subjective effects of tobacco/nicotine-containing product use (Carter et al., 2009, Cobb et al., 2010, Cox et al., 2001, Gray et al., 2008, Hardie et al., 2022, Hatsukami et al., 2004, Kotlyar et al., 2007, McDermott et al., 2023). Therefore, a sample size of approximately 48 participants (24 completed participants per each of the menthol and non-menthol groups) is considered adequate for the current study design.

5. RANDOMIZATION

Participants will be randomized at 1:1:1:1:1:1 ratio into 1 of 6 study product sequences as listed below. At least 60 participants will be randomized to ensure approximately 48 completed participants, with approximately 24 menthol and 24 non-menthol cigarette smokers. Every attempt will be made to enroll no less than 40% of either sex for each cigarette flavor (menthol or non-menthol). Participants will be stratified by sex and cigarette flavor for each of the sequences.

A 6x6 Latin Square with the following sequences will be used for the randomization:

Sequence 1 = ABFCED
Sequence 2 = BCADFE
Sequence 3 = CDBEAF
Sequence 4 = DECFBA

Sequence 5 = EFDACB
Sequence 6 = FAEBDC

Participants will be randomized to the above sequences on the day of Check-in (Day -1).

6. ANALYSIS POPULATIONS

Enrolled Population will include all participants who signed the ICF. Screen failure participants will be included in the Enrolled Population.

Safety Population will include all participants who used any study product. Participants who participated in the product trial only will be included in the Safety Population but summarized separately.

Pharmacokinetic (PK) Population will include all participants who used any study product and have both product baseline pre-use and at least one post-use plasma nicotine concentration values.

Subjective Measures Population will include all participants who used any study product and have both product baseline pre-use (Tobacco/Nicotine Withdrawal) and at least one post-use (Product Liking, Tobacco/Nicotine Withdrawal, Direct Effects of Product, Use the Product Again, and mCEQ) Questionnaire response scores.

Heart Rate Population will include all participants who used any study product and have product baseline pre-use and at least one post-use physiological heart rate measurement during the morning *ad libitum* product use PK test session.

Product Use Population will include all participants who used any study product and have at least one puff count value.

For any participant who is pregnant during the study, that participant's data will only be listed but will be excluded from all analyses.

7. STUDY PRODUCT DESCRIPTIONS

A description of the study products is presented in Table 7–1. The study products will be listed in the TFLs according to the long or the short description, as applicable.

Table 7–1: Study Products

Study Product	Long Description	Short Description	Route of Administration	Manufacturer	
				Device	Sticks
A	Ploom® 3.1 HTP - Menthol HTS; MX3 (681) (Test Product)	Menthol MX3 HTS	Inhalation	PT. Pegatron Technology	JTI
B	Ploom® 3.1 HTP - Menthol HTS; MX5 (706) (Test Product)	Menthol MX5 HTS	Inhalation	PT. Pegatron Technology	JTI
C	Ploom® 3.1 HTP - Tobacco HTS; R8 (120) (Test Product)	Tobacco R8 HTS	Inhalation	PT. Pegatron Technology	JTI
D	Ploom® 3.1 HTP - Tobacco HTS; RX4 (953) (Test Product)	Tobacco RX4 HTS	Inhalation	PT. Pegatron Technology	JTI
E	Nicorette® 4 mg Mint Nicotine Gum (Reference Product)	Nicotine Gum	Oral	N/A	N/A
F	Combustible Cigarette (menthol or non-menthol), participant's usual brand (Reference Product)	UBCC	Inhalation	N/A	Various

The HTP (devices and sticks; Products A, B, C, and D) and nicotine gum (Product E) will be sourced by Altria Client Services LLC. The heated tobacco sticks (HTS) for Products A, B, C, and D were manufactured by [redacted]). Participants' UBCC (Product F) will be sourced by the participant prior to Check-in.

8. PHARMACOKINETIC ANALYSIS

8.1 Measurements and Collection Schedule

8.1.1 Plasma Nicotine

On Days 1 through 6, venous blood samples (~4 mL per sample) for PK analysis of plasma nicotine concentrations will be collected approximately 5 minutes prior to and 3, 5, 7, 10, 15, 30, 45, 60, 120, and 180 minutes following the start of each morning *ad libitum* product use episode. The allowed window for PK blood sampling is defined in Table 4 of the protocol.

8.1.2 Plasma NNN

On Days 1 through 6, blood samples (~10 mL per sample) for PK analysis of plasma NNN concentrations will be collected approximately 5 minutes prior to and 5, 7, and 10 minutes following the start of each controlled products use episode.

8.2 Bioanalytical Method

Plasma nicotine concentrations will be analyzed by the validated procedure "The Determination of Nicotine, Cotinine, Trans-3'-Hydroxycotinine Concentrations in Human Plasma by liquid chromatography-mass spectrometry (LC-MS/MS)" by [redacted] Lincoln, Nebraska. Sample analysis shall be conducted in compliance with the agreed upon protocol, analytical plan, and [redacted] Bioanalytical Laboratory's SOPs. The International Council for Harmonisation (ICH) Harmonised Guideline M10, Bioanalytical Method Validation and Study Sample Analysis (24 May 2022) will be used as a reference for sample conduct.

Plasma NNN concentrations will be analyzed by LC-MS/MS at ABF GmbH, Planegg, Germany, using validated procedures according to the ICH M10 guideline on bioanalytical method validation and study sample analysis and US FDA Guidance for Industry on bioanalytical method validation.

8.3 Pharmacokinetic Concentrations

8.3.1 Plasma Nicotine

Plasma concentrations of nicotine as determined at the collection times and per the bioanalytical method described in Section 8.1 and Section 8.2, respectively, will be used for the calculation of the baseline-adjusted plasma nicotine concentration. Concentrations below the lower limit of quantitation (BLQ) will be set to ½ the lower limit of quantitation (LLOQ) prior to baseline adjustment. However, for calculation of Kel from unadjusted data (to be used for baseline adjustment), concentrations BLQ will be set to 0 for pre-administration and prior to the first measurable concentration, and set to missing thereafter (if applicable). Baseline adjustment of plasma nicotine concentrations will be performed using the following equation:

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

Where:

C_t = corrected concentration at time t,

$C_{t\ uncorrected}$ = the uncorrected concentration at time t,

C_0 = the pre-product administration concentration,

kel [£] = the apparent elimination rate constant obtained from each participant's uncorrected concentrations (for this estimation, values that are BLQ are set to zero pre-administration and prior to the first measurable concentration, and set to missing thereafter),

t = actual sampling time since start of product administration, and

t1 = time elapsed since pre-product administration sampling (i.e., actual time of C_0 + time between pre-product administration sampling and start time of product use).

[£] Note: the adjustment is participant - and product-specific. If a Kel cannot be estimated for a participant, the mean kel value from other participants for that product will be used.

After correction for pre-product administration values, some concentrations may be BLQ 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.

Baseline-adjusted plasma nicotine concentrations 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 listed and discussed in the CSR.

8.3.2 Plasma N-nitrosonornicotine (NNN)

Plasma concentrations of NNN as determined at the collection times and per the bioanalytical method described in Section 8.1 and Section 8.2, respectively, will be used for the calculation of the plasma NNN concentration. Concentrations that are BLQ will be set to ½ the LLOQ prior to the correction for pre-product administration values (subtraction of the pre-product administration value from each post-product administration value.

After correction for pre-product administration values, some concentrations may be BLQ 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.

8.4 Noncompartmental Pharmacokinetic Analysis and Parameter Calculation

8.4.1 Plasma Nicotine Pharmacokinetic Analysis

The appropriate noncompartmental PK parameters will be calculated from the baseline-adjusted plasma nicotine concentration-time data using Phoenix® WinNonlin® Version 8.3.4 or higher. Actual sample times will be used in the calculations of the PK parameters. The calculation of the actual time for plasma nicotine will be in respect to the start of product use. All PK parameters included in

the protocol are listed in Table 8–1 below, and are defined as appropriate for study design.

Table 8–1 Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters

Parameter	Label to be Used in the Text, Tables and Figures*	Definition	Method of Determination
$AUC_{(0\text{-}180)}$	AUC(0-180)	Area under the nicotine concentration-time curve calculated using linear trapezoidal summation from time zero (defined as the start of product use) to 180 minutes (or the last quantifiable concentration during that interval)	Calculated using the Linear Trapezoidal with Linear Interpolation Method
C_{max}	Cmax	Maximum measured plasma concentration over the duration of the measurement interval.	Taken directly from baseline-adjusted bioanalytical data
T_{max}	Tmax	Time of the maximum measured plasma concentration over the duration of the measurement interval. T_{max} is defined as the first time point with this value.	Taken from clinical database as the difference in the time of start of product use and the time of the blood draw which is associated with the C_{max}
K_{el}	Kel	Apparent first-order terminal elimination rate constant (will be reported for both adjusted and unadjusted data)	Calculated by linear least-squares regression analysis using the maximum number of points in the terminal log-linear period (e.g., three or more non-zero plasma concentrations).
$T_{½}$	T½	Apparent first-order elimination half-life.	Calculated as $\ln 2/K_{el}$

* In the text of the CSR, subscripts may be used in parameter names, as appropriate.

Pharmacokinetic parameters will not be calculated for participants with less than 3 consecutive post-product administration time points with quantifiable concentrations. Participants for whom there are insufficient data to calculate the PK parameters will be included in the concentration tables only and excluded from the summary statistics, statistical analysis, and mean profiles.

The Kel will be determined using linear regressions composed of at least 3 data points. The Kel will not be calculated if 1) the terminal elimination phase is not apparent, 2) if Cmax is one of the 3 last data points, or 3) if the R^2 value is less than 0.75. In cases where the Kel interval is not calculated, the values of T½ will not be reported.

8.4.2 Plasma NNN Pharmacokinetic Analysis

The following PK parameters will be calculated for the change from baseline (concentrations adjusted by subtraction of baseline values) plasma NNN concentration-time data following HTP and UBCC use using SAS® software (Version 9.4 or higher).

Table 8–2 Baseline-Adjusted Plasma N-nitrosonornicotine (NNN) Pharmacokinetic Parameter

Parameter	Label to be Used in the Text, Tables and Figures*	Definition	Method of Determination
$C_{max\text{-}NNN}$	Cmax-NNN	Maximum baseline-adjusted NNN concentration over the duration of the measurement interval	Maximum numerical value after subtracting the NNN baseline value from every post product use NNN concentration

* In the text of the CSR, subscripts may be used in parameter names, as appropriate.

8.5 Data Summarization and Presentation

SAS® software (Version 9.4 or higher) will be used for all data presentation and summarization including statistical analyses, summary tables, figures, and data listings. Plasma concentrations and PK parameters descriptive statistics will be generated.

The plasma nicotine and NNN concentrations will be listed for all participants and presented with the same level of precision as received from the bioanalytical laboratory. Plasma nicotine and NNN concentrations will be summarized by study product for all participants in the PK Population. Summary statistics, including sample size (n), n missing (number of participants with a missing result), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), minimum, median, maximum, and 90% confidence interval (90% CI of Mean), will be calculated for each nominal time point for both baseline-adjusted and unadjusted concentrations. Excluded participants will be included in the concentration listings, but will be excluded from the summary statistics and noted as such in the tables. Concentration values that are BLQ will be set to one half (½) of the

limit of quantitation for the calculation of the descriptive statistics of unadjusted plasma nicotine and NNN concentrations. Unadjusted values that are BLQ 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 and NNN PK parameters will be listed by participant and summarized by study product for all participants in the PK Population. Pharmacokinetic parameters will be reported to 3 significant figures for individual parameters, with the exception of T_{max}, which will be presented with 2 decimal places. Summary statistics will be reported, including n, n missing, Mean, SD, CV%, SEM, minimum, median, maximum, and 90% CI of Mean by study product. In addition, geometric mean (geom mean), geometric CV% (geom CV%) and the 90% CI of geometric mean will be provided for the C_{max} and plasma nicotine $AUC_{(0\text{-}180)}$ parameters by study product, as applicable.

Excluded participants 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 the bioanalytical data (concentrations) or as mentioned above for the PK parameters, mean/median/geom mean in one more level of precision than minimum/maximum, SD/SEM in one more level of precision than mean/median, n/n missing will be presented as an integer, CV% and geom CV% will be presented to the nearest tenth and 90% CIs will be presented with two decimals.

Missing data will be treated as missing and no data imputation will be conducted.

Note that the NNN concentrations for nicotine gum collected up to 10 minutes following start of product use do not appear meaningful for analysis because the gum use goes over 30 minutes. Therefore, no PK parameters will be presented for NNN for nicotine gum.

8.6 Statistical Analysis of PK Parameters

A linear mixed model for analysis of variance will be performed on the natural log (ln) transformed plasma nicotine PK parameters C_{max} and $AUC_{(0\text{-}180)}$ The model will include sequence, study product, and study day as fixed effects and participant-nested-within-sequence as a random effect. Sequence will be tested using participant-nested-within-sequence as the error term. Geometric least-square means (LSMs) and 90% CIs will be provided for the PK parameters of C_{max} and $AUC_{(0\text{-}180)}$ by study product. Geometric LSM ratio, 90% CIs of geometric LSM ratio, and p-values will be provided for the study product comparisons among each of the test HTP products and

the reference products (UBCC and nicotine gum, respectively) for C_{max} and $AUC_{(0-\infty)}$.

The above statistical analyses will be performed using the following sample SAS® code:

```
Proc mixed data=< >;
class participant sequence day product;
model log(parameter) = sequence day product / ddfm=KR;
random participant (sequence);
lsmeans product/diff cl alpha=0.10;
run;
```

9. SUBJECTIVE MEASURES ANALYSIS

9.1 Measurements and Collection Schedule

On Day 1 through Day 6, the following subjective effects questionnaires will be conducted during morning *ad libitum* product use sessions.

Product Liking Questionnaire will be administered at 5, 15, 30, 60, and 180 minutes after the start of morning *ad libutum* product use.

Tobacco/Nicotine Withdrawal Questionnaire will be administered at prior to product use, and at 5, 15, 30, and 60 minutes after the start of morning *ad libutum* product use.

Direct Effects of Product Questionnaire will be administered at 5, 15, 30, and 60 minutes after the start of morning *ad libutum* product use.

Use the Product Again Questionnaire will be administered at 60 minutes after the start of morning *ad libutum* product use.

The Modified Cigarette Evaluation Questionnaire (mCEQ) Questionnaire will be administered at 180 minutes after the start of morning *ad libutum* product use.

9.2 Data Collection

The response scores of Product Liking, Tobacco/Nicotine Withdrawal, Direct Effects of Product, and Use the Product Again Questionnaires will be recorded on the VAS scales, and on the 7-point scale for mCEQ Questionnaire.

The study questionnaires will be captured in the Medrio ePRO system. Paper copies of the questionnaires should only be used in the event the Medrio system is not available. Data entry will be done through EDC in the event questionnaires are completed on paper.

9.3 Analysis Variables

9.3.1 Product Liking (PL) Questionnaire

Ratings of the participants' PL question (At this moment, how much do you like the product?) recorded on VAS scales (where 0 = strongly dislike, 50 = neither like nor dislike, and 100 = strongly like) will be used to calculate the following parameters:

Table 9–1 Subjective Effects - Product Liking (PL) Questionnaire Analysis Parameters

Parameter	Label to be Used in the Text, Tables and Figures*	Definition	Method of Determination
$E_{max\text{-}PL}$	Emax-PL	Maximum product liking in VAS score during each morning *ad libitum* product use.	Maximum numerical VAS score value over 180 minutes for each morning *ad libitum* product use.
$AUEC_{\text{-}PL}$	AUEC-PL	Area under the effect curve for product liking from 5 minutes to 180 minutes after the start of each morning *ad libitum* product use.	Calculated using the Linear Trapezoidal with Linear Interpolation Method in Drug Effect (220) module as AUC_above B, where "B" is the baseline specified as 0.

*In the text of the CSR, subscripts may be used in parameter names, as appropriate.

9.3.2 Tobacco/Nicotine Withdrawal (TNW) Questionnaire

Ratings of the participants' TNW questions recorded on VAS scales (where 0 = not at all and 100 = extremely) will be used to calculate the following parameter for each of the two TNW questionnaire items (1. Urges to Smoke, 2. Craving a Cigarette):

Table 9–2 Subjective Effects - Tobacco/Nicotine Withdrawal (TNW) Questionnaire Analysis Parameter

Parameter	Label to be Used in the Text, Tables and Figures*	Definition	Method of Determination
$E_{max\text{-}TNW}$	Emax-TNW	Maximum reduction in VAS score from baseline pre-use to post-use (i.e., VASpre-use – VASpost-use) for each morning *ad libitum* product use.	Maximum numerical value after subtracting every post product use VAS score value from the baseline VAS score value for each *ad libutum* use episode

*In the text of the CSR, subscripts may be used in parameter names, as appropriate.

9.3.3 Direct Effects of Product (DEP) Questionnaire

Ratings of the participants' DEP£ questionnaires recorded on VAS scales (where 0 = not at all and 100 = extremely) will be used to calculate the following parameter for each of the eight DEP questionnaire items:

Table 9–3 Subjective Effects - Direct Effects of Product (DEP) Questionnaire Analysis Parameter

Parameter	Label to be Used in the Text, Tables and Figures*	Definition	Method of Determination
$E_{max\text{-}DEP}$	Emax-DEP	The largest VAS score recorded for each morning *ad libitum* product use	Maximum numerical VAS score value over the 60-minute measurement period for each morning *ad libutum* product use episode

*In the text of the CSR, subscripts may be used in parameter names, as appropriate.

£Direct Effects of Product Questionnaire

1. Is the product "Pleasant" right now?
2. Is the product "Satisfying" right now?
3. Is the product making you feel "Calm" right now?
4. Is the product helping you "Concentrate" right now?
5. Is the product making you feel more "Awake" right now?
6. Is the product making you feel "Sick" right now?
7. Is the product reducing your "Hunger" for food right now?
8. Would you like "More" of the product right now?

9.3.4 Use the Product Again (UPA) Questionnaire

Ratings of the participants' willingness to use the product again recorded on a 100 mm VAS scale ranging from "Definitely Would Not" (0) to "Don't Care" (50) to "Definitely Would" (100) will be reported.

In addition, responses to UPA questionnaire will also be treated as a bipolar variable. The bipolar score will be calculated by subtracting 50 from the original VAS score, then categorizing into three categories: -50 to < 0, 0, and > 0 to 50.

9.3.5 Modified Cigarette Evaluation Questionnaire (mCEQ)

Responses to the mCEQ questionnaire for all products following each morning *ad libitum* product use episode will be assessed as a 7-point scale (where 1 = not at all, 2 = very little, 3 = a little, 4 = moderately, 5 = a lot, 6 = quite a lot, and 7 = extremely) and treated as a continuous variable. The responses to the mCEQ Questionnaire as defined in study protocol will be presented as the following factor scores which will be calculated as the average of the original score from individual questions:

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

9.4 Data Summarization and Presentation

SAS® software (Version 9.4 or higher) will be used for all subjective measures data presentation and summarization, including the calculation of E_{max} parameters.

For all subjective measures, original data will be presented with the same precision as reported in the clinical database. Factor scores that are averages of responses to more than 1 question will be presented with one more level of precision that the clinical database. E_{max} parameters will be presented with the same precision as the original data. The level of precision for each statistic will be presented as follows: minimum/maximum in same precision as in the clinical database, mean, median, Q1, and Q3 in one more level of precision than minimum/maximum, SD/SEM in one more level of precision than mean/median, n/n missing will be presented as an integer, CV% will be presented to the nearest tenth and 90% CI of the arithmetic mean will be presented with two decimals.

Missing data will be treated as missing and no data imputation will be conducted.

9.4.1 Product Liking (PL)

Descriptive statistics (n, mean, SD, CV%, SEM, minimum, Q1, median, Q3, and maximum) of the PL original VAS scores will be provided by study product and assessment time point. Descriptive statistics of $E_{max\text{-}PL}$ and AUEC-$_{PL}$ will be provided by study product. Individual response scores and analysis parameters will be listed.

9.4.2 Tobacco/Nicotine Withdrawal (TNW)

Descriptive statistics (n, mean, SD, CV%, SEM, minimum, Q1, median, Q3, and maximum) of the TNW original VAS scores will be provided by study product and assessment time point. Descriptive statistics of $E_{max\text{-}TNW}$ will be provided by study product. Individual response scores and analysis parameters will be listed.

9.4.3 Direct Effects of Product (DEP)

Descriptive statistics (n, mean, SD, CV%, SEM, minimum, Q1, median, Q3, and maximum) of the DEP original VAS scores to each questionnaire item will be provided by study product and assessment time point. Descriptive statistics of $E_{max\text{-}DEP}$ will be provided by study product. Individual response scores and analysis parameters will be listed.

9.4.4 Use Product Again (UPA) Questionnaire

The VAS responses treated as bipolar categorical variables (-50 to <0, 0, >0 to 50) will be summarized by study product using frequency count tables. The bipolar score for the Use the Product Again questionnaire is calculated by subtracting 50 from the original VAS score.

The original VAS response scores and bipolar scores in each category (except Category 0) will also be treated as continuous variables and summarized using descriptive statistics of n, mean, SD, CV%, SEM, minimum, Q1, median, Q3, maximum, and 90% CI by study product. Individual response scores and bipolar scores will be listed.

9.4.5 Modified Cigarette Evaluation Questionnaires (mCEQ)

Descriptive statistics (n, mean, SD, CV%, SEM, minimum, median, maximum, Q1, Q3, and 90% CIs) of the factor scores as defined in Section 9.3.5 will be provided by study product. Individual original response scores and factor scores will be listed.

9.5 Statistical Analysis of Subjective Effects Measures

For the maximum response scores to Product Liking questionnaire ($E_{max\text{-}PL}$ and AUEC-$_{PL}$), the maximum reduction response scores to each question item of the Tobacco/Nicotine Withdrawal questionnaire ($E_{max\text{-}TNW}$), and the maximum response scores to each question item of the Direct Effects of Product questionnaire ($E_{max\text{-}DEP}$)

following each *ad libitum* product use, a linear mixed model for analysis of variance will be performed. The model will include sequence, study product, and study day as fixed effects and participant-nested-within-sequence as a random effect. Sequence will be tested using participant-nested-within-sequence as the error term. The LSM, 90% CIs, and p-values will be provided for the study products in each response. For **exploratory** purposes only, the LSM difference, 90% CIs for the difference, and p-values will be provided for the study product comparisons among each of the test HTP products and the reference products UBCC and Nicotine gum (NRT), respectively.

The above statistical analyses will be performed using the following sample SAS® code:

```
Proc mixed data=< >;
class participant sequence day product;
model parameter = sequence day product / ddfm=KR;
random participant (sequence);
lsmeans product/diff cl alpha=0.10;
run;
```

10. PRODUCT USE ANALYSIS

Product Trial Period

Participants will receive all four varieties of HTS on Day -6 and begin the at-home product trial. Participants are required to use each HTS variety at least once a day *ad libitum* for a minimum of 20 HTS uses over 5 days.

Day -1 Afternoon to Day 6

For UBCC use, the cigarette dispensed, the number of puffs per combustible cigarette, and the start time of the first puff and end time of the last puff will be documented for the 5-minute *ad libitum* product use during the morning *ad libitum* product use PK Test Session (manually documented). During the afternoon product use session (no more than approximately 6 hours afternoon *ad libitum* product use), the number of cigarettes used will be documented (manually).

For HTP use, the HTS dispensed, the number of puffs per stick, and the start time of the first puff and the stop time of the last puff, will be documented for the 5-minute *ad libitum* product use session during the morning *ad libitum* product use PK test session (manually documented). During the afternoon product use session (no more than approximately 6 hours *ad libitum* product use), the number of sticks used will be documented (manually).

For nicotine gum, the product dispensed, the start time of use (when participant places the gum in the mouth) and the use stop time (when participant takes the gum out of the mouth) will be documented for the 30-minute *ad libitum* product use during

the morning *ad libitum* product use PK test session (manually documented). During the afternoon product use sessions (no more than approximately 6 hours *ad libit*um product use), the number of pieces of gum used will be documented (manually).

10.1 Analysis Variables

Product Trial

- Number of each HTS product used during the Product Trial

Morning *Ad libitum* Product Use Episodes

- Total product use duration during PK test session which calculated from the start time of the first puff and stop time of last puff for each product use during a morning *ad libitum* product use PK test session.
- Puff count during the morning *ad libitum* product use PK test sessions for UBCC and HTP products

Afternoon *Ad Libitum* Product Use Episodes

- Number of HTS, UBCC, and nicotine gum used

10.2 Data Summarization and Presentation

The individual product use variables in Section 10.1 will be listed. Individual product use durations will be rounded to 1 decimal for presentation and calculation of summary statistics. Descriptive statistics (n, mean, SD, CV%, SEM, minimum, Q1, median, Q3, and maximum) will be provided for the product use variables listed above (Section 10.1).

11. PHYSIOLOGICAL HEART RATE ANALYSIS

11.1 Measurements and Collection Schedule

On Days 1 through 6, heart rate will be measured after participant remained seated for at least 5 minutes, at approximately 5 minutes prior to the start of each morning *ad libitum* product use episode (prior to the blood draw) and approximately 1 minute prior to the scheduled blood draw time point at 5, 15, 30, 60, and 180 minutes following the start of each morning *ad libitum* product use episode.

11.2 Method Used to Calculate the Baseline-Adjusted Heart Rate Parameters

Baseline-adjusted heart rate will be calculated by subtracting the baseline heart rate value (prior to the start of each morning *ad libitum* product use episode) from every post product use heart rate value. Negative values will be used as is.

Baseline-adjusted heart rate will be used for the calculation of the heart rate parameters.

11.3 Heart Rate Analysis Parameters

The appropriate noncompartmental heart rate (HR) parameters will be calculated from the baseline-adjusted heart rate data using SAS Version 9.4 or higher. Actual heart rate times will be used in the calculations of the Heart Rate parameters. The calculation of the actual time for heart rate will be in respect to the start of controlled product use. All heart rate parameters included in the protocol are listed in Table 11-1 below, and are defined as appropriate for study design.

Table 11-1 Physiological Baseline-Adjusted Heart Rate Analysis Parameters

Parameter	Label to be Used in the Text, Tables and Figures*	Definition	Method of Determination
$E_{max\text{-}HR}$	Emax-HR	Maximum heart rate change from baseline	Maximum numerical value after subtracting the baseline heart rate value from every post product use heart rate value. If an entire profile is negative, the Emax-HR will be 0.
TE_{max}	TEmax	Time of the Emax-HR. If the maximum value occurs at more than one time point, TEmax will be 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 heart rate which is associated with the $E_{max\text{-}HR}$

*In the text of the CSR, subscripts may be used in parameter names, as appropriate.

Heart Rate parameters will not be calculated for subjects with less than 3 consecutive post-product-use administration time points. Subjects for whom there are insufficient data to calculate the Heart Rate parameters will be included in the listings only and excluded from the statistical analysis.

Baseline-adjusted negative values will be used as is without imputation.

11.4 Data Summarization and Presentation

SAS® software (Version 9.4 or higher) will be used for all data presentation and summarization including statistical analyses, summary tables, figures, and data listings.

Original heart rate and baseline-adjusted heart rate will be listed by participant and summarized by study product and time point using descriptive statistics. Summary statistics, including n, n missing, mean, SD, CV%, 90% CI, SEM, median, minimum, and maximum will be calculated for each nominal time point for both baseline-adjusted and unadjusted results. Excluded participants will be included in the listings, but will be excluded from the summary statistics.

Mean (with and without SD) and individual unadjusted and baseline-adjusted heart rate-time profiles will be presented on linear scale.

Heart Rate parameters will be listed by subject and summarized by study product for all subjects in the Heart Rate Population. Heart rate parameters will be reported to 3 significant figures for individual parameters, with the exception of TE_{max} which will be presented with 2 decimal places. Summary statistics will be reported, including n, mean, SD, CV%, SEM, minimum, median, maximum, and 90% CI by study product. In addition, geom mean, geom CV%, and the 90% CI of geom mean will be provided for $E_{max\text{-}HR}$ parameter by study product.

Excluded subjects will be listed in the heart rate parameter listings, but will be excluded from the summary statistics.

The level of precision for each heart rate measurement statistics will be presented as follows: minimum/maximum in same precision as in the dataset, mean/median/geom mean in one more level of precision than minimum/maximum, SD/SEM in one more level of precision than mean/median, n will be presented as an integer, CV% and geom CV% will be presented to the nearest tenth and 90% CI will be presented with two decimals.

Missing data will be treated as missing and no data imputation will be conducted.

11.5 Statistical Analysis of Heart Rate Parameters

A linear mixed model for analysis of variance will be performed on the log-transformed $E_{max\text{-}HR}$ parameter. A similar statistical method to the PK analyses will be used for the heart rate parameter analysis. All pairwise comparisons among the study products that are performed for the PK parameter analysis will also be performed for $E_{max\text{-}HR}$ analysis for exploratory purposes.

12. SAFETY ANALYSIS

No inferential statistics will be performed on the safety data.

All clinical safety data will be listed by participant. The following items will be summarized using n, arithmetic mean, SD, minimum, median, and maximum for continuous data and frequency counts for categorical data. The analysis will be performed for Safety Population.

- Participant disposition (product trial period, by sequence and overall)
- Participant demographics (product trial period, by sequence and overall)
- Tobacco/nicotine product use history (product trial period, by sequence and overall)
- Adverse experiences (product trial period, by product and overall)
- Clinical laboratory tests (overall)
- Vital signs (overall): This will only include safety vital signs, and physiological serial heart rates as described in Section 11 will be summarized separately.

Level of precision will be presented as follows.

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

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

12.1 Participant Discontinuation

The number of participants enrolled, number who completed the study, and number who did not complete the study (overall and reasons for early withdrawal) will be tabulated by randomized sequence and overall. The number of participants who received each study product and who did not receive study product at each visit will be tabulated. Participants only enrolled in the product trial and dropped prior to randomization will be summarized separately. Screen failures will be listed.

12.2 Protocol Deviations and Heated Product Issues

Protocol deviations and heated product issues occurred during the study will be recorded in the EDC and listed by participant.

12.3 Demographics

Descriptive statistics will be reported for continuous variables (age, weight, height, and body mass index [BMI]) and frequency counts will be tabulated for categorical variables (sex, ethnicity, and race). Summarization will be done by randomized sequence and overall. Participants only enrolled in the product trial and dropped prior to randomization will be summarized separately. Screen failures will be listed.

12.4 Usual Brand Attributes

Usual brand attributes will be summarized with descriptive statistics for continuous variables based on the Screening results. Frequency counts will be presented for categorical variables. The continuous variables will include number of cigarettes smoked per day and number of years of smoking cigarettes and the categorical variables will include usual cigarette brand, and flavor.

Participants only enrolled in the product trial and dropped prior to randomization will be summarized separately. Screen failures will be listed.

12.5 Fagerström Test for Cigarette Dependence

Fagerström Test for Cigarette Dependence (FTCD) will be assessed at Screening and listed by participant. The responses for individual questions and total score will be directly collected on the CRF page. Total score will be summarized with descriptive statistics. Individual values will be listed by participant.

12.6 Adverse Experiences

All AEs will be coded (to the preferred term) with Medical Dictionary for Regulatory Activities (MedDRA®) Version 25.1.

All experiences captured in the database will be listed in by-participant data listings. However, only study product use-emergent adverse experiences (PUEAEs) will be summarized.

A PUEAE is defined as an AE that is starting or worsening at the time of or after study product administration. Each PUEAE will be attributed to a product based on the onset date and time of the AE. AEs occurring prior to the first *ad libitum* product use episode on Day -1 but after the product trial has started will be attributed to the product trial.

Frequencies of participants with PUEAEs, regardless of relationship to study product will be summarized by study product and sorted by system organ class and preferred term. The number of PUEAEs will be tabulated in a similar manner. Tables which summarize the number of PUEAEs and number of participants by severity and relationship to study product will also be included.

Participants only enrolled in the product trial and dropped prior to randomization will be summarized separately.

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

12.7 Clinical Laboratory Tests (Serum Chemistry, Hematology, Urinalysis)

Clinical laboratory evaluations will be performed at Screening. All clinical laboratory information will be listed by participant. Numeric results will be summarized using descriptive statistics. Participants only enrolled in the product trial and dropped prior to randomization will be summarized separately.

12.8 Vital Signs

Vital signs (blood pressure, heart rate, respiratory rate, and body temperature) will be measured for safety purposes at Screening, Check-in (Day -1), and End-of-Study (Day 6). If applicable, an Early Termination assessment will be performed.

Descriptive statistics will be reported for vital sign measurements (blood pressure, heart rate, respiration rate, and body temperature) by time point. Post-product use (after the start of *ad libitum* product use on Day -1) recheck values will not be used for calculation of descriptive statistics. Similarly, post-product use unscheduled and early termination results will not be used for calculation of descriptive statistics. Participants only enrolled in the product trial and dropped prior to randomization will be summarized separately.

Serial heart rate measurements are described in Section 11 and will be summarized separately.

12.9 Electrocardiogram

A 12-lead electrocardiograms (ECG) will be obtained during Screening. ECG information will be listed by participant.

12.10 Concomitant Medications

All concomitant medications recorded during the study will be coded with the World Health Organization (WHO) Dictionary Version Global B3 September 1, 2022 and listed.

12.11 Physical Examination

Physical examinations will be performed at Screening. Symptom-driven physical examinations and/or oral examination will be performed between Check-in (Day -1) and End-of-Study (Day 6) at the discretion of the Investigator. Physical examinations will be listed by participant and time point of collection. Abnormal findings will be discussed in the CSR.

13. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

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

14. 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 summary tables and figures will be generated using SAS® Version 9.4 or higher.

The following is a list of table and figure titles that will be included in Section 14 of the report. Table and figure titles 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 Population)
Table 14.1.2	Disposition of Participants (Safety Population)
Table 14.1.3	Summary of Demographic Characteristics (Safety Population)
Table 14.1.4	Usual Brand Attributes Summary (Safety Population)
Table 14.1.5	Fagerström Test for Cigarette Dependence Summary (Safety Population)

14.2 PK, Subjective Measures, Product Use Behavior, and Heart Rate Measurements Data Summary Tables and Figures

14.2.1.1 Pharmacokinetic Tables – Plasma Nicotine

Table 14.2.1.1.1	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Menthol HTS; MX3 (681) (Product A, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.2	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Menthol HTS; MX5 (706) (Product B, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.3	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Tobacco HTS; R8 (120) (Product C, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.4	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Tobacco HTS; RX4 (953) (Product D, Test)

	During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.5	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Nicotine Gum (Product E, Reference) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.6	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Participant's UBCC (Product F, Reference) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.7	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Menthol HTS; MX3 (681) (Product A, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.8	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Menthol HTS; MX5 (706) (Product B, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.9	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Tobacco HTS; R8 (120) (Product C, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.10	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Tobacco HTS; RX4 (953) (Product D, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.11	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Nicotine Gum (Product E, Reference) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.12	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Participant's UBCC (Product F, Reference) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.13	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Menthol HTS; MX3 (681)

	(Product A, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.14	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Menthol HTS; MX5 (706) (Product B, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.15	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Tobacco HTS; R8 (120) (Product C, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.16	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Tobacco HTS; RX4 (953) (Product D, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.17	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Nicotine Gum (Product E, Reference) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.18	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Participant's UBCC (Product F, Reference) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.19	Unadjusted Plasma Nicotine Kel Values During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.1.20	Statistical Summary of Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Cmax and AUC(0-180) by Product (Pharmacokinetic Population)
Table 14.2.1.1.21	Statistical Comparison of Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Cmax and AUC(0-180) (Pharmacokinetic Population)

14.2.1.2 Pharmacokinetic Tables – Plasma NNN

Table 14.2.1.2.1	Unadjusted and Baseline-Adjusted Plasma NNN Concentrations (ng/mL) Following Menthol HTS; MX3 (681) (Product A, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.2.2	Unadjusted and Baseline-Adjusted Plasma NNN Concentrations (ng/mL) Following Menthol HTS; MX5 (706) (Product B, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.2.3	Unadjusted and Baseline-Adjusted Plasma NNN Concentrations (ng/mL) Following Tobacco HTS; R8 (120) (Product C, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.2.4	Unadjusted and Baseline-Adjusted Plasma NNN Concentrations (ng/mL) Following Tobacco HTS; RX4 (953) (Product D, Test) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.2.5	Unadjusted and Baseline-Adjusted Plasma NNN Concentrations (ng/mL) Following Participant's UBCC (Product F, Reference) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Table 14.2.1.2.6	Baseline-Adjusted Plasma NNN Pharmacokinetic Parameter Cmax-NNN Following HTP and UBCC Products (Products A, B, C, D, and F) During and After the Morning ad Libitum Product Use Episode (Pharmacokinetic Population)

14.2.2.1 Pharmacokinetic Figures – Plasma Nicotine

Figure 14.2.2.1.1	Mean (SD) Unadjusted Plasma Nicotine Concentrations Versus Time (Linear Scale) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)

Figure 14.2.2.1.2	Mean Unadjusted Plasma Nicotine Concentrations Versus Time (Linear Scale) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Figure 14.2.2.1.3	Mean Unadjusted Plasma Nicotine Concentrations Versus Time (Semi-Log Scale) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Figure 14.2.2.1.4	Mean (SD) Baseline-Adjusted Plasma Nicotine Concentrations Versus Time (Linear Scale) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Figure 14.2.2.1.5	Mean Baseline-Adjusted Plasma Nicotine Concentrations Versus Time (Linear Scale) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Figure 14.2.2.1.6	Mean Baseline-Adjusted Plasma Nicotine Concentrations Versus Time (Semi-Log Scale) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)

14.2.2.2 Pharmacokinetic Figures – Plasma NNN

Figure 14.2.2.2.1	Mean (SD) Unadjusted Plasma NNN Concentrations Versus Time (Linear Scale) During and After the Morning ad Libitum Product Use Episode (Pharmacokinetic Population)
Figure 14.2.2.2.2	Mean Unadjusted Plasma NNN Concentrations Versus Time (Linear Scale) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Figure 14.2.2.2.3	Mean (SD) Baseline-Adjusted Plasma NNN Concentrations Versus Time (Linear Scale) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)
Figure 14.2.2.2.4	Mean Baseline-Adjusted Plasma NNN Concentrations Versus Time (Linear Scale) During and After the Morning Ad Libitum Product Use Episode (Pharmacokinetic Population)

14.2.3 Subjective Measures Tables

Product Liking	
Table 14.2.3.1	Summary of Product Liking VAS Scores During and After the Morning Ad Libitum Product Use Episode by Study Product and Timepoint (Subjective Measures Population)
Table 14.2.3.2	Summary of Product Liking VAS Parameters (Emax_PL and AUEC-PL) During and After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)
Table 14.2.3.3	Statistical Summary of Product Liking VAS Parameters (Emax-PL and AUEC-PL) by Study Product (Subjective Measures Population)
Table 14.2.3.4	Statistical Comparison of Product Liking VAS Parameters (Emax-PL and AUEC-PL) (Subjective Measures Population)
Tobacco/Nicotine Withdrawal (TNW)	
Table 14.2.3.5	Summary of Tobacco/Nicotine Withdrawal VAS Scores and Difference From Pre-use During and After the Morning Ad Libitum Product Use Episode (Urges to Smoke) by Study Product and Timepoint (Subjective Measures Population)
Table 14.2.3.6	Summary of Tobacco/Nicotine Withdrawal VAS Scores and Difference From Pre-use During and After the Morning Ad Libitum Product Use Episode (Craving a Cigarette) by Study Product and Timepoint (Subjective Measures Population)
Table 14.2.3.7	Summary of Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (Emax-TNW) During and After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

Table 14.2.3.8	Statistical Summary of Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (Emax-TNW) by Study Product (Subjective Measures Population)
Table 14.2.3.9	Statistical Comparison of Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (Emax-TNW) (Subjective Measures Population)
Direct Effects of Product (DEP)	
Table 14.2.3.10	Summary of Direct Effects of Product VAS Scores During and After the Morning Ad Libitum Product Use Episode by Study Product and Timepoint (Subjective Measures Population)
Table 14.2.3.11	Summary of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)
Table 14.2.3.12	Statistical Summary of Direct Effects of Product Emax-DEP by Study Product (Subjective Measures Population)
Table 14.2.3.13	Statistical Comparison of Direct Effects of Product Emax-DEP (Subjective Measures Population)
Use Product Again Questionnaire	
Table 14.2.3.14	Frequency Counts of Responses to Use Product Again VAS Scores in Each Category After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)
Table 14.2.3.15	Summary of Responses to Use Product Again VAS Scores in Each Category After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

Table 14.2.3.16	Summary of Responses to Use the Product Again VAS Original Scores After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)
Modified Cigarette Evaluation Questionnaires (mCEQ)	
Table 14.2.3.17	Summary of Modified Cigarette Evaluation Questionnaire Factor Scores After the Afternoon Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

14.2.4 Subjective Measures Figures

Product Liking	
Figure 14.2.4.1	Bar Chart of Product Liking VAS Parameter (Emax-PL) During and After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)
Tobacco/Nicotine Withdrawal (TNW)	
Figure 14.2.4.2	Bar Chart of Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (Emax-TNW) During and After the Morning Ad Libitum Product Use Episode (Urges to Smoke) by Study Product (Subjective Measures Population)
Figure 14.2.4.3	Bar Chart of Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (Emax-TNW) During and After the Morning Ad Libitum Product Use Episode (Craving a Cigarette) by Study Product (Subjective Measures Population)

Direct Effects of Product (DEP)	
Figure 14.2.4.4	Bar Chart of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode (Pleasant) by Study Product (Subjective Measures Population)
Figure 14.2.4.5	Bar Chart of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode (Satisfying) by Study Product (Subjective Measures Population)
Figure 14.2.4.6	Bar Chart of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode (Feel Calm) by Study Product (Subjective Measures Population)
Figure 14.2.4.7	Bar Chart of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode (Help Concentrate) by Study Product (Subjective Measures Population)
Figure 14.2.4.8	Bar Chart of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode (Feel More Awake) by Study Product (Subjective Measures Population)
Figure 14.2.4.9	Bar Chart of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode (Feel Sick) by Study Product (Subjective Measures Population)
Figure 14.2.4.10	Bar Chart of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode (Reduce Hunger) by Study Product (Subjective Measures Population)
Figure 14.2.4.11	Bar Chart of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode (Like More Products) by Study Product (Subjective Measures Population)

14.2.5 Product Use Tables

Table 14.2.5.1	Summary of Product Use During Product Trial Period by Study Product (Product Use Population)
Table 14.2.5.2	Summary of Product Use Behavior Characteristics During the Morning Ad Libitum Product Use Episode by Study Product (Product Use Population)
Table 14.2.5.3	Summary of Product Use Behavior Characteristics During the Afternoon Ad Libitum Product Use Episode by Study Product (Product Use Population)

14.2.6 Physiological Heart Rate Measurement Tables

Table 14.2.6.1	Summary of Unadjusted Heart Rates During the Morning Ad Libitum Product Use Episode by Study Product and Timepoint (Physiological Heart Rate Population)
Table 14.2.6.2	Summary of Baseline-Adjusted Heart Rates During the Morning Ad libitum Product Use Episode by Study Product (Physiological Heart Rate Population)
Table 14.2.6.3	Baseline-Adjusted Heart Rate Parameters Following Menthol HTS; MX3 (681) (Product A, Test) During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)
Table 14.2.6.4	Baseline-Adjusted Heart Rate Parameters Following Menthol HTS; MX5 (706) (Product B, Test) During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)
Table 14.2.6.5	Baseline-Adjusted Heart Rate Parameters Following Tobacco HTS; R8 (120) (Product C, Test) During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)
Table 14.2.6.6	Baseline-Adjusted Heart Rate Parameters Following Tobacco HTS; RX4 (953) (Product D, Test) During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)

Table 14.2.6.7	Baseline-Adjusted Heart Rate Parameters Following Nicotine Gum (Product E, Reference) During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)
Table 14.2.6.8	Baseline-Adjusted Heart Rate Parameters Following Participant's UBCC (Product F, Reference) During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)
Table 14.2.6.9	Statistical Summary of Baseline-Adjusted Heart Rate Parameter Emax-HR by Product (Physiological Heart Rate Population)
Table 14.2.6.10	Statistical Comparison of Baseline-Adjusted Heart Rate Parameter Emax-HR by Product (Physiological Heart Rate Population)

14.2.7 Heart Rate Measurement Figures

Figure 14.2.7.1	Mean (SD) Heart Rate Measurement During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)
Figure 14.2.7.2	Mean Heart Rate Measurement During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)
Figure 14.2.7.3	Mean (SD) Baseline-Adjusted Heart Rate Measurement (Linear Scale) During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)
Figure 14.2.7.4	Mean Baseline-Adjusted Heart Rate Measurement (Linear Scale) During and After the Morning Ad Libitum Product Use Episode (Physiological Heart Rate Population)

14.3 Safety Data Summary Tables

14.3.1 Displays of Adverse Experiences

Table 14.3.1.1	Adverse Experience Frequency by Study Product – Number of Participants Reporting the Experience (% of Participants Who Received Study Product) (Safety Population)
Table 14.3.1.2	Adverse Experience Frequency by Study Product – Number of Adverse Experiences (% of Total Adverse Experiences) (Safety Population)
Table 14.3.1.3	Adverse Experience Frequency by Study Product, Severity, and Relationship to Study Product – Number of Participants Reporting the Experience (Safety Population)
Table 14.3.1.4	Adverse Experience Frequency by Study Product, Severity, and Relationship to Study Product – Number of Adverse Experiences (Safety Population)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Experiences

Table 14.3.2.1	Serious Adverse Experiences (Safety Population) (if no serious adverse experience occurred, a statement 'There were no serious adverse experiences recorded during the study.')

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

14.3.5 Display of Clinical Laboratory and Vital Signs

Table 14.3.5.1	Clinical Laboratory Summary – 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)

14.1 Section 16 Data Listings

Note: Hepatitis and HIV results that are provided by the clinical laboratory will not be presented in participant 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 Participant Data Listings

16.2.1 Participant Discontinuation

Appendix 16.2.1.1	Participant Disposition (Safety Population)
Appendix 16.2.1.2	Participant Disposition (Screen Failures)

16.2.2 Protocol Deviations

Appendix 16.2.2.1	Protocol Deviations
Appendix 16.2.2.2	Heated Tobacco Product Issues

16.2.3 Participants Excluded from Pharmacokinetic, Subjective Effects, Product Use Behavior, and Heart Rate Measurements Analysis

Appendix 16.2.3.1	Participants Excluded from Pharmacokinetic, Subjective Effects, Product Use Behavior, and Heart Rate Measurement Analysis
Appendix 16.2.3.2	Participant Population Information (Safety Population)

Note: Appendix 16.2.3.1 is generated in MS Word for inclusion in the study report.

16.2.4 Demographic Data

Appendix 16.2.4.1	Demographics (Safety Population)
Appendix 16.2.4.2	Demographics (Screen Failures)
Appendix 16.2.4.3	Physical Examination (Safety Population)
Appendix 16.2.4.4	Symptom Driven Physical Examination (Safety Population)
Appendix 16.2.4.5	Medical History (Safety Population)
Appendix 16.2.4.6	Usual Brand Attributes (Safety Population)
Appendix 16.2.4.7	Reproductive Status (Safety Population)
Appendix 16.2.4.8	Fagerström Test for Cigarette Dependence (Safety Population)

16.2.5 Compliance, Product Use, and/or Blood Sample Collection Data

Appendix 16.2.5.1	Participant Eligibility (Safety Population)
Appendix 16.2.5.2	At Home Product Trial (Safety Population)
Appendix 16.2.5.3	Randomization (Safety Population)
Appendix 16.2.5.4	Morning Ad Libitum Product Use (Safety Population)
Appendix 16.2.5.5	Afternoon Ad Libitum Product Use (Safety Population)
Appendix 16.2.5.6	Concomitant Medications (Safety Population)
Appendix 16.2.5.7	Plasma Nicotine Pharmacokinetic Blood Draw Times and Concentration Data (Safety Population)
Appendix 16.2.5.8	Plasma NNN Pharmacokinetic Blood Draw Times and Concentration Data (Safety Population)

16.2.6 Individual Pharmacokinetic, Subjective Measures Response, Product Use Behavior, and Heart Rate Data

Appendix 16.2.6.1	Individual Unadjusted Plasma Nicotine Concentrations Versus Time (Linear and Semi-Log Scales) (Pharmacokinetic Population)
Appendix 16.2.6.2	Individual Baseline-Adjusted Plasma Nicotine Concentrations Versus Time (Linear and Semi-Log Scales) (Pharmacokinetic Population)
Appendix 16.2.6.3	Individual Unadjusted Plasma NNN Concentrations Versus Time (Linear Scale) (Pharmacokinetic Population)
Appendix 16.2.6.4	Individual Baseline-Adjusted Plasma NNN Concentrations Versus Time (Linear Scale) (Pharmacokinetic Population)
Appendix 16.2.6.5	Intervals (Minutes) Used for the Determination of Unadjusted Plasma Nicotine Kel Values (Pharmacokinetic Population)
Appendix 16.2.6.6	Intervals (Minutes) Used for the Determination of Unadjusted Plasma Nicotine Kel Values (Pharmacokinetic Population)
Appendix 16.2.6.7	Individual Responses to Product Liking Questionnaire (Safety Population)
Appendix 16.2.6.8	Individual Responses to Product Liking Questionnaire - Maximum VAS Score (Emax-PL) (Safety Population)
Appendix 16.2.6.9	Individual Responses to Tobacco/Nicotine Withdrawal Questionnaire (Safety Population)
Appendix 16.2.6.10	Individual Responses to Tobacco/Nicotine Withdrawal Questionnaire – Maximum Reduction in VAS Score (Emax-TNW) (Safety Population)
Appendix 16.2.6.11	Individual Responses to Direct Effects of Product Questionnaire (Safety Population)
Appendix 16.2.6.12	Individual Responses to Direct Effects of Product Questionnaire – Maximum VAS Score (Emax-DEP) (Safety Population)
Appendix 16.2.6.13	Individual Responses to Use Product Again Questionnaire (Safety Population)

Appendix 16.2.6.14	Individual Responses to Modified Cigarette Evaluation Questionnaire (Safety Population)
Appendix 16.2.6.15	Individual Factor Score to Modified Cigarette Evaluation Questionnaire (Safety Population)
Appendix 16.2.6.16	Individual Unadjusted and Baseline-Adjusted Heart Rate (Safety Population)

16.2.7 Adverse Experiences Listings

Appendix 16.2.7.1	Adverse Experiences (Safety Population)
Appendix 16.2.7.2	Serious Adverse Experiences (Safety Population)

16.2.8 Listings of Individual Laboratory Measurements and Other Safety Observations

Appendix 16.2.8.1	Clinical Laboratory Report - Chemistry (Safety Population)
Appendix 16.2.8.2	Clinical Laboratory Report - Hematology (Safety Population)
Appendix 16.2.8.3	Clinical Laboratory Report - Urinalysis (Safety Population)
Appendix 16.2.8.4	Alcohol, Drug, and Cotinine Screen (Safety Population)
Appendix 16.2.8.5	Pregnancy Test (Safety Population)
Appendix 16.2.8.6	Serology (Safety Population)
Appendix 16.2.8.7	Exhaled Carbon Monoxide (Safety Population)
Appendix 16.2.8.8	Vital Signs (Safety Population)
Appendix 16.2.8.9	12-Lead Electrocardiogram (Safety Population)

15. TABLE AND FIGURE SHELLS

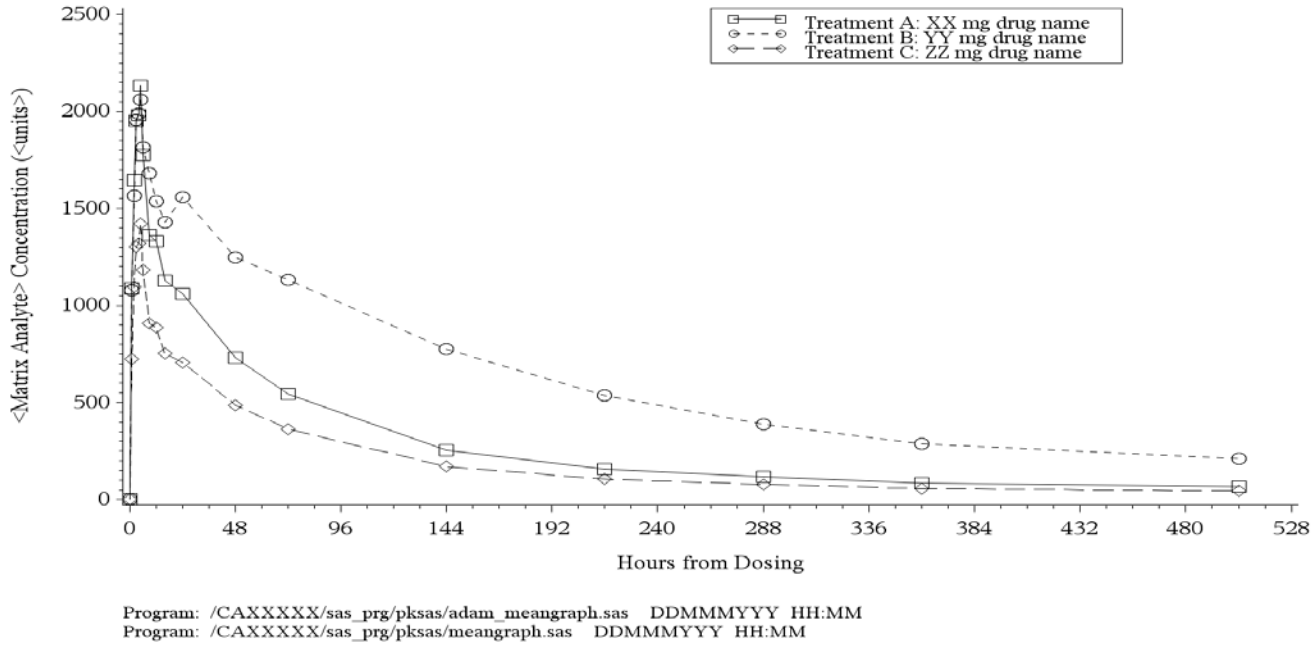
The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables that will be presented and included in the final report. Unless otherwise noted, all tables will be presented in Times New Roman font size 9. Tables and figures will be generated as RTF for inclusion in the CSR. In compliance [redacted] SOP/PG, SAS® outputs will not be manually edited. Tables will be generated from ADaM datasets created in accordance with CDISC guidance (ADaM Model 2.1 and ADaM implementation Guide 1.1).

The source dataset used in each table will be added as footnote in the table.

15.1 Figure Shells

Figures 14.2.2.1.2, 14.2.2.1.5, 14.2.2.2.2, and 14.2.2.2.4 will have the following format:
Internal template: Figure PFPConc2

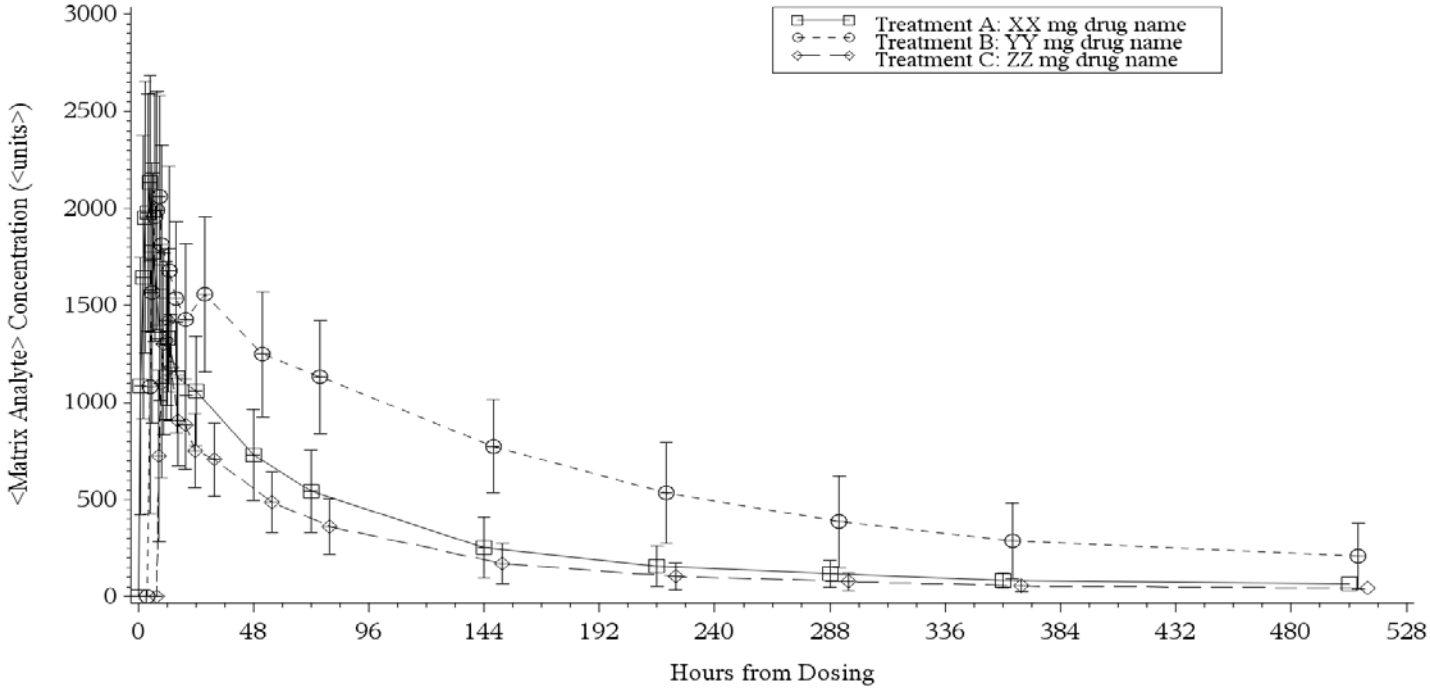
Figure Table 14.2.2.1.2 Mean Unadjusted Plasma Nicotine Concentrations Versus Time (Linear Scale) During and After the Morning ad Libitum Product Use Episode (Pharmacokinetic Population)



Programming note : the legend will present the 6 products 'Product X: Product Description'
The x-axis title will be: 'Time From Start of Product Use (min)'.
The x-axis title will be: 'Time From Start of Product Use (min)'.The y-axis title will be Unadjusted/Baseline-Adjusted Plasma Nicotine/NNN Concentration (ng/mL).

Figures 14.2.2.1.1, 14.2.2.1.4, 14.2.2.2.1, and 14.2.2.2.3 will have the following format:
Internal template: Figure PFPConc1

Figure Table 14.2.2.1.1 Mean (SD) Unadjusted Plasma Nicotine Concentrations Versus Time (Linear Scale) During and After the Morning ad Libitum Product Use Episode (Pharmacokinetic Population)

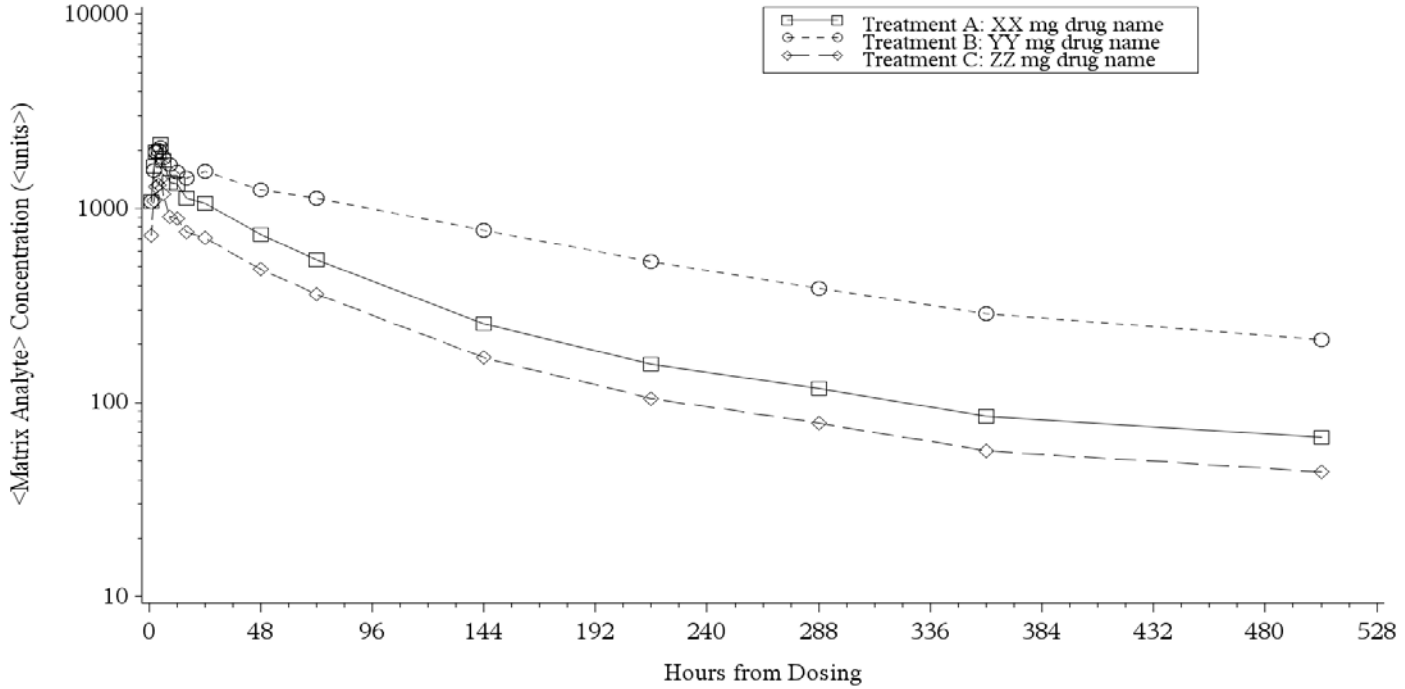


Treatments B and C are shifted to the right for ease of reading
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYY HH:MM

Programming note : the legend will present the 6 products 'Product X: Product Description'
The x-axis title will be: 'Time From Start of Product Use (min)'.
The y-axis title will be Unadjusted/Baseline-Adjusted Plasma Nicotine/NNN Concentration (ng/mL).

Figures 14.2.2.1.3 and 14.2.2.1.6 will have the following format:
Internal template: Figure PFPConc3

Figure Table 14.2.2.1.3 Mean Unadjusted Plasma Nicotine Concentrations Versus Time (Semi-Log Scale) During and After the Morning ad Libitum Product Use Episode (Pharmacokinetic Population)



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

Programming note : the legend will present the 6 products 'Product X: Product Description'
The x-axis title will be: 'Time From Start of Product Use (min)'.
The y-axis title will be Unadjusted/Baseline-Adjusted Plasma Nicotine/NNN Concentration (ng/mL).

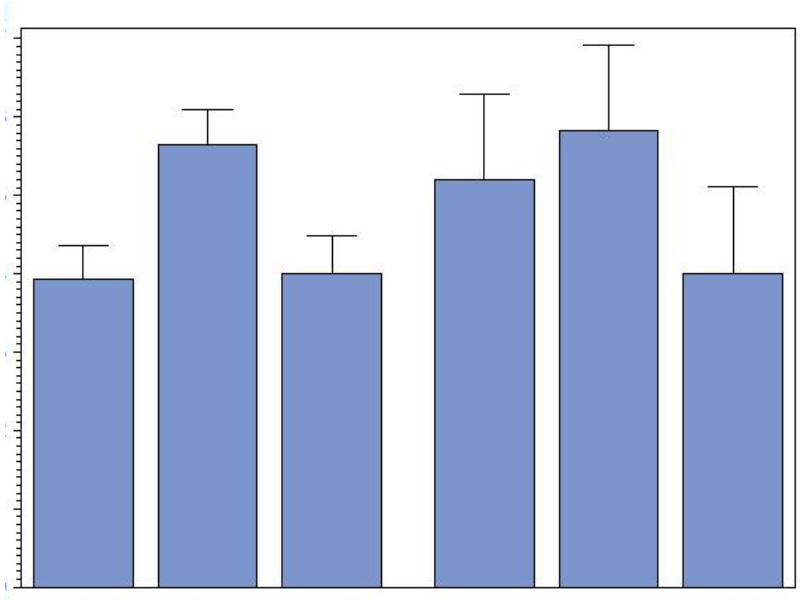
Note: Figure 14.2.4.1 for Product Liking Maximum VAS Score (Emax-PL), Figures 14.2.4.2 and 14.2.4.3 for Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (Emax-TNW) and Figures 14.2.4.4 through 14.2.4.11 for Direct Effects of Product Maximum VAS Scores (Emax-DEP) will be presented as follows:

Figure of histogram bar charts will be included to present Product Liking Maximum VAS score (Emax-PL) LS Mean and 90% CI with all 6 products.

Figures of histogram bar charts will be included to present each Tobacco/Nicotine Withdrawal Maximum Reduction in VAS score (Emax-TNW) LS Mean and 90% CI with all 6 products within one figure per each TNW Question (a total of 2 figures).

Figures of histogram bar charts will be included to present each Direct Effects of Product Maximum VAS Score (Emax-DEP) LS Mean and 90% CI with all 6 products within one figure per each DEP Question (a total of 8 figures).

The format of the fugures will be histogram bar chart similar to the below. The X-axis will show the six products and the Y-axis will show the LS Means with upper CI of VAS parameters (Emax-PL, Emax-TNW, or Emax-DEP). Also a footnote will be added as follows: Refer to Table 14.2.3.x for the pairwise comparisons between products.

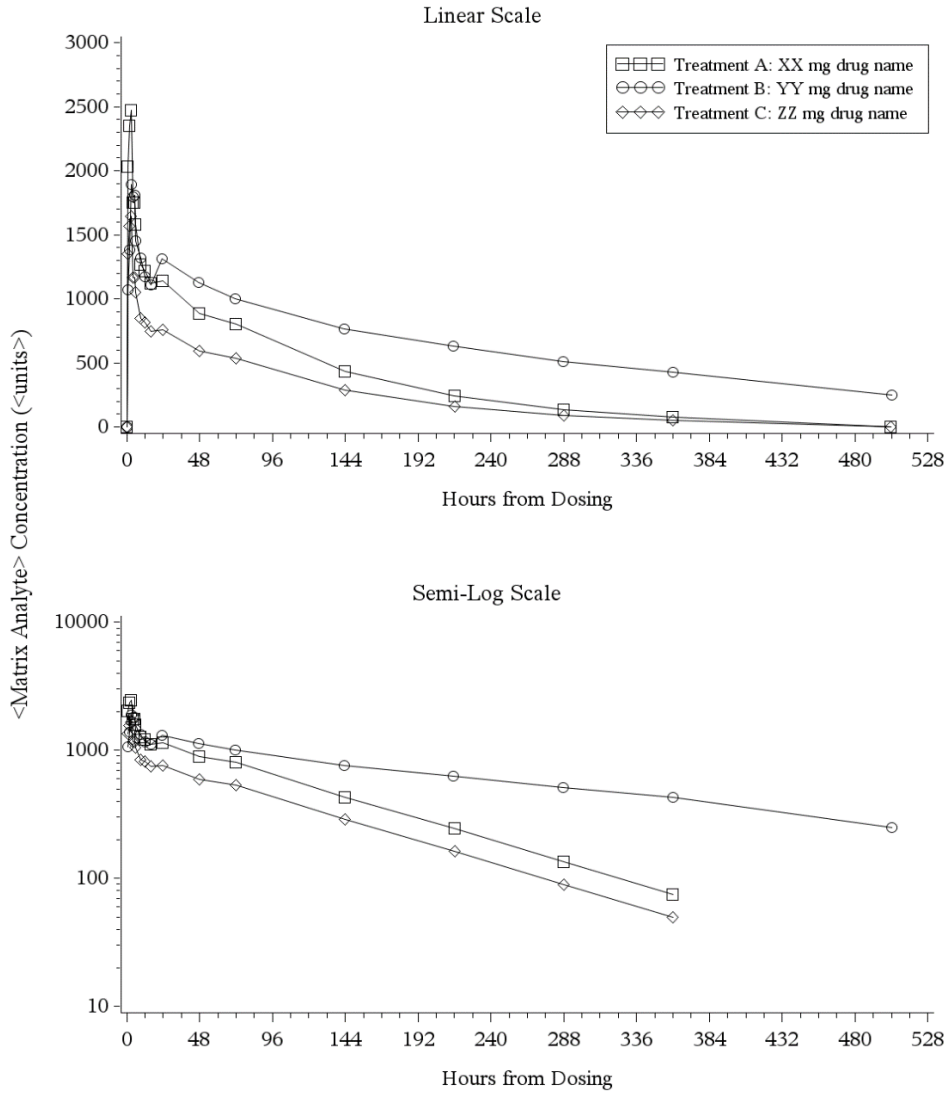


Linear and Semi-log Figures in Appendix 16.2.6.1 and 16.2.6.2 will have the following format:

Internal template: Figure PFPConc3

Appendix 16.2.6.1

Individual Unadjusted Plasma Nicotine Concentrations Versus Time
(Linear and Semi-Log Scales) (Pharmacokinetic Population)



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Program: /CAXXXXX/sas_prg/pksas/indgraph-all.sas DDMMMYYY HH:MM

Programming note : the legend will present the 6 products 'Product X: Product Description'
The x-axis title will be: 'Time From Start of Product Use (min)'.
The y-axis title will be Unadjusted/Baseline-Adjusted Plasma Nicotine/NNN Concentration (ng/mL).
Figures 16.2.6.3 and 16.2.6.4 will be presented in Linear Scale only.

15.2 Section 14 Summary Tables Shells

Table 14.1.1 Summary of Disposition (Safety Population)

		Randomized Product Sequence						
Category	Product Trial*	ABFCED	BCADFE	CDBEAF	DECFBA	EFDACB	FAEBDC	Overall#
Enrolled	XX	XX	XX	XX	XX	XX	XX	XX
Completed	XX	XX	XX	XX	XX	XX	XX	XX
Discontinued Early	X	X	X	X	X	X	X	X
<Reason1>	X	X	X	X	X	X	X	X
<Reason2>	X	X	X	X	X	X	X	X
<Reason3>	X	X	X	X	X	X	X	X

Product A: Ploom® 3.1 HTP - Menthol HTS; MX3 (681) (Test Product)
Product B: Ploom® 3.1 HTP - Menthol HTS; MX5 (706) (Test Product)
Product C: Ploom® 3.1 HTP - Tobacco HTS; R8 (120) (Test Product)
Product D: Ploom® 3.1 HTP - Tobacco HTS; RX4 (953) (Test Product)
Product E: Nicorette® 4 mg Mint Nicotine Gum (Reference Product)
Product F: Combustible Cigarette (menthol or non-menthol), participant's usual brand (Reference Product)
*Only includes participants that enrolled in the Product Trial period and dropped prior to randomization.
Participants who only participated in the Product Trial period are excluded from the Overall summary.

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Table 14.1.2 Disposition of Participants (Safety Population)

Participant Number	Randomized Product Sequence	Study Product Administered							Study Completion	
		Trial	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Status	Date
X	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Terminated Study Prematurely	DDMMMYYYY
X	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY
X	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY
X	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY
X	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY
X	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY
X	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY
X	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY
X	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY
XX	XXXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY
XX*		Yes	No	No	No	No	No	No	Dropped prior to randomization	DDMMMYYYY
XX*		Yes	No	No	No	No	No	No	Dropped prior to randomization	DDMMMYYYY
		XX	XX	XX	XX	XX	XX	XX		

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
*Participant enrolled in the Product Trial period and dropped prior to randomization.

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

Table 14.1.3 Summary of Demographic Characteristics (Safety Population)

Trait		Product Trial*	Randomized Product Sequence						Overall#
			ABFCED	BCADFE	CDBEAF	DECFBA	EFDACB	FAEBDC	
Sex	Male	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	Female	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Race	XXXXXXXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	XXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	XXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Ethnicity	Hispanic or Latino	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	Not Hispanic or Latino	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Age (yrs)	n	X	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX	XX	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
*Only includes participants that enrolled in the Product Trial period and dropped prior to randomization.
Participants who only participated in the Product Trial period are excluded from the Overall summary.

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

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

Table 14.1.4 Usual Brand Attributes Summary (Safety Population)

Trait		Product Trial*	Randomized Product Sequence						
			ABFCED	BCADFE	CDBEAF	DECFBA	EFDACB	FAEBDC	Overall#
Cigarette Brand	XXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	XXXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Cigarette Flavor	XXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	XXXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Number of Cigarettes Smoked per Day	n	X	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XXX.XX	X.XXX.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX	XX	XX
Number of Years of Smoking Cigarettes	n	X	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX	XX	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
*Only includes participants that enrolled in the Product Trial period and dropped prior to randomization.
Participants who only participated in the Product Trial period are excluded from the Overall summary.

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

Table 14.1.5 Fagerström Test for Cigarette Dependence Summary (Safety Population)

	Product Trial*	Randomized Product Sequence						
		ABFCED	BCADFE	CDBEAF	DECFBA	EFDACB	FAEBDC	Overall#
n	X	X	X	X	X	X	X	X
Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
Minimum	XX	XX	XX	XX	XX	XX	XX	XX
Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
Maximum	XX	XX	XX	XX	XX	XX	XX	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
*Only includes participants that enrolled in the Product Trial period and dropped prior to randomization.
Participants who only participated in the Product Trial period are excluded from the Overall summary.

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

Note: Plasma Nicotine Concentration Tables (Tables 14.2.1.1.1-14.2.1.1.6 for unadjusted, and Tables 14.2.1.1.7-14.2.1.1.12 for baseline-adjusted) and Plasma NNN Concentration Tables, both unadjusted and baseline-adjusted (Tables 14.2.1.2.1-14.2.1.2.5) will have the following format:
Internal template: Table CPConc1

Table 14.2.1.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Menthol HTS; MX3 (681) (Product A, Test) During and After the Morning ad Libitum Product Use Episode (Pharmacokinetic Population)

Participant Number	Randomized Product Sequence	Study Visit	Sample Times (minutes) Pre-use	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
XX	XXXXXX	X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
XX	XXXXXX	X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
XX	XXXXXX	X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
n			X	X	X	X	X	X	X	X	X	X	X
n missing			X	X	X	X	X	X	X	X	X	X	X
Mean			X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
SD			X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
CV(%)			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
Minimum			XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
Median			X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
Maximum			XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
90% CI Lower			X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
90% CI upper			X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX

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

Programming Notes: For the 90% CI (of Mean), the lower and upper limits may be presented on different rows if the space limit requires it.
Footnotes to include under the table, as appropriate:
<. = Concentration value missing or not reportable.>
The following footnote will only be included in the unadjusted plasma nicotine tables: <Concentration values that were below the limit of quantitation (BLQ) of 0.200 ng/mL were set to one-half of the limit of quantitation for the calculation of summary statistics.>
The following footnote will only be included in the baseline-adjusted plasma nicotine tables: < Prior to baseline adjustment, concentration values that were below the limit of quantitation (BLQ) of 0.200 ng/mL were set to one-half of limit of quantitation. After baseline adjustment, any negative values were assigned a value of zero and all other values obtained were reported as is (even if lower than the original limit of quantitation of 0.200 ng/mL) for the calculation of the descriptive statistics.>

Sample Times are listed in Section 8.1. Descriptive statistics precision is specified in Section 8.5.

Note: Plasma Nicotine Pharmacokinetic Parameter Tables (Tables 14.2.1.1.13-14.2.1.1.18), Plasma NNN Pharmacokinetic Parameter Table 14.2.1.2.6), and Heart Rate Parameter Tables (Tables 14.2.6.3-14.2.6.8) will have the following format:

Internal template: Table CPPar1

Table 14.2.1.1.13 Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Menthol HTS; MX3 (681) (Product A, Test) During and After the Morning ad Libitum Product Use Episode (Pharmacokinetic Population)

Participant Number	Randomized Product Sequence	Study Visit	Parameters: Parm 1 <unit>	Parm 2 <unit>	Parm 3 <unit>	Parm 4 <unit>	Parm X <unit>
XX	XXXXXX	X	X.XX	X.XX	X.XX	X.XX	X.XX
XX	XXXXXX	X	X.XX	X.XX	X.XX	X.XX	X.XX
XX	XXXXXX	X	X.XX	X.XX	X.XX	X.XX	X.XX
n			X	X	X	X	X
n missing			X	X	X	X	X
Mean			X.X	X.X	X.X	X.X	X.X
SD			X.XX	X.XX	X.XX	X.XX	X.XX
CV(%)			XX.X	XX.X	XX.X	XX.X	XX.X
SEM			X.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
90% CI Lower			X.XX	X.XX	X.XX	X.XX	X.XX
90% CI Upper			X.XX	X.XX	X.XX	X.XX	X.XX
Geom. Mean			X.X	X.X	X.X	X.X	X.X
Geom. CV%			XX.X	XX.X	XX.X	XX.X	XX.X
Geom. 90% CI Lower			X.XX	X.XX	X.XX	X.XX	X.XX
Geom. 90% CI Upper			X.XX	X.XX	X.XX	X.XX	X.XX

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

Programming Note: Footnote to include under the table, as appropriate: <. = Parameter value missing or not reportable.>

The plasma nicotine PK Parameters are AUC(0-180) (ng*min/mL), Cmax (ng/mL), Tmax (min), kel (1/min), and T½ (min). The plasma NNN PK parameter will be Cmax-NNN (unit/mL). The heart rate parameters are Emax-HR (bpm) and TEmax (min).
Descriptive statistics precision is specified in Section 8.5.
Geometric mean, geometric CV% and 90% CI of Geom. Mean will be calculated only for Cmax, AUC(0-180), and Cmax.

Unadjusted Kel table (Table 14.2.1.1.19) will have the following format:

Table 14.2.1.1.19 Unadjusted Plasma Nicotine Kel Values During and After the Morning ad Libitum Product Use Episode (Pharmacokinetic Population)

Participant Number	Randomized Product Sequence	Study Visit	kel (1/min) Product A	Product B	Product C	Product D
XX	XXXXXX	X	X.XX	X.XX	X.XX	X.XX
XX	XXXXXX	X	X.XX	X.XX	X.XX	X.XX
XX	XXXXXX	X	X.XX	X.XX	X.XX	X.XX
n			X	X	X	X
n missing			X	X	X	X
Mean			X.X	X.X	X.X	X.X
SD			X.XX	X.XX	X.XX	X.XX
CV(%)			XX.X	XX.X	XX.X	XX.X
SEM			X.XX	X.XX	X.XX	X.XX
Minimum			XX	XX	XX	XX
Median			X.X	X.X	X.X	X.X
Maximum			XX	XX	XX	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
Program: /CAXXXXX/sas_prg/pksas/PROGRAMNAME.SAS DDMMMYYYY HH:MM

Programming Note: Footnote to include under the table, as appropriate: <. = Parameter value missing or not reportable.>
There will also be results for Products E and F in this table.
Descriptive statistics precision is specified in Section 8.5.

Note: Plasma nicotine kel interval tables (Appendix 16.2.6.5 for unadjusted and Appendix 16.2.6.6 for baseline-adjusted data) will have the following format:
Internal template: Table CPKel1:

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Appendix 16.2.6.5 Intervals (Minutes) Used for the Determination of Unadjusted Plasma Nicotine Kel Values
(Pharmacokinetic Population)

Participant Number	Randomized Product Sequence	Product A Interval	Product A R^2	Product A n	Product B Interval	Product B R^2	Product B n
X	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XX	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XX	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XX	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XX	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XX	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XX	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XX	XXXXXX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X

Product A: <Long product description>
Product B: <Long product description>
Product C: <Long product description>
Product D: <Long product description>
Product E: <Long product description>
Product F: <Long product description>
R^2 = Coefficient of determination
n = Number of points used in Kel calculation
Source: ADaM.ADPP
Program: /XXXXXXX/sas_prg/pksas/adam_kel.sas DDMMMYYYY HH:MM

Programming Note:

- Interval start and stop times will be presented to 1 decimal or 3 sig figures min;
- R2 will be presented to 3 decimals;
- n will be presented as an integer (with no decimal)
- Set up the table to two pages, one page for A, B, and C and one for D, E, and F.

Note: Statistical summary of plasma nicotine PK parameters by product (Table 14.2.1.1.20) and the Heart Rate parameter table (Table 14.2.6.9) will have the following format:

Table 14.2.1.1.20 Statistical Summary of Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Cmax and AUC(0-180) by Product (Pharmacokinetic Population)

Product	Parameter	n	Geometric LS Mean	90% Confidence Interval	p-value
A	Cmax	x	X.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180)	x	X.XX	XX.XX – XXX.XX	X.XXXX
B	Cmax	x	X.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180)	x	X.XX	XX.XX – XXX.XX	X.XXXX
C	Cmax	x	X.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180)	x	X.XX	XX.XX – XXX.XX	X.XXXX
D	Cmax	x	X.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180_	x	X.XX	XX.XX – XXX.XX	X.XXXX
E	Cmax	x	X.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180)	x	X.XX	XX.XX – XXX.XX	X.XXXX
F	Cmax	x	X.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180)	x	X.XX	XX.XX – XXX.XX	X.XXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
The mixed model includes product sequence, study day, and product as fixed effects and participant nested within product sequence as a random effect. Mixed model with a default (variance component) covariance structure was used.
Parameters are ln-transformed prior to analysis.
Geometric least-squares means (LS Means) are calculated by exponentiating the LS Means from the ANOVA.
n = Number of observations used in the analysis

Program: /CAXXXXX/sas_prg/pksas PROGRAMNAME.SAS DDMMMYYYY HH:MM
Programming note: Geometric LS Means be presented to same precision as Mean in the PK parameter table. Geometric Mean Ratio and 90% confidence intervals will be presented to 2 decimal places; p-value will be presented to 4 decimals.

Note: Statistical comparison of PK parameters (Table 14.2.1.1.21) and the Heart Rate parameters (Table 14.2.6.10) will have the following format:

Table 14.2.1.1.21 Statistical Comparison of Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Cmax and AUC(0-180) (Pharmacokinetic Population)

Comparison	Parameter	Geometric LS Means Test (n)	Geometric LS Means Reference (n)	% Geometric LS Mean Ratio (Test/Reference)	90% Confidence Interval for %GMR	p-value
Product A vs Product E	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Product B vs Product E	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Product C vs Product E	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Product D vs Product E	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	AUC(0-180)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
The mixed model includes product sequence, study day, and product as fixed effects and participant nested within product sequence as a random effect. Mixed model with a default (variance component) covariance structure was used.
Parameters are ln-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/Reference)
Test = The first product in the comparison
Reference = The second product in the comparison
n = Number of observation used in the analysis

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

Programming note: Geometric LS Means to be presented to same precision as Mean in the PK parameter table. Geometric Mean Ratio and 90% confidence intervals will be presented to 2 decimal places; p-value will be presented to 4 decimals.
Programming note: All pairwise comparison will be included in the table, by displayed order of: Testing product vs references, followed by among references, followed by among testing products.
Programming note: Add asterisk to the p-value column to flag significant values when p < 0.1 and add footnote to state this.

Note: Subjective measure tables for Product Liking VAS Scores (14.2.3.1) will have the following format.

Table 14.2.3.1 Summary of Product Liking VAS Scores During and After the Morning Ad Libitum Product Use Episode by Study Product and Timepoint (Subjective Measures Population)

		Product Use Sample Times (minute)				
Product	Statistic	5	15	30	60	180
A	n	X	X	X	X	X
	n missing	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Q1	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X
	Q3	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Programmer Note: Products B, C, D, E, and F will also be presented in the table.

Note: Subjective measure tables for Product Liking Maximum VAS Scores (14.2.3.2) will have the following format.

Table 14.2.3.2 Summary of Product Liking VAS Parameters (Emax-PL and AUEC-PL) During and After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

Parameter	Statistic	Product A	Product B	Product C	Product D	Product E	Product F
Emax-PL	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Q1	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
Emax-PL = Maximum value of the VAS score across all timepoints.

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

Programmer Note: AUEC-PL will also be presented in the table.

Note: Statistical summary table of Product Liking maximum VAS score by product (Table 14.2.3.3) will have the following format:

Table 14.2.3.3 Statistical Summary of Product Liking VAS Parameters (Emax-PL and AUEC-PL) by Study Product (Subjective Measures Population)

Product	Parameter	n	LS Mean	90% Confidence Interval	p-value
A	Emax-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
B	Emax-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
C	Emax-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
D	Emax-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
E	Emax-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
F	Emax-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X	X.XX	XX.XX – XXX.XX	X.XXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
n = Number of observation used in the analysis
The mixed model includes product sequence, study day, and product as fixed effects and participant nested within product sequence as a random effect. Mixed model with a default (variance component) covariance structure was used.
Least-squares means (LS Means) are calculated from the ANOVA.

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

Note: Statistical comparison table of Product Liking maximum reduction in VAS (Table 14.2.3.4) will have the following format:

Tables 14.2.3.4 Statistical Comparison of Product Liking VAS Parameters (Emax-PL and AUEC-PL) (Subjective Measures Population)

Comparison	Parameter	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test - Reference)	90% CI for LS Mean Difference	p-value
Product A vs Product E	Emax-PL	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Product B vs Product E	Emax-PL	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Product C vs Product E	Emax-PL	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Product D vs Product E	Emax-PL	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	AUEC-PL	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
The mixed model includes product sequence, study day, and product as fixed effects and participant nested within product sequence as a random effect. Mixed model with a default (variance component) covariance structure was used.
Least-squares means (LS Means) are calculated from the ANOVA.
Test = The first product in the comparison
Reference = The second product in the comparison
n = Number of observation used in the analysis

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

Note: Subjective measure tables for Tobacco/Nicotine Withdrawal VAS Scores (14.2.3.5 and 14.2.3.6) will have the following format.

Table 14.2.3.5 Summary of Tobacco/Nicotine Withdrawal VAS Scores and Difference From Pre-use During and After the Morning Ad Libitum Product Use Episode (Urges to Smoke) by Study Product and Timepoint (Subjective Measures Population)

		----Product Use Sample Times (minute)----					---------Pre-Use – Post-Use----			
Product	Statistics	Pre-use	5	15	30	60	5	15	30	60
A	n	XX	XX	XX	XX	XX	XX	XX	XX	XX
	n missing	X	X	X	X	X	X	X	X	X
	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	XXX.X	XXX.X	XXX.X	XXX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	X	X	X	X	X	-XX	-XX	-XX	-XX
	QX	XX.X	XX.X	XX.X	XX.X	XX.X	X.X	X.X	X.X	X.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	X.X	XX.X	XX.X	XX.X
	QX	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XXX	XXX	XXX	XXX	XXX	XX	XX	XXX	XX
	XX% CI Lower	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	XX% CI Upper	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
B	n	XX	XX	XX	XX	XX	XX	XX	XX	XX
	n missing	X	X	X	X	X	X	X	X	X
	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	XXX.X	XXX.X	XXX.X	XXX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	X	X	X	X	X	-XX	-XX	-XX	-XX
	QX	XX.X	XX.X	XX.X	XX.X	XX.X	X.X	X.X	X.X	X.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	X.X	XX.X	XX.X	XX.X
	QX	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XXX	XXX	XXX	XXX	XXX	XX	XX	XXX	XX
	XX% CI Lower	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	XX% CI Upper	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Programmer Note: Products B, C, D, E, and F will also be presented in the table.

Note: Subjective measure tables for Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (14.2.3.7) will have the following format.

Table 14.2.3.7 Summary of Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (Emax-TNW) During and After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

Assessment	Statistics	Product A	Product B	Product C	Product D	Product E	Product F
Urges to Smoke	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Q1	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
Emax-TNW = Maximum value of the VAS score across all timepoints.

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

Programmer Note: Craving a Cigarette will also be presented in the table.

Note: Statistical summary table of Tobacco/Nicotine Withdrawal maximum reduction in VAS score by product (Table 14.2.3.8) will have the following format:

Table 14.2.3.8 Statistical Summary of Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (Emax-TNW) by Study Product (Subjective Measures Population)

		Emax-TNW			
Product	Assessment	n	LS Mean	90% Confidence Interval	p-value
A	Urges to Smoke	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Craving a Cigarette	X	X.XX	XX.XX – XXX.XX	X.XXXX
B	Urges to Smoke	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Craving a Cigarette	X	X.XX	XX.XX – XXX.XX	X.XXXX
C	Urges to Smoke	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Craving a Cigarette	X	X.XX	XX.XX – XXX.XX	X.XXXX
D	Urges to Smoke	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Craving a Cigarette	X	X.XX	XX.XX – XXX.XX	X.XXXX
E	Urges to Smoke	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Craving a Cigarette	X	X.XX	XX.XX – XXX.XX	X.XXXX
F	Urges to Smoke	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Craving a Cigarette	X	X.XX	XX.XX – XXX.XX	X.XXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
n = Number of observation used in the analysis
The mixed model includes product sequence, study day, and product as fixed effects and participant nested within product sequence as a random effect. Mixed model with a default (variance component) covariance structure was used.
Least-squares means (LS Means) are calculated from the ANOVA.

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

Note: Statistical comparison table of Tobacco/Nicotine Withdrawal maximum reduction in VAS (Table 14.2.3.9) will have the following format:

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Tables 14.2.3.9 Statistical Comparison of Tobacco/Nicotine Withdrawal Maximum Reduction in VAS Score (Emax-TNW) (Subjective Measures Population)

		Emax-TNW				
		LS Means		LS Mean Difference	90% CI for	
Comparison	Assessment	Test (n)	Reference (n)	(Test - Reference)	LS Mean Difference	p-value
Product A vs Product E	Urges to Smoke	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Craving a Cigarette	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
Product B vs Product E	Urges to Smoke	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Craving a Cigarette	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
Product C vs Product E	Urges to Smoke	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Craving a Cigarette	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
Product D vs Product E	Urges to Smoke	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Craving a Cigarette	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
The mixed model includes product sequence, study day, and product as fixed effects and participant nested within product sequence as a random effect. Mixed model with a default (variance component) covariance structure was used.
Least-squares means (LS Means) are calculated from the ANOVA.
Test = The first product in the comparison
Reference = The second product in the comparison
n = Number of observation used in the analysis

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

Programming Note: The comparisons between A vs F, B vs F, C vs F, and D vs F will also be included in the table.

Note: Subjective measure tables for Direct Effects of Product VAS Scores (14.2.3.10) will have the following format.

Table 14.2.3.10 Summary of Direct Effects of Product VAS Scores During and After the Morning Ad Libitum Product Use Episode by Study Product and Timepoint (Subjective Measures Population)

Question	Product	Statistics	Product Use Sample Times (minute) 5	15	30	60
Is the Product "Pleasant" Right Now?	A	n	X	X	X	X
		n missing	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Q1	X.X	X.X	X.X	X.X
		Median	X.X	X.X	X.X	X.X
		Q3	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
		90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X
	B	n	X	X	X	X
		n missing	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Q1	X.X	X.X	X.X	X.X
		Median	X.X	X.X	X.X	X.X
		Q3	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
		90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Programmer Note: Products B, C, D, E, and F will also be presented in the table. All questions in the Direct Effects of Product will be presented in the table.

Note: Subjective measure tables for Direct Effects of Product Maximum VAS Scores Emax-DEP (14.2.3.11) will have the following format.

Table 14.2.3.11 Summary of Direct Effects of Product Maximum VAS Scores (Emax-DEP) During and After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

Question	Statistics	Product A	Product B	Product C	Product D	Product E	Product F
Is the Product "Pleasant" Right Now?	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Q1	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Programmer Note: All questions in the Direct Effects of Product will be presented in the table.

Note: Statistical summary table of Direct Effects of Product maximum VAS score (Emax-DEP) by product (Table 14.2.3.12) will have the following format:

Table 14.2.3.12 Statistical Summary of Direct Effects of Product Emax-DEP by Study Product (Subjective Measures Population)

			Emax-DEP		
Product	Assessment	n	LS Mean	90% Confidence Intervals	p-Value
A	Pleasant	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Satisfying	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Feel Calm	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Help Concentrate	X	X.XX	XX.XX – XXX.XX	X.XXXX
	More Awake	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Feel Sick	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Reducing Hunger	X	X.XX	XX.XX – XXX.XX	X.XXXX
	Like More Product	X	X.XX	XX.XX – XXX.XX	X.XXXX
B	<repeat for products B through G>				

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
n = Number of observation used in the analysis
The mixed model includes product sequence, visit, and product as fixed effects and participant nested within product sequence as a random effect. Mixed model with a default (variance component) covariance structure was used.
Least-squares means (LS Means) are calculated from the ANOVA.

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

Note: Statistical comparison table of Direct Effects of Product maximum VAS score (Emax-DEP) (Table 14.2.3.13) will have the following format:

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Tables 14.2.3.13 Statistical Comparison of Direct Effects of Product Emax-DEP (Subjective Measures Population)

		Emax-DEP				
		LS Means		LS Mean Difference	90% CI for	
Comparison	Assessment	Test (n)	Reference (n)	(Test - Reference)	LS Mean Difference	p-Value
Product A vs Product E	Pleasant	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Satisfying	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Feel Calm	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Help Concentrate	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	More Awake	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Feel Sick	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Reducing Hunger	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Like More Product	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
Product B vs Product E	Pleasant	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Satisfying	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Feel Calm	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Help Concentrate	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	More Awake	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Feel Sick	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Reducing Hunger	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Like More Product	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
<Same for remaining comparisons>						

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
The mixed model includes product sequence, study day, and product as fixed effects and participant nested within product sequence as a random effect. Mixed model with a default (variance component) covariance structure was used.
Least-squares means (LS Means) are calculated from the ANOVA.
Test = The first product in the comparison
Reference = The second product in the comparison
n = Number of observation used in the analysis

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

Programming Note: The comparison between test products and reference products will be included in the table.

Note: Subjective measure tables for Use the Product Again VAS Scores (14.2.3.14 through 14.2.3.16) will have the following format.

Table 14.2.3.14 Frequency Counts of Responses to Use Product Again VAS Scores in Each Category After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

Product	Statistics	---- Use the Product Again Response Category ---- -50 to <0	0	>0 to 50
A	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
B	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
C	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
D	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
E	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
F	n (%)	XX(XX%)	XX(XX%)	XX(XX%)

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

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

Table 14.2.3.15 Summary of Responses to Use Product Again VAS Scores in Each Category After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

Use the Product Again Response Category	Statistics	Product A	Product B	Product C	Product D	Product E	Product F
-50 to <0	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Q1	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X
>0 to 50	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Q1	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Table 14.2.3.16 Summary of Responses to Use the Product Again VAS Original Scores After the Morning Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

Statistics	Product A	Product B	Product C	Product D	Product E	Product F
n	X	X	X	X	X	X
n missing	X	X	X	X	X	X
Mean	X.X	X.X	X.X	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
Minimum	XX	XX	XX	XX	XX	XX
Q1	X.X	X.X	X.X	X.X	X.X	X.X
Median	X.X	X.X	X.X	X.X	X.X	X.X
Q3	X.X	X.X	X.X	X.X	X.X	X.X
Maximum	XX	XX	XX	XX	XX	XX
90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Note: Subjective measure tables for Modified Cigarette Evaluation Questionnaire factor scores (Table 14.2.3.17) will be in the following format.

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Table 14.2.3.17 Summary of Modified Cigarette Evaluation Questionnaire Factor Scores After the Afternoon Ad Libitum Product Use Episode by Study Product (Subjective Measures Population)

Subscale	Statistics	Product A	Product B	Product C	Product D	Product E	Product F
Product Use	n	X	X	X	X	X	X
Satisfaction	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Q1	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Factors will be populated with Product Use Satisfaction, Psychological Reward, Aversion, Enjoyment of the Sensation, and Craving Reduction
The following footnote will be added:
Response Scale: 1 = Not at all, 2 = Very little, 3 = A little, 4 = Moderately, 5 = A lot, 6 = Quite a lot, 7 = Extremely

Table 14.2.5.1 Summary of Product Use During Product Trial Period by Study Product (Product Use Population)

Variable	Statistics	Product A	Product B	Product C	Product D
Number of HTS used	n	X	X	X	X
	n missing	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	SEM	XX.X	XX.X	XX.X	XX.X
	Minimum	X.X	X.X	X.X	X.X
	Q1	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Q3	XX	XX	XX	XX
	Maximum	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >

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

Table 14.2.5.2 Summary of Product Use Behavior Characteristics During the Morning Ad Libitum Product Use Episode by Study Product (Product Use Population)

Variable	Statistics	Product A	Product B	Product C	Product D	Product E	Product F
Total Duration	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Minimum	X.X	X.X	X.X	X.X	X.X	X.X
	Q1	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Q3	XX	XX	XX	XX	XX	XX
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Programming Note: Puff count will also be presented in the table. The puff count for nicotine gum will be NA as Not Applicable.

Table 14.2.5.3 Summary of Product Use Behavior Characteristics During the Afternoon Ad Libitum Product Use Episode by Study Product (Product Use Population)

Variable	Statistics	Product A	Product B	Product C	Product D	Product E	Product F
Number of Product Used	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Minimum	X.X	X.X	X.X	X.X	X.X	X.X
	Q1	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Q3	XX	XX	XX	XX	XX	XX
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Note: Heart Rate tables (14.2.6.1 and 14.2.6.2) will have the following format.

Table 14.2.6.1 Summary of Heart Rates During the Morning Ad Libitum Product Use Episode by Study Product and Sex
(Physiological Heart Rate Population)

Time Point	Statistics	Product A	Product B	Product C	Product D	Product E	Product F
Pre-use	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Minimum	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X
5 minutes	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Minimum	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	90% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Programming Note: Summaries for all time points will be included in the table. On the Baseline-adjusted table the Pre-use time point will not be presented.

Table 14.3.1.1 Adverse Experience Frequency by Study Product – Number of Participants Reporting the Experience (% of Participants Who Received Study Product) (Safety Population)

	Product Trial#	Product						
Adverse Experience	(N=XX)	A (N=XX)	B (N=XX)	C (N=XX)	D (N=XX)	E (N=XX)	F (N=XX)	Overall^ (N=XX)
Number of Participants With Adverse Experiences	X(X%)	X(XX%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Number of Participants Without Adverse Experiences	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%)

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

*Adverse experiences are classified according to MedDRA Version 25.1.
#Only include the adverse experiences that occurred during the product trial period. The Product Trial period includes the at home product trial up until the first ad libitum use on Day -1.
^Adverse experiences that occurred during the product trial period are excluded from Overall summary.

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

Programmer Note: Product Trial should include all AE's in the database prior to ad libitum use on Day -1, inclusive of if the participant was a screen failure or enrolled in the study.

Table 14.3.1.2 Adverse Experience Frequency by Study Product – Number of Adverse Experiences (% of Total Adverse Experiences)
(Safety Population)

Adverse Experience*	Product Trial#	Product A	B	C	D	E	F	Overall^
Number of Adverse Experiences	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%)

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
*Adverse experiences are classified according to MedDRA Version 25.1.
#Only include the adverse experiences that occurred during the product trial period. The Product Trial period includes the at home product trial up until the first ad libitum use on Day -1.
^Adverse experiences that occurred during the product trial period are excluded from Overall summary.

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

Programmer Note: Product Trial should include all AE's in the database prior to ad libitum use on Day -1, inclusive of if the participant was a screen failure or enrolled in the study.

Table 14.3.1.3 Adverse Experience Frequency by Study Product, Severity, and Relationship to Study Product – Number of Participants Reporting the Experience (Safety Population)

Adverse Experience*	Study Product	Number of Participants With AEs	Severity			Relationship to Study Product				
			Mild	Moderate	Severe	Not Related	Unlikely	Possible	Likely	Definitely
Abdominal pain	X	X	X	X	X	X	X	X	X	X
Dry throat	X	X	X	X	X	X	X	X	X	X
Product Trial#		X	X	X	X	X	X	X	X	X
Study Product A		X	X	X	X	X	X	X	X	X
Study Product B		X	X	X	X	X	X	X	X	X
Study Product C		X	X	X	X	X	X	X	X	X
Study Product D		X	X	X	X	X	X	X	X	X
Study Product E		X	X	X	X	X	X	X	X	X
Study Product F		X	X	X	X	X	X	X	X	X
Overall^		X	X	X	X	X	X	X	X	X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

*Adverse experiences are classified according to MedDRA Version 25.1.
#Only include the adverse experiences that occurred during the product trial period. The Product Trial period includes the at home product trial up until the first ad libitum use on Day -1.
^Adverse experiences that occurred during the product trial period are excluded from Overall summary.
When a participant 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 participant 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.

Program: /CAXXXXX/sas_prg/stsas/tab cdash_tblae4a_auto.sas DDMMMYYYY HH:MM

Programmer Note: Product Trial should include all AE's in the database prior to ad libitum use on Day -1, inclusive of if the participant was a screen failure or enrolled in the study.

Table 14.3.1.4 Adverse Experience Frequency by Study Product, Severity, and Relationship to Study Product – Number of Adverse Experiences (Safety Population)

Adverse Experience*	Study Product	Number of AEs	Severity			Relationship to Study Product				
			Mild	Moderate	Severe	Not Related	Unlikely	Possible	Likely	Definitely
Abdominal pain	X	X	X	X	X	X	X	X	X	X
Dry throat	X	X	X	X	X	X	X	X	X	X
Product Trial#		X	X	X	X	X	X	X	X	X
Study Product A		X	X	X	X	X	X	X	X	X
Study Product B		X	X	X	X	X	X	X	X	X
Study Product C		X	X	X	X	X	X	X	X	X
Study Product D		X	X	X	X	X	X	X	X	X
Study Product E		X	X	X	X	X	X	X	X	X
Study Product F		X	X	X	X	X	X	X	X	X
Overall^		X	X	X	X	X	X	X	X	X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
*Adverse experiences are classified according to MedDRA Version 25.1.
#Only include the adverse experiences that occurred during the product trial period. The Product Trial period includes the at home product trial up until the first ad libitum use on Day -1.
^Adverse experiences that occurred during the product trial period are excluded from Overall summary.

Program: /CAXXXXX/sas_prg/stsas/tab cdash_tblae4a_auto.sas DDMMMYYYY HH:MM

Programmer Note: Product Trial should include all AE's in the database prior to ad libitum use on Day -1, inclusive of if the participant was a screen failure or enrolled in the study.

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

Table 14.3.2.1 Serious Adverse Experiences (Safety Population)

There were no serious adverse experiences recorded during the study.

Programmer Note: If there are Serious adverse experiences follow the shell associated with Appendix 16.2.7.2

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

Hematology and urinalysis summary tables (Table 14.3.5.2 and 14.3.5.3) will be in the following format.

Table 14.3.5.1 Clinical Laboratory Summary – Chemistry (Safety Population)

		Screening	
		Product	
Laboratory (units)	Statistic	Trial*	Randomized#
Testname (unit)	n	X	X
	Mean	X.X	X.X
	SD	X.XX	X.XX
	Minimum	XX	XX
	Median	X.X	X.X
	Maximum	XX	XX
Testname (unit)	n	X	X
	Mean	X.X	X.X
	SD	X.XX	X.XX
	Minimum	XX	XX
	Median	X.X	X.X
	Maximum	XX	XX
Testname (unit)	n	X	X
	Mean	X.X	X.X
	SD	X.XX	X.XX
	Minimum	XX	XX
	Median	X.X	X.X
	Maximum	XX	XX

*Only includes participants that enrolled in the Product Trial period and dropped prior to randomization.
#Participants who only participated in the Product Trial period are excluded from the summary.

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

Table 14.3.5.4 Vital Sign Summary (Safety Population)

Vital Sign (units)	Statistic	Screening/ Product Trial*	Time Point# Screening	Check-in	End of Study
Testname (unit)	n	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
Testname (unit)	n	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
Testname (unit)	n	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX

*Only includes participants that enrolled in the Product Trial period and dropped prior to randomization.
#Participants who only participated in the Product Trial period are excluded from the summaries.

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

16. 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. Listings will generated from data created in accordance with SDTM Model 1.4 with Implementation Guide 3.2 or CDASH data structure. Listings with derived data may be created from the ADaM data. All listings will be presented in Times New Roman size font 9 in RTF format. Time point information (visit, day, hour) will match that found in the CRF.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

Laboratory Group	Test Name	Sex	Age Category	Reference Range	Unit
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

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

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

Appendix 16.2.1.1 Participant Disposition (Safety Population)

Participant Number	Date of Completion/Discontinuation	Participant Status	Specify Reason for Participant Status	Last Visit Completed	Reason Not Randomized
X	DDMMMYYYY	Completed			
X	DDMMMYYYY	Completed			
X	DDMMMYYYY	Completed			
X	DDMMMYYYY	Completed			
X	DDMMMYYYY	Withdrawal by Participant	XXXXXXXXXX	Day X	XXXXXXXXXXX
X	DDMMMYYYY	Completed			
X	DDMMMYYYY	Completed			
X	DDMMMYYYY	Completed			

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

Appendix 16.2.1.2 Participant Disposition (Screen Failures)

Participant Number	Date of Completion/Discontinuation	Participant Status	Specify Reason for Participant Status	Were all Eligibility Criteria Met?	Criterion Not Met	Reason Not Randomized
X	DDMMMYYYY	Screen Failure	XXXXXXXXX	No	INCXX	XXXXXXXXX
X	DDMMMYYYY	Screen Failure	XXXXXXXXX	No	EXCXX	
X	DDMMMYYYY	Screen Failure	XXXXXXXXX	No	EXCXX	
X	DDMMMYYYY	Screen Failure	XXXXXXXXX	No	INCXX	
X	DDMMMYYYY	Screen Failure	XXXXXXXXX	No	INCXX	
X	DDMMMYYYY	Screen Failure	XXXXXXXXX	No	EXCXX	

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

Appendix 16.2.2.1 Protocol Deviations

Participant Number	Any Deviation?	Study Visit	Study Product	Deviation Start Date	Time-point	Deviation Classification	Eligibility Category	Informed Consent Category	Study Conduct Procedures	Safety Deviation Category	Protocol Deviation Reported Term	Protocol Deviation Importance
X	XXX	XXX	X	DDMMMYYYY	XXXX	XXXX	XXX	XXX	XXX	XXX	XXXXXX	XXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Appendix 16.2.2.2 Heated Tobacco Product Issues

Participant Number	Any Deviation?	Study Visit	Study Product	Heated Tobacco Product Issue	Date	Pattern of Issue	Action taken with Device
X	XXX	XXX	X	XXXXXXXX	DDMMMYYYY	XXXXX	XXXXXXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >

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

Appendix 16.2.3.2 Participant Population Information

Participant Number	Randomized Product Sequence	Population				
		Safety	PK	Subjective Measures	Heart Rate	Product Use
X	XXXXXXXX	Yes	Yes	Yes	Yes	Yes
X	XXXXXXXX	Yes	Yes	Yes	Yes	Yes
X	XXXXXXXX	Yes	No	No	No	Yes
X	XXXXXXXX	Yes	Yes	Yes	Yes	Yes

Promgrammer Note: This listing will not be produced until all participant populations have been determined.

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
PK = Pharmacokinetics

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

Appendix 16.2.4.1 Demographics (Safety Population)

Participant Number	Randomized Randomized Sequence	Year of Birth	Age (yrs)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	BMI (kg/m^2)	Informed Consent Date
X	XXXXXXX	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMMYYYY
X	XXXXXXX	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMMYYYY
X	XXXXXXX	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMMYYYY
X	XXXXXXX	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMMYYYY
X	XXXXXXX	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMMYYYY
X	XXXXXXX	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMMYYYY
X	XXXXXXX	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMMYYYY

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
BMI = Body mass index

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

Appendix 16.2.4.2 Demographics (Screen Failures)

Participant Number	Year of Birth	Age (yrs)	Sex	Race	Ethnicity	Informed Consent Date
X	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXX	DDMMMYYYY
X	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	DDMMMYYYY
X	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	DDMMMYYYY
X	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	DDMMMYYYY
X	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	DDMMMYYYY
X	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	DDMMMYYYY
X	YYYY	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	DDMMMYYYY

BMI = Body mass index

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

Appendix 16.2.4.3 Physical Examination (Safety Population)

Participant Number	Study Visit	Was PE Performed?	Date	Reason Not Performed?	Were All Required Findings From the Physical Exam Entered as Medical History?
X	Screening	Yes	DDMMMYYYY		
	X	Yes	DDMMMYYYY		XXX
	X	No	DDMMMYYYY		

PE = Physical examination

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

Appendix 16.2.4.4 Symptom Driven Physical Examination (Safety Population)

Participant Number	Study Visit	Was a Symptom Driven PE Performed?	Date	Were There Any New Findings or Findings That Have Worsened?
X	XX	Yes	DDMMMYYYY	XXXXXXX

PE = Physical examination

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

Appendix 16.2.4.5 Medical History (Safety Population)

Participant Number	Any History?	Study Visit	Condition or Event	Date Start	Date End	Ongoing?	If Ongoing, are There any CM Being Taken?	MTSTYR
X	XXX	Screening	XXXXXXXXXXX	DDMMMYYYY		YES	No	XXX
			XXXXXXXXXXXX	DDMMMYYYY	DDMMMYYYY	NO		
X	XXX	Screening	XXXXXXXXXXXX	MMMYYYY	MMMYYYY	NO		

CM = Concomitant medications

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

Appendix 16.2.4.6 Usual Brand Attributes (Safety Population)

Participant Number	Visit	Usual Cigarette Brand	Other Brand, Specify	Flavor	Number of Cigarettes per day	Number of Years Smoked	UPC Code	Color Image of Usual Brand Obtained?
X	Screening	XXXXX	XXXXX	XXX	XX	XX	XXX	XXX

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

Appendix 16.2.4.7 Reproductive Status (Safety Population)

Participant Number	Visit	What is the Participant's menopausal Status?	Is the Participant of Child-bearing Potential?	What is the Contraceptive Method Used by the Participant?	What was postmenopausal status Confirmed by an FSH Test?	Date of FSH Sample
X	Screening	XXXXXXXXXXXXXXX	XXXX	XXXXXXXXXXXXXXXXX	XXXXXXXXXX	DDMMMYYYY

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

Appendix 16.2.4.8 Fagerström Test for Cigarette Dependence (Safety Population)

Participant Number	Visit	FTCD Completed?	Date	Time	Question# 1	2	3	4	5	6	Total Score
X	Screening	XXX	DDMMMYYYY	HH:MM	XXX	XXX	XXX	XXX	XXX	XXX	X

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

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

Appendix 16.2.5.1 Participant Eligibility (Safety Population)

Participant Number	Visit	Were all Eligibility Criteria Met?	Criterion Not Met
X	Screening	No	EXCXX
X	Screening	Yes	
X	Screening	Yes	
X	Screening	No	INCXX

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

Appendix 16.2.5.2 At Home Product Trial (Safety Population)

Participant Number	Dispensed On Day -6*	Used at least Once per Day for 5 Days?	Date Dispensed	Product	Amount Dispensed	Unit	Date Return	Amount Return	Amount Used*
X	XXX	XXX	DDMMMYYYY	A	XX	Stick	DDMMMYYYY	XX	XX
				B	XX	Stick	DDMMMYYYY	XX	XX
				C	XX	Stick	DDMMMYYYY	XX	XX
				D	XX	Stick	DDMMMYYYY	XX	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
* Was the participant dispensed study product for home trial use at Day-6?
*Calculated as Amount Dispensed – Amount Returned

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

Appendix 16.2.5.3 Randomization (Safety Population)

Participant Number	Date of Randomization	Randomization Group	Sex	Randomization Number	Randomized Product Sequence	Actual Product Sequence
X	DDMMMYYYY	XXXXXX	XXXX	XXXXX	XXXXXX	XXXXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Appendix 16.2.5.4 Morning Ad Libitum Product Use (Safety Population) (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Visit Performed?	Reason Not Done	Study Product	Date	Start Time	End Time	Number of Puffs	Amount of Used Gum	Product Collected?	Reason Not Collected
X	XXXXXX	Day X	XXX		X	DDMMMYYYY	HH:MM	HH:MM	XX	XX	XXX	

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Appendix 16.2.5.5 Afternoon Ad Libitum Product Use (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Date	Start Time	End Time	Number of Stick Used	Number of Cigarettes Used	Number of Gum Used	Used Product Collected?	Reason Not Collected
X	XXXXXX	Day X	X	DDMMMYYYY	HH:MM	HH:MM	XX Sticks	XX Cigarettes	XXX Gums	XXX	

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

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

Appendix 16.2.5.6 Concomitant Medications (Safety Population)

Participant Number	Any Med?	Study Product	Medication (WHO* Term)	Dosage	Route	Start Date	End Date	Frequency	Indication	Ongoing?	Related AE/MH
X	XXX	X	XXXXXXXXXXXX (XXXXXXXXXXXX)	XXX mg	XXXXX	DDMMMYYYY	DDMMMYYYY	XXXXXX	XXXXXXXXX	No	XXXXXXXXXXXXXXXXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
*Concomitant medications are coded with WHO Dictionary Version Global B3 September 1, 2022.
MH = Medical history; AE = Adverse experience; WHO = World Health Organization

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

Programmer note: Specified unit, frequency, and route will also be presented, if applicable.

Appendix 16.2.5.8 will resemble the format of Appendix 16.2.5.7.

Appendix 16.2.5.7 Plasma Nicotine Pharmacokinetic Blood Draw Times and Concentration Data (Safety Population)

Participant Number	Study Visit	Study Product	CRF Day	CRF Time point	Blood Draw Date	Blood Draw Time	Elapsed Time From Start Morning Product Use (units)	Unadjusted Concentration (units)	Baseline_ Adjusted Concentration (units)	Not Done?	Reason for Not Done
1	1	A	1	XXXXXX	DDMONYYYY	HH:MM:SS	0.0	X.XX	X.XX		
				XXXXX	DDMONYYYY	HH:MM:SS	0.265	X.XX	X.XX		
				XXXXX	DDMONYYYY	HH:MM:SS	0.590	X.XX	X.XX		
			< >								

<similar for all other time points and participants>

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >

Program: /CAXXXXX/sas_prg/pksas/standardlis/pk_bld.sas DDMMMYYYY HH:MM
Programmer Notes:

- Population: Safety population will be used in this listing.

Appendix 16.2.6.7 Individual Responses to Product Liking Questionnaire (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Time Point	Date	Time	VAS Score
X	XXXXXX	X	X	XXXXX	DDMMMYYYY	HH:MM	XX
				XXXXX	DDMMMYYYY	HH:MM	XX
				XXXXX	DDMMMYYYY	HH:MM	XX
				XXXXX	DDMMMYYYY	HH:MM	XX
		X	X	XXXXX	DDMMMYYYY	HH:MM	XX
				XXXXX	DDMMMYYYY	HH:MM	XX
				XXXXX	DDMMMYYYY	HH:MM	XX
				XXXXX	DDMMMYYYY	HH:MM	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
Response scale: 0 = Not at all; 100 = Extremely

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

Appendix 16.2.6.8 Individual Responses to Product Liking Questionnaire - Maximum VAS Score (Emax-PL) (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Date	Emax-PL
X	XXXXXX	X	X	DDMMMYYYY	XX
		X	X	DDMMMYYYY	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
VAS scale: 0 = Not at all; 100 = Extremely

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

Appendix 16.2.6.9 Individual Responses to Tobacco/Nicotine Withdrawal Questionnaire (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Time Point	Date	Time	Original Scale: Urges to Smoke	Original Scale: Craving a Cigarette	Pre-Use – Post-Use: Urges to Smoke	Pre-Use – Post-Use: Craving a Cigarette
X	XXXXXX	X	X	Pre-Use	DDMMMYYYY	HH:MM	XX	XX		
				XXXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX
				XXXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX
				XXXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX
				XXXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX
		X	X	Pre-Use	DDMMMYYYY	HH:MM	XX	XX		
				XXXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX
				XXXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX
				XXXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX
				XXXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
VAS Response scale: 0 = Not at all; 100 = Extremely

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

Appendix 16.2.6.10 Individual Responses to Tobacco/Nicotine Withdrawal Questionnaire – Maximum Reduction in VAS Score (Emax-TNW)
(Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Emax-TNW: Urges to Smoke	Emax-TNW: Craving a Cigarette
X	XXXXXX	X	X	XX	XX
		X	X	XX	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
Emax-TNW = Maximum value of the differences (VASpre-use – VASpost-use)

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

Appendix 16.2.6.11 Individual Responses to Direct Effects of Product Questionnaire (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Time Point	Date	Time	Pleasant	Satisfying	Feel Calm	Helping Concentrate	More Awake	Feel Sick	Reducing Hunger	Like More
X	XXXX	X	X	XXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX
				XXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX
				XXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX
				XXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX
		X	X	XXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX
				XXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX
				XXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX
				XXXX	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
VAS Response scale: 0 = Not at all; 100 = Extremely

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

Appendix 16.2.6.12 Individual Responses to Direct Effects of Product Questionnaire – Maximum VAS Score (Emax-DEP) (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Emax-DEP: Pleasant	Satisfying	Feel Calm	Helping Concentrate	More Awake	Feel Sick	Reducing Hunger	Like More
X	XXXXXX	X	X	XX	XX	XX	XX	XX	XX	XX	XX
X	XXXXXX	X	X	XX	XX	XX	XX	XX	XX	XX	XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
Emax-DEP = Maximum value of the VAS scores
Response scale: 0 = Not at all, 100 = Extremely

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

Appendix 16.2.6.13 Individual Responses to Use Product Again Questionnaire (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Date	Time	If Given the Opportunity, I Would Want to Use This Product Again	Response as Bipolar Variable
X	XXXXXX	X	X	DDMMMYYYY	HH:MM	XXX	>0 to 50
		X	X	DDMMMYYYY	HH:MM	XXX	-50 to <0

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
Response scale: 0 = Definitely would not; 50 = Don’t care; 100 = Definitely would
Bipolar score = Original VAS score – 50

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

Appendix 16.2.6.14 Individual Responses to Modified Cigarette Evaluation Questionnaire (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Date	Time	Question* 1	2	3	4	5	6	7	8	9	10	11	12
X	XXXXXX	X	X	DDMMMYYYY	HH:MM	X	X	X	X	X	X	X	X	X	X	X	X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
*Questions: 1. Was using the product satisfying?; 2. Did the product taste good?;
3. Did you enjoy the sensations in your mouth?; 4. Did using the product calm you down?;
5. Did using the product make you feel more awake?; 6. Did using the product make you feel less irritable?;
7. Did using the product help you concentrate?; 8. Did using the product reduce your hunger for food?;
9. Did using the product make you dizzy?; 10. Did using the product make you nauseous?;
11. Did using the product immediately relieve your craving for your usual brand smokeless produc?; 12. Did you enjoy using the product?
Response scale: 1 = Not at all; 2 = Vey little; 3 = A little; 4 = Moderately; 5 = A lot; 6 = Quite a lot; 7 = Extremely

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

Appendix 16.2.6.15 Individual Factor Score to Modified Cigarette Evaluation Questionnaire (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Date	Time	Product Use Satisfaction	Psychological Reward	Aversion	Enjoyment of Sensation	Craving Reduction
X	XXXXXX	X	X	DDMMMYYYY	HH:MM	X	X	X	X	X
		X	X	DDMMMYYYY	HH:MM	X	X	X	X	X
		X	X	DDMMMYYYY	HH:MM	X	X	X	X	X
		X	X	DDMMMYYYY	HH:MM	X	X	X	X	X

Product A = < >
Product B = < >
Product C = < >
Product D = < >
Product E = < >
Product F = < >
Product use satisfaction: average of scores from 1, 2, and 12
Psychological reward: average of scores from 4 to 8
Aversion: average of scores from 9 and 10;
Enjoyment of sensation: score from 3
Craving Reduction: score from 11
Refer to Appendix 16.2.6.14 for question descriptions.

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

Appendix 16.2.6.16 Individual Unadjusted and Baseline-Adjusted Heart Rate (Safety Population)

Participant Number	Actual Product Sequence	Study Visit	Study Product	Time Point	Date	Time	Heart Rate (bpm)	Baseline-Adjusted Heart Rate (bpm)	Not Done
X	XXXXXX	X	X	XXXXXXX	DDMMMYYYY	HH:MM:SS	XX		
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
		X	X	XXXXXXX	DDMMMYYYY	HH:MM:SS	XX		
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	
				XXXXX	DDMMMYYYY	HH:MM:SS	XX	XX	

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
Baseline is the value at pre-use of each product use episode.
Baseline-adjusted = post-use – pre-use

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

Appendix 16.2.7.1 Adverse Experiences (Safety Population)

Participant Number	Age/ Sex	Study Product	PUE?	System Organ Class/ Preferred Term (Verbatim)	Time From Start Product Use (DD:HH:MM)	Date:Time Start/ Last End/ Duration (DD:HH:MM)	Ongoing	Serious/ Outcome	Severity	Study Product Relationship/ Action	CM Given/ Cause Discon.
1	30/F			None							
2	24/M			None							
3	52/M	X	Yes	XXXXXXXXXXXX/ XXXXXXXXXXXXXXXX (XXXXXXXXXXX)	XX:XX:XX	DDMONYYYY:HH:MM/ DDMONYYYY:HH:MM 00:23:15	XXX	No/ Recovered/ Resolved	Moderate	Related/ XXXXX	XXX/ XXX
		X	Yes	<similar to above>							

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
PT = Adverse experiences occurred during the product trial period. The product trial period includes the at home product trial up until the first ad libitum use on Day -1.
^Abbreviation for study product use-emergent (PUE), PUE is assigned to last product used prior to AE (Adverse experience) start.
*Adverse experiences are classified according to the MedDRA Version 25.1.
CM = Comcomitant medication; Discon = Discontinuation.

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

Appendix 16.2.7.2 Sevious Adverse Experiences (II of II) (Safety Population)

Participant Number	Study Product	PUE?^	System Organ Class >Preferred Term* >>Adverse Experience	Date:Time Start/ End Duration (DD:HH:MM)	Serious AE?	Congenital Anomaly/ Birth Defect?	Persistent or Significant Disability or Incapacity?	Hospital- ization?	Life- Threat?	Important Medical Event?	Death?
X	X	XXX	XXXXXXXXXXXXX >XXXXXXXXX >>XXXXXXXXXXXXXXXX	DDMONYYYY:HH:MM/ DDMONYYYY:HH:MM 00:23:15	Yes	No	No	Yes	No	Yes: < >	No

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Product F: < >
PT = Adverse experiences occurred during the product trial period. The product trial period includes the at home product trial up until the first ad libitum use on Day -1.
^Abbreviation for study product use-emergent (PUE), PUE is assigned to last product used prior to AE (Adverse experience) start.
*Adverse experiences are classified according to the MedDRA Version 25.1.
CM = Concomitant medication

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

Appendices 16.2.8.1 to 16.2.8.3 will have the following format.

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Appendix 16.2.8.1 Clinical Laboratory Report - Chemistry (Safety Population)

Participant Number	Age/ Sex	Visit	Fasting?	Date	Time	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)
X	XX/X	Screening	XXX	DDMMMYYYY	HH:MM	XX H	XX	XX	XX	XX L

Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study. Fasting column will only be presented for chemistry panel.

H = Above reference range; L = Below reference range

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

Appendix 16.2.8.4 Alcohol, Drug, and Cotinine Screen (Safety Population)

Participant Study Number	Visit	Lab Test	Date	Result*	Lab Name	Specimen Type	Not Done?
X	Screening	XXXXXXXX	DDMMMYYYY	XXXXXX	XXXXXX	XXXXXXXX	

*Cotinine result response is to the question 'Was the result of the cotinine test >500 ng/mL?'

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

Appendix 16.2.8.5 Pregnancy Test (Safety Population)

Participant Number	Study Visit	Date	Was Test Perfomed?	Specimen Type	Result	Lab Name
X	Screening	DDMMMYYYY	XXX	XXXXXXXX	XXXXXX	XXXXXX

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

Appendix 16.2.8.6 Serology (Safety Population)

Participant Number	Study Visit	Was Test Perfomed?	Date of Collection
X	Screening	XXX	DDMMMYYYY

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

Appendix 16.2.8.7 Exhaled Carbon Monoxide (Safety Population)

Participant Number	Study Visit	Was ECO Test Perfomed?	Date	Result (ppm)	Lab Name	Specimen Type
X	Screening	XXX	DDMMMYYYY	XXX	XXXXX	Expired Air

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

Appendix 16.2.8.8 Vital Signs (Safety Population)

Participant Number	Study Visit	Day	Date	Time	Were Vitals Performed?	Blood Pressure (mmHg) Systolic/Diastolic	Heart Rate (bpm)	Respiration (rpm)	Temperature (°C)
X	Screening		DDMMMYYYY	HH:MM	XXX	XXX/ XX	XX	XX	XX.X
	X	-X	DDMMMYYYY	HH:MM	XXX	XXX/ XX	XX	XX	XX.X
	X	X	DDMMMYYYY	HH:MM	XXX	XXX/ XX	XX	XX	XX.X

Programmer Note: The physiological heart rate measrements will not be included in this listing.

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

Appendix 16.2.8.9 12-Lead Electrocardiogram (Safety Population)

Participant Number	Study Visit	Date	Time	What was the Interpretation of the ECG?	If Abnormal, Specify	Was the ECG Clinically Significant?
X	Screening	DDMMMYYYY	HH:MM	XXXXXXXXX		

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

17. REFERENCES

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