A Randomised, Cross-Over, Nicotine Pharmacokinetic and Pharmacodynamic Study of Heated Tobacco and Heated Herbal Products Compared with Combustible Cigarettes

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STATISTICAL ANALYSIS PLAN

A Randomised, Cross-Over, Nicotine Pharmacokinetic and Pharmacodynamic Study of Heated Tobacco and Heated Herbal Products Compared with Combustible Cigarettes

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STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

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As the statistical analysis plan was executed using the Veeva platform, please find the e-signature page at the end of the document.

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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 Imperial Brands PLC will be considered out of scope and must be described in the CSR.

2. OBJECTIVES AND ENDPOINTS

2.1 Objectives

Primary

1. To evaluate and compare the maximum plasma nicotine concentration (C_{max}) and the area under the plasma nicotine concentration-time curve at the last time point measured (AUC_t) following controlled use of each Heated Tobacco Product (HTP), Heated Herbal Product (HHP), or cigarette comparator.

Secondary

1. To evaluate other pharmacokinetic (PK) parameters of nicotine after the controlled use of each HTP, HHP, or cigarette comparator.

2. To evaluate the change in smoking urges observed after the controlled use of each HTP, HHP, or cigarette comparator.

3. To evaluate product perception and preference using subjective assessments.

4. To evaluate the tolerability and safety of each of the products used.

5. To investigate usage behaviour for each product using measurements of topography parameters (puff count, puff duration, puff volume, peak puff flow rate, average puff flow rate, inter puff interval) for each product following *ad libitum* product use sessions.

2.2 Study Endpoints Including Key Assessments and Summarization

Pharmacokinetics:

For each morning product use session on Days 1 through 5, plasma nicotine PK parameters (AUC_{inf}, AUC_{0-90}, AUC_{0-240}, AUC_t, C_{max}, C_{last}, T_{max}, $T_{1/2}$) will be computed from the individual plasma concentrations for each study product. Baseline adjustments will be performed.

Nicotine concentrations and PK parameters will be listed by subject and summarised using descriptive statistics.

Subjective Effects:

Intent to Use (ITU)

Descriptive statistics of the visual analogue scale (VAS) will be provided by study product and product use session. Individual responses will be listed by subject.

Urge to Smoke

Responses and derived parameters (E_{max}, TE_{max}, $AUEC_{0-240}$) will be listed by subject and summarised using descriptive statistics.

Product Evaluation Scale

Responses will be considered as a 7-point scale, and will be presented as factors outlined in Section 9.2.

Descriptive statistics of the subscales will be provided by study product and product use session. Individual responses will be listed.

Puff Topography:

Puff topography will be assessed using a SPA-M topography device. Since the device collects topography data for approximately 60 minutes, it will need to reset at 60 minutes in order to collect 2 hours of topography data. Topography parameters (puff count, puff duration, puff volume, peak puff flow rate, average flow rate, inter-puff interval) will be listed by subject and summarised using descriptive statistics.

Product Use Behaviour:

All product use data, including the number HTP/HHP sticks used and the number of Subject's own brand combustible cigarettes (OBCCs) smoked (Days -1 through Day 5), will be summarised using descriptive statistics.

Incidence of device malfunction(s) will also be tabulated.

Safety:

Safety will be monitored in-study through physical examination (symptom-driven), vital signs measurements, electrocardiogram (ECGs), and clinical laboratory tests (serum chemistry, haematology, and urinalysis).

Adverse events (AEs) spontaneously reported by the subjects or observed by the Investigator or other study personnel will be monitored from Screening until the follow-up.

AEs will be tabulated and summary statistics for vital signs and clinical laboratory tests may be computed and provided, as deemed clinically appropriate.

3. STUDY DESIGN

This study is designed to meet the objectives outlined in Section 2.1.

This will be a randomised, cross-over, open-label, confinement study conducted in 25 adult male or female smokers of combustible cigarettes. The study will investigate OBCC, HTPs, and HHPs, in a cross-over design, incorporating PK evaluation, subjective effects assessments, usage behaviour, and puff topography. The study will also incorporate a product use safety evaluation.

Subjects will perform a Screening Visit and 1 Study Visit, including a 6-day confinement period and finally a follow-up telephone call approximately 7 days after the final study product use.

Visit 1 (Screening)

Screening procedures will be performed within 28 days prior to study procedures on Day -1 and will include an eligibility check, review of health status and assessment of nicotine consumption habits. Medical and tobacco-use histories and demographic data will be collected. Other screening procedures include a physical examination (including oral cavity and oropharynx), vital signs, ECG, body mass index (BMI), clinical laboratory tests (haematology, serum chemistry, urinalysis), serology, urine/saliva drug, urine/breath alcohol, cotinine screen, exhaled carbon monoxide (CO), and pregnancy and follicle-stimulating hormone (FSH) tests (for females as appropriate). If required, subjects will be offered smoking cessation advice and contact information for a smoking cessation support service.

Visit 2 (In-clinic period, Day -1 to Day 5)
At Visit 2, subjects who successfully complete the screening procedures and meet all the inclusion criteria and none of the exclusion criteria will be eligible to check in to the clinical research unit (CRU) on Day -1 and will remain at the clinic until Day 5 for daily study

product use, PK sampling, subjective questionnaire assessments, puff topography (as applicable), and safety assessments.

On Day -1, following eligibility confirmation, subjects will undertake a familiarisation session of the study products and questionnaires. The clinical team will explain how the HTPs and HHPs will be used. Subjects will have the opportunity to see the products/devices and packaging and will participate in a Product Trial where they will take 5 puffs on a single one HTP stick (flavour chosen by subject) and 5 puffs on a single HHP stick (flavour chosen by subject). All products/devices used in the trial session will not be used in the clinical study but will be retained as demonstration samples for accountability purposes. An explanation of how the questionnaires will be administered to the subjects will be given. After the familiarisation session and completion of check-in procedures, subjects will be allowed to smoke their own cigarettes *ad libitum* but will abstain from use of any tobacco- or nicotine-containing products for at least 12 hours prior to the start of the morning controlled product use session on Day 1.

In the morning of Days 1 through 5, after pre-use assessments and confirmation of eligibility, subjects will use their randomly-assigned study product under controlled conditions by completely using a single unit (one stick, approximately 10 puffs) of the assigned study product, with puffs taken at 30-second intervals and of 3-second duration. PK samples will be collected within 5 minutes pre-study product use (timepoint '0') and at 2, 4, 6, 8, 10, 15, 30, 45, 60, 120, and 240 minutes following the start of study product use. Questionnaires will be administered to the subject at defined intervals throughout the day. Safety will be monitored throughout the day.

On Days 1 through 5, following the 4-hour PK blood collection, subjects will start a 4-hour *ad libitum* product use session (no limits on cigarette, HTP or HHP consumption) with the same study product used during the morning controlled use session.

On Days 1 through 5, puff topography will be performed over the last 2-hour period during the 4-hour *ad libitum* product use session. The Sodim Smoking Puff Analyzer Mobile (SPA-M) topography device will collect data (puff count, puff duration, puff volume, peak puff flow rate, average puff flow rate, inter-puff interval) for 2 hours. The SPA-M topography device will be reset at 60 minutes in order to collect 2 hours of data.

The *ad libitum* product use session on Days 1 through 5 will start at approximately the same time each day, with lunch served at the start of the *ad libitum* product use session, at approximately the same time each day. After completion of the *ad libitum* use session, subjects will be allowed to smoke their own cigarettes (*ad libitum*) but will abstain from use of any tobacco- or nicotine-containing products for at least 12 hours prior to the start of the morning controlled product use scheduled on the following day.

A new/unused device will be provided to the subjects on each day of HTP/HHP use (i.e., the same device will be used for the morning controlled product use and *ad libitum* product use sessions on the same day).

On Day 5, following completion of study assessments, subjects will be allowed to smoke their own cigarettes and will leave the CRU after completing all final check out requirements.

Visit 3 (Follow-up telephone call)

A follow-up telephone call (Visit 3) will be made by the CRU in an attempt to contact all subjects who used at least one study product (including subjects who terminate the study early) using their standard procedures approximately 7 days after the final product use to determine if any AE has occurred since the last study visit.

Subjects will not be forced to use any tobacco/nicotine products at any time during the study.

4. SAMPLE SIZE ESTIMATION

The sample size chosen for this study was selected without statistical considerations. It has been determined adequate to meet the study objectives.

5. SUBJECT RANDOMISATION

Subjects who complete the study screening assessments and meet all the eligibility criteria and are randomised will be assigned a unique randomisation identification number on Day -1 and will receive study products according to the randomisation scheme.

The sequences to be used in the randomisation will be ABECD, BCADE, CDBEA, DECAB, and EADBC, with 5 subjects randomly assigned to each sequence.

6. ANALYSIS POPULATIONS

Safety Population will include all subjects who have successfully completed eligibility requirements after checking in to the CRU and used at least one study product.

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

7. STUDY PRODUCT DESCRIPTIONS

All subjects will use Products A through E

The following products will be tested in this study:

Study Product	Short Description	Long Description
A	[redacted] stick	[redacted] device with [redacted] stick
B	[redacted] stick	[redacted] device with [redacted] stick
C	[redacted] stick	[redacted] device with [redacted] stick
D	[redacted] stick	[redacted] device with [redacted] stick
E	Cigarette	Subject's own brand combustible cigarette (OBCC)

Products A and B are HTPs ([redacted]).

Products C and D are HHPs ([redacted]).

8. PHARMACOKINETIC ANALYSIS

8.1 Measurements and Collection Schedule

On each of Days 1 through 5, venous blood samples (~4 mL per sample) for plasma nicotine analysis will be collected within 5 minutes pre-study product use (timepoint '0') and at 2, 4, 6, 8, 10, 15, 30, 45, 60, 120, and 240 minutes following the start of controlled study product use .

8.2 Bioanalytical Method

Plasma nicotine will be analysed by LC-MS/MS at Celerion Bioanalytical Services Lincoln, Nebraska, using validated analytical methods with appropriate quality controls according to the Food and Drug Administration (FDA) Guidance for Industry (Title 21 CFR Part 58). Additionally, processing of samples will completed by a non-tobacco user.

8.3 Pharmacokinetic Concentrations

For the concentration tables, unadjusted plasma nicotine concentrations that are below the limit of quantification (BLQ) will be set to one-half of the lower limit of quantitation for the calculation of descriptive statistics.

Individual nicotine concentrations will be adjusted for baseline nicotine ("baseline-adjusted") and all PK parameters will be calculated based on the adjusted concentrations. Baseline adjustment will be performed by subtraction of the pre-existing nicotine concentration from

each nicotine concentration obtained after test product administration in that period/day for each subject using the following equation:

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

where C_t is the adjusted concentration at time t, $C_{t\ unadjusted}$ is the observed concentration at time t, C_0 is the pre-product use concentration (-5 minutes), $K_{el} = \frac{\ln(2)}{T½}$, $T_{½}$ is 2 hours (average nicotine half-life), t is the actual sampling time since product administration, and t1 is the actual sampling time since the time of the pre-product use sample.

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 the descriptive statistics and the 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.

8.4 Noncompartmental Pharmacokinetic Analysis and Parameter Calculation

The appropriate noncompartmental PK parameters will be calculated from the baseline-adjusted plasma nicotine concentration-time data using Phoenix® WinNonlin® Version 8.1 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. Noncompartmental Pharmacokinetic Parameters to be Calculated

Parameter	Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
AUC_{0-90}	AUC0-90	Area under the baseline-adjusted nicotine concentration-time curve from time zero (defined as the start of the product use session) to the 90-minutes time point. If the 90-minutes plasma concentration is missing, BLQ, or not reportable, then interpolation and/or extrapolation will be conducted, as appropriate. If interpolation and/or extrapolation cannot be reliably performed, then this parameter cannot be calculated.	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC_{0-240}	AUC0-240	Area under the baseline-adjusted nicotine concentration-time curve from time zero (defined as the start of the product use session) to the to the 240-minutes time point. If the 240-minutes plasma concentration is missing, BLQ, or not reportable, then interpolation and/or extrapolation will be conducted, as appropriate. If interpolation and/or extrapolation cannot be reliably performed, then this parameter cannot be calculated.	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC_t	AUCt	Area under the baseline-adjusted nicotine concentration-time curve from time zero (defined as the start of the product use session) to the time of the last measurable non-zero concentration.	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC_{inf}	AUCinf	Area under the baseline-adjusted concentration-time curve from time 0 extrapolated to infinity	Calculated as: $AUC_t + (C_{last}/ K_{el})$ where C_{last} is the last observed/measured concentration

Parameter	Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
$AUC_{\%extrap}$	AUC%extrap	Percent of AUC_{inf} extrapolated to infinity	Calculated as: $(1 - AUC_t/AUC_{inf}) \times 100$
C_{max}	Cmax	Maximum baseline-adjusted plasma concentration over the duration of the measurement interval.	Taken from bioanalytical data adjusted for baseline
C_{last}	Clast	Plasma baseline-adjusted nicotine concentration at last time point measured.	Taken from bioanalytical data adjusted for baseline
T_{max}	T_{max}	Time to reach the maximum baseline-adjusted plasma concentration. If the maximum value occurs at more than one time point, T_{max} is defined as the first time point with this value	Taken from clinical database as the difference in the time of administration and the time of the blood draw which is associated with the C_{max}
$T_{½}$	T½	Apparent first-order terminal elimination half-life.	Calculated as $\ln 2/K_{el}$
K_{el}	Kel	Apparent first-order terminal elimination rate constant	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).

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

The K_{el} will be determined using linear regressions composed of least 3 data points. The K_{el} will not be calculated if 1) the terminal elimination phase is not apparent, 2) if C_{max} is one of the 3 last data points, or 3) if the R^2 value is less than 0.75. In cases where the K_{el} interval is not calculated, the values of $T_{½}$, AUC_{inf}, and $AUC_{\%extrap}$ will not be reported.

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, graphs, and data listings. Descriptive statistics will be generated for plasma concentrations and PK parameters.

The plasma nicotine concentrations will be listed for all subjects and presented with the same level of precision as received from the bioanalytical laboratory. Plasma nicotine concentrations will be summarised by study product and time point for all subjects in the outcomes population, by sex and overall using descriptive statistics. Summary statistics, including sample size (n), arithmetic mean (mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), minimum, median, and maximum will be calculated for all nominal time point for both baseline-adjusted and unadjusted concentrations. Excluded subjects or timepoints will be included in the concentration tables, but will be excluded from the summary statistics and noted as such in the tables. All BLQ values will be presented as "BLQ" in the concentration tables and footnoted accordingly.

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

Plasma nicotine PK parameters will be listed and summarised by product (overall and by sex) for all subjects in the Outcomes Population. Pharmacokinetic parameters will be reported to 3 significant figures for individual parameters, with the exception of T_{max}, which will be presented with 2 decimal places. Summary statistics will be reported, including n, mean, SD, CV%, SEM, minimum, median, and maximum by study product (overall and by sex). In addition, geometric mean (geom mean) and geometric CV% (geom CV%) will be provided for the C_{max} and AUCt parameters by study product (overall and by sex).

Excluded subjects or any PK parameter data, as applicable, 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 will be presented as an integer, CV% and geom CV% will be presented to the nearest tenth.

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

8.6 Statistical Analysis of Pharmacokinetic Parameters

A linear mixed model for analysis of variance (ANOVA) will be performed on the natural log-transformed PK parameters C_{max} and AUCt following the controlled (morning) product use session on each of Days/Periods 1, 2, 3, 4, and 5. The model will include sequence, product, and study period as fixed effects and subject-nested-within-sequence as a random

effect. Sequence will be tested using subject-nested-within-sequence as the error term for informational purposes. Geometric least-squares means (LSM) and 95% confidence intervals (CIs) will be provided for the PK parameters of C_{max} and AUCt by study product. Geometric LSM ratio, 95% CIs of geometric LSM ratio, and p-values will be provided for the study product comparisons in C_{max} and AUCt. The comparisons of interest will include each product compared to every other product (pairwise comparisons).

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

```
Proc mixed data=< >;
class subject sequence period product;
model  log(parameter) = sequence period product / ddfm=KR;
random  subject (sequence);
lsmeans product/cl alpha=0.05;
estimate “Product A versus Product E” Product 1 0 0 0 -1/cl alpha=0.05;
estimate “Product B versus Product E” Product 0 1 0 0 -1/cl alpha=0.05;
estimate “Product C versus Product E” Product 0 0 1 0 -1/cl alpha=0.05;
estimate “Product D versus Product E” Product 0 0 0 1 -1/cl alpha=0.05;
estimate “Product A versus Product D” Product 1 0 0 -1 0/cl alpha=0.05;
estimate “Product B versus Product D” Product 0 1 0 -1 0/cl alpha=0.05;
estimate “Product C versus Product D” Product 0 0 1 -1 0/cl alpha=0.05;
estimate “Product A versus Product C” Product 1 0 -1 0 0/cl alpha=0.05;
estimate “Product B versus Product C” Product 0 1 -1 0 0/cl alpha=0.05;
estimate “Product A versus Product B” Product 1 -1 0 0 0/cl alpha=0.05;
run;
```

Note: Protocol defined the study as Days 1-5 and the CRF had periods 1-5 (each have one day), respectively. Period will be used in the database and therefore in the statistical analysis.

Geometric LSMs will be presented in one more precision level than the associated PK parameter. GMRs and 95% CIs will be presented with 2 decimal places and intra-subject CV% will be presented to 2 decimal places.

Non-parametric analysis of T_{max} will be performed. The nonparametric Wilcoxon Signed Rank Test will be performed and the p-value will be presented for the same comparisons calculated in the ANOVA model above.

The Hodges-Lehmann estimate for the median of the differences in T_{max}, and the 95% CI will be presented for the comparisons. The Hodges-Lehmann estimator is given by the median of all possible pairwise averages (Walsh averages) of the differences in T_{max}. The CI will be constructed using Walsh averages and the appropriate quantile of the Wilcoxon Signed Rank Test Statistic. Note that T_{max} will not be ln-transformed for these analyses.

8.7 Preliminary Data and Interim Analysis

Celerion Biometrics will not perform preliminary or interim analyses.

9. SUBJECTIVE EFFECTS ASSESSMENTS

9.1 Urge to Smoke (UTS)

The Urge to Smoke (visual analogue scale (VAS)) questionnaire will be completed at Time 0 (pre-product use) and at 4, 8, 15, 45, 60, 120, and 240 minutes relative to the start of controlled product use on Days 1, 2, 3, 4, and 5.

Ratings of the subjects' 'Right now, how much would you like to smoke a cigarette?' recorded on a 100 mm VAS scale ranging from "Not at all" (0) to "A great deal" (100) will be reported.

The following parameters will be calculated for the urge to smoke assessments:

E_{max}	The maximum change from baseline VAS score (VAS_{preuse} - $VAS_{postuse}$).
TE_{max}	Time of the E_{max}. If the maximum value occurs at more than one time point, TE_{max} will be defined as the first time point with this value.
$AUEC_{0-240}$	The area under the change from baseline VAS score versus time curve from time 0 to 240 minutes.

Baseline (VAS_{preuse}) will be the VAS result closest and prior to product use for the respective product. Responses, change from baseline, and derived parameters will be listed by subject and summarised by product, by sex and overall using descriptive statistics (n, mean, SD, CV%, SEM, minimum, Q1, median, Q3, maximum, and 95% CI.)

A linear mixed model for ANOVA will be performed on the urge to smoke parameters (no data transformation). The model will include sequence, product, and study period as fixed effects and subject-nested-within-sequence as a random effect. Sequence will be tested using subject-nested-within-sequence as the error term for informational purposes. LSMs and 95% CIs will be provided for E_{max} and $AUCEC_{0-240}$ by study product. LSM differences, 95% CIs of LSM differences, and p-values will be provided for the study product comparisons in E_{max} and $AUCEC_{0-240}$. The same comparisons from PK analysis detailed above will be used.

The ANOVA analysis will be performed using the same SAS® code as outlined in the Statistical Analysis of Pharmacokinetic Parameters section above.

9.2 Product Evaluation Scale (PES)

The Product Evaluation Scale questionnaire will be completed at 240 minutes for each product use on Days 1, 2, 3, 4, and 5.

Product Evaluation will be considered as a 7-point scale (1 = not at all, 2 = very little, 3 = a little, 4 = moderately, 5 = a lot, 6 = quite a lot, and 7 = extremely). Responses will be presented as the following factor scores:

a) Satisfaction: average of the response scores from questions 1, 2, 3, and 12;

b) Psychological reward: average of the response scores from questions 4 to 8;

c) Aversion: average of the response scores from questions 9, 10, 16, and 18;

d) Relief: average of items 11, 13, 14, 15, and reversed for item 20 (i.e., not at all = 7, extremely = 1);

e) Items 17, 19, 21 will be summarised as individual item scores.

Descriptive statistics of the subscales will be provided by study product, by sex and overall. Individual responses will be listed by subject.

9.3 Intent to Use (ITU)

The Intent to Use (VAS) questionnaire will be completed at 240 minutes for each product use on Days 1, 2, 3, 4, and 5.

Ratings of the subjects' 'If available, how likely are you to buy your assigned study product in the future?' recorded on a 100 mm VAS scale ranging from "Not at all" (0) to "Extremely" (100) will be reported.

In addition, responses to the ITU 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.

Descriptive statistics of the VAS raw score and bipolar score will be provided by study product. Individual responses will be listed by subject. A frequency count table will be presented for the categories of the bipolar scores.

10. PUFF TOPOGRAPHY

On Days 1 through 5, puff topography measurements will be performed for a 2 hour period during the last 2 hours of the 4-hour *ad libitum* product use session.

The following per-puff topography parameters will be recorded using Sodim Smoking Puff Analyzer Mobile (SPA-M) devices:

- Puff count
- Puff duration
- Puff volume
- Peak puff flow rate

- Average puff flow rate
- Inter-puff interval

The following per-product topography parameters will then be derived:

- Total number of puffs
- Total puff duration
- Average puff duration
- Total puff volume
- Average puff volume
- Average peak flow rate
- Average flow rate
- Total inter-puff interval
- Average inter-puff interval

Topography parameters will be listed by subject and per-product parameters will be summarised by study product, overall and by sex using descriptive statistics (n, mean, SD, CV%, SEM, minimum, Q1, median, Q3, maximum, and 95% CI).

A linear mixed model for ANOVA will be performed on the per-product topography parameters (no data transformation). The model will include sequence, product, and study period as fixed effects and subject-nested-within-sequence as a random effect. Sequence will be tested using subject-nested-within-sequence as the error term for informational purposes. LSMs and 95% CIs will be provided for the parameters by study product. LSM differences, 95% CIs of LSM differences, and p-values will be provided for the study product comparisons in per-product topography parameters. The same comparisons from PK analysis detailed above will be used.

The ANOVA analysis will be performed using the same SAS® code as outlined in the Statistical Analysis of Pharmacokinetic Parameters section above.

11. PRODUCT USE BEHAVIOUR

On Days 1 through 5, subjects will use their randomised product (same product as the morning session) *ad libitum* for 4 hours starting after the 4-hour PK blood draw.

The number of cigarettes smoked, will be documented from Check-in until beginning of smoking abstinence (Day -1, until at least 12 hours prior to the start of morning controlled

product use on Day 1; Days 1 through 5, 8 hours post morning controlled use session IP start until at least 12 hours prior to the start of morning controlled product use scheduled on the following day). The number of cigarettes smoked and the number of HTP/HHP sticks used will be documented during each 4-hour *ad libitum* product use session (Days 1 through 5). The number of inhalations and reasons for missed puffs will also be documented.

The number of HTP/HHP sticks used (*ad libitum* product use session), the number of OBCCs smoked (Days -1 through 5), and the number of puffs (morning controlled product use session) will be listed by subject and summarised by study product, product use session, using descriptive statistics.

Incidence of device malfunction(s) will also be tabulated.

12. SAFETY

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

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

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

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

Baseline will be the result closest and prior to the first product use on Day 1 unless otherwise stated. Summaries for post-baseline time points will not include rechecks, unscheduled, or early termination measurements.

Tables summarising safety data by assessment time point will only include summaries for baseline and post-baseline time points.

12.1 Subject Disposition

Subjects will be summarised by the number and percent of subjects enrolled, randomised, completed the study, and discontinued the study (with discontinuation reasons) by randomised product sequence and overall.

Individual product use status (i.e., which products were administered to each subject) will also be provided along with their study completion status and date of study completion or

discontinuation. The number of subjects with product use for each study product (i.e. A, B, C, D, and E) will also be presented.

12.2 Protocol Deviations

Protocol deviations are captured by the clinical site and provided in the CSR in a similar format to that provided by the clinical site. Protocol deviations are not edited or processed in SAS®.

12.3 Demographics

Descriptive statistics will be calculated for continuous variables (age, body mass index, height, and weight) by randomised product sequence and overall. Age will be approximated by subtracting the year of birth from the year of informed consent. If year of informed consent – year of birth is one more than the protocol maximum age (65) then the age approximation will be year of informed consent – year of birth – 1. Descriptive statistics for body mass index, height, and weight will be calculated using screening measurements.

Frequency counts will be provided for categorical variables (sex, race, and ethnicity) for each randomised product sequence and overall.

12.4 Smoking History and Usual Brand Attributes

Smoking history and usual brand attributes will be summarised with descriptive statistics for continuous variables by randomised product sequence and overall. Frequency counts will be presented for categorical variables for each randomised product sequence and overall. The continuous variables will include number of cigarettes smoked per day, number of years of cigarettes smoked, and the categorical variables will include usual cigarette brand, brand style, cigarette length and flavour. Subjects that only enrolled in the product trial and dropped prior to randomisation will be summarised separately.

Number of years smoked is calculated as stop year (year portion of Stop Date) – start year (year portion of Start Date). Where stop date is missing (i.e. smoking is ongoing), stop year is equal year of informed consent.

12.5 Adverse Events

All AEs occurring during this clinical trial will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 26.1.

All AEs captured in the database will be listed in a by-subject data listing including verbatim term, coded term, product, onset date/time, resolution date/time, frequency, severity, relationship to study product, and action; however, only product use-emergent AEs (PUEAEs) will be summarised.

PUEAE is defined as an AE that is starting or worsening at the time of or after the first study product use. Each PUEAE will be attributed to a product based on the onset date and time of

the AE compared to that of the respective product administration date and time. An AE that occurs between products will be considered product use-emergent to the last product administered prior to onset of the AE. AEs occurring prior to the first product use episode on Day 1 but after the product trial has started on Day -1 will be attributed to the product trial.

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

PUEAEs will be tabulated by System Organ Class (SOC) and Preferred Term. Summary tables will include the number of subjects reporting the PUEAE and as a percent of the number of subjects that used study product by product and overall. The number of PUEAEs will be tabulated in a similar manner. A table, which summarises the number of PUEAEs by Preferred Term, severity, and relationship to study product, will also be included.

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

12.6 Clinical Laboratory Tests (Chemistry, Hematology, and Urinalysis)

Clinical laboratory tests will be measured at the following time points:

Clinical Laboratory Panels	Time Point		
	Period	CRF/Listing Day and Hour	Table
Chemistry, Haematology, Urinalysis	Screening		NA
	Check-in	Day -1 Hour -22.50	Baseline
	5	Day 1 Hour 8.67	End of Study

Time points in the CRF/Listing column are approximated/based on the blank CRF and it should be noted that the data listings will reflect the data found in the final subject CRFs.
If applicable, an early termination assessment will be performed.
NA = Not applicable (individual result(s) may be required for baseline)

Clinical laboratory results will be presented in standard international (SI) units. Out-of-reference range flags will be recorded as follows: high (H) and low (L) for numerical results and did-not-match (*) for categorical results.

Out-of-reference range values and corresponding recheck results will be listed.

For all numeric laboratory values, descriptive statistics will be presented for each laboratory test by assessment time point. Change from baseline will be summarised in a similar manner. For all numeric laboratory tests, the mean value calculated for each assessment time point will be compared to the reference range and flagged if outside of the reference range (* if

above the reference range and ^ if below the reference range). In the event there is more than one reference range for a laboratory test, the comparison will be made against the lowest of the lower ranges and the highest of the higher ranges.

12.7 Vital Signs

Vital signs will be measured at the following time points:

Parameter	Time Point		
	Period	CRF/Listing Day and Hour	Table
Blood Pressure, Pulse, Respiration, Temperature	Screening		NA
	Check-in	Day -1 Hour -22.00	NA
	1	Day 1 Hour -0.50	Baseline
	2	Day 1 Hour -0.50	Day 2 Preuse
	3	Day 1 Hour -0.50	Day 3 Preuse
	4	Day 1 Hour -0.50	Day 4 Preuse
	5	Day 1 Hour -0.50	Day 5 Preuse
Blood Pressure, Pulse	5	Day 1 Hour 8.50	End of Study

Time points in the CRF/Listing column are approximated/based on the blank CRF and it should be noted that the data listing will reflect the data found in the final subject CRFs.
If applicable, an early termination assessment will be performed.
NA = Not applicable (individual result(s) may be required for baseline)

Descriptive statistics will be presented for vital signs measurements by assessment time point. Change from baseline will be summarised in a similar manner.

12.8 Electrocardiogram

ECGs will be measured at the following time points:

Parameter	Time Point		
	Period	CRF/Listing Day and Hour	Table
HR, RR, PR, QRS, QT, QTcF	Screening		NA
	Check-in	Day -1 Hour -22.25	Baseline
	5	Day 1 Hour 8.33	End of Study

Time points in the CRF/Listing column are approximated/based on the blank CRF and it should be noted that the data listing will reflect the data found in the final subject CRFs.
If applicable, an early termination assessment will be performed.
NA = Not applicable (individual result(s) may be required for baseline)

Descriptive statistics will be presented for ECG measurements by assessment time point. Change from baseline will be summarised in a similar manner.

All ECG data will be listed by subject where QTc values > 450 msec and increase from baseline > 30 msec will be flagged.

12.9 Prior and Concomitant Medications

Prior and concomitant medications recorded during the study will be coded with the World Health Organization (WHO) Drug Dictionary Version 01-Sep-2023_b3 and listed.

12.10 Oral and Physical Examination

Abnormal physical examination findings will be reported as medical history or AEs. All data found in the CRF will be listed.

12.11 Exhaled Carbon Monoxide

Exhaled Carbon Monoxide (CO) levels will be measured using a Bedfont Micro+ Smokerlyzer or similar device, at Screening and at Check-in. Exhaled CO data will be listed by subject and assessment timepoint.

12.12 Device Malfunction

Incidence of device malfunction(s) will be listed by subject and tabulated by product.

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, FIGURES, AND LISTINGS

Summary tables, figures, and listings are numbered following the International Council 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, figures, and listings will be generated using SAS® Version 9.4 or higher, as appropriate.

14.1 Section 14 Tables and Figures

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

Number	Title	Shell
Table 14.1.1	Disposition Summary (Safety Population)	CDS
Table 14.1.2	Subject Product Use Status and Study Disposition (Safety Population)	SDS
Table 14.1.3	Demographic Summary (Safety Population)	CDEM

Number	Title	Shell
Table 14.1.4	Smoking History and Usual Brand Attributes Summary (Safety Population)	CSHUB

14.2 Pharmacokinetic, Subjective Effects, Topography, and Product Use Behaviour Summary Tables and Figures

14.2.1 Pharmacokinetic Tables – Plasma Nicotine

Number	Title	Shell
Table 14.2.1.1	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPConc1
Table 14.2.1.2	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPConc1
Table 14.2.1.3	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPConc1
Table 14.2.1.4	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPConc1
Table 14.2.1.5	Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of Subject's OBCC (Outcomes Population)	CPConc1
Table 14.2.1.6	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPConc1
Table 14.2.1.7	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPConc1
Table 14.2.1.8	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPConc1
Table 14.2.1.9	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPConc1

Table 14.2.1.10	Baseline-Adjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of Subject's OBCC (Outcomes Population)	CPConc1
Table 14.2.1.11	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPPar1
Table 14.2.1.12	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPPar1
Table 14.2.1.13	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPPar1
Table 14.2.1.14	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Controlled Product Use of [redacted] Stick (Outcomes Population)	CPPar1
Table 14.2.1.15	Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Controlled Product Use of Subject's OBCC (Outcomes Population)	CPPar1
Table 14.2.1.16	Statistical Summary of Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Cmax and AUCt Following Controlled Product Use (Outcomes Population)	CPStatSum
Table 14.2.1.17	Statistical Comparison of Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Cmax and AUCt Following Controlled Product Use (Outcomes Population)	CPStat1
Table 14.2.1.18	Nonparametric Statistical Comparison of Plasma Nicotine Pharmacokinetic Parameter Tmax Following Controlled Product Use (Outcomes Population)	CPStat2

14.2.2 Pharmacokinetic Figures – Plasma Nicotine

Number	Title	Shell
Figure 14.2.2.1	Arithmetic Mean (SD) Unadjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Linear Scale) (Outcomes Population)	PFPConc1
Figure 14.2.2.2	Arithmetic Mean Unadjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Linear Scale) (Outcomes Population)	PFPConc2
Figure 14.2.2.3	Arithmetic Mean Unadjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Semi-Log Scale) (Outcomes Population)	PFPConc3
Figure 14.2.2.4	Arithmetic Mean (SD) Baseline-Adjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Linear Scale) (Outcomes Population)	PFPConc1
Figure 14.2.2.5	Arithmetic Mean Baseline-Adjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Linear Scale) (Outcomes Population)	PFPConc2
Figure 14.2.2.6	Arithmetic Mean Baseline-Adjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Semi-Log Scale) (Outcomes Population)	PFPConc3

14.2.3 Subjective Effects Tables

14.2.3.1 Urge to Smoke Tables

Number	Title	Shell
Table 14.2.3.1.1	Summary of Urge to Smoke VAS Scores Following Controlled Product Use by Sex and Product (Outcomes Population)	UTSS
Table 14.2.3.1.2	Summary of Urge to Smoke VAS Score Differences from Pre-use to Following Controlled Product Use by Sex and Product (Outcomes Population)	UTSS
Table 14.2.3.1.3	Summary of Urge to Smoke VAS Parameters Following Controlled Product Use by Sex and Product (Outcomes Population)	UTSP
Table 14.2.3.1.4	Statistical Summary of Urge to Smoke VAS Parameters Emax and AUEC0-240 Following Controlled Product Use (Outcomes Population)	SUTSP

Number	Title	Shell
Table 14.2.3.1.5	Statistical Comparison of Urge to Smoke VAS Parameters Emax and AUEC0-240 Following Controlled Product Use (Outcomes Population)	SCUTS

14.2.3.2 PES Subscales Tables

Number	Title	Shell
Table 14.2.3.2.1	Summary of PES Factor Scores Following Controlled Product Use by Product (Outcomes Population)	PESS

14.2.3.3 Intent to Use Tables

Number	Title	Shell
Table 14.2.3.3.1	Summary of Intent to Use VAS Raw Scores Following Controlled Product Use by Sex and Product (Outcomes Population)	ITUS
Table 14.2.3.3.2	Summary of Intent to Use VAS Bipolar Scores Following Controlled Product Use by Sex and Product (Outcomes Population)	ITUS
Table 14.2.3.3.3	Frequency of Intent to Use VAS Bipolar Scores in Each Category Following Controlled Product Use by Sex and Product (Outcomes Population)	ITUF

14.2.4 Puff Topography Tables

Number	Title	Shell
Table 14.2.4.1	Summary of Per-Product Puff Topography Parameters by Sex and Product (Outcomes Population)	PUFS
Table 14.2.4.2	Statistical Summary of Per-Product Puff Topography Parameters Following Ad Libitum Product Use (Outcomes Population)	SPUFS
Table 14.2.4.3	Statistical Comparison of Per-Product Puff Topography Parameters Following Ad Libitum Product Use (Outcomes Population)	SCPUF

14.2.5 Product Use Behaviour Tables

Number	Title	Shell
Table 14.2.5.1	Summary of Total Number of HTP/HHP Sticks Used During the Ad Libitum Product Use by Sex and Product (Outcomes Population)	PUBS
Table 14.2.5.2	Summary of Total Number of OBCCs Smoked on Days -1 through 5 During the Ad Libitum Product Use by Sex and Study Period (Outcomes Population)	SPUBS
Table 14.2.5.3	Summary of Total Number of Puffs During the Controlled Product Use by Sex and Product (Outcomes Population)	SCPUB

14.3 Safety Data Summary Tables

14.3.1 Displays of Adverse Events

Number	Title	Shell
Table 14.3.1.1	Product Use-Emergent Adverse Event Frequency by Product – Number of Subjects Reporting the Event (% of Subjects Who Received Study Product) (Safety Population)	CAES
Table 14.3.1.2	Product Use-Emergent Adverse Event Frequency by Product – Number of Adverse Events (% of Total Adverse Events) (Safety Population)	CAEE
Table 14.3.1.3	Product Use-Emergent Adverse Event Frequency by Product, Severity, and Relationship to Study Product – Number of Adverse Events (Safety Population)	CAESR

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Number	Title	Shell
Table 14.3.2.1	Serious Adverse Events (Safety Population)	16.2.7

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

14.3.4 Abnormal Laboratory Value Listing (each subject)

Number	Title	Shell
Table 14.3.4.1	Out-of-Range Values and Recheck Results – Chemistry (Safety Population)	CLBO
Table 14.3.4.2	Out-of-Range Values and Recheck Results – Haematology (Safety Population)	
Table 14.3.4.3	Out-of-Range Values and Recheck Results – Urinalysis (Safety Population)	

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

Number	Title	Shell
Table 14.3.5.1	Clinical Laboratory Summary and Change From Baseline – Chemistry (Safety Population)	CLBD
Table 14.3.5.2	Clinical Laboratory Summary and Change From Baseline – Haematology (Safety Population)	CLBD
Table 14.3.5.3	Clinical Laboratory Summary and Change From Baseline – Urinalysis (Safety Population)	CLBD
Table 14.3.5.4	Vital Sign Summary and Change From Baseline (Safety Population)	CVS
Table 14.3.5.5	12-Lead Electrocardiogram Summary and Change From Baseline (Safety Population)	CEG
Table 14.3.5.6	Incidence of Device Malfunction by Product (Safety Population)	CDM

14.2 Section 16 Data Listings

Note: Hepatitis and HIV results that are provided by the clinical laboratory will not be presented in subject data listings and will not be included in any database transfer. All data will be presented as outline in the CRF (i.e., time point information will be consistent with the CRF data).

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

16.1.9 Statistical Methods

Number	Title
Appendix 16.1.9.1	Statistical Analysis Plan
Appendix 16.1.9.2	Statistical Methods

16.1.10 Clinical Laboratory Reference Ranges

Number	Title
Appendix 16.1.10	Clinical Laboratory Reference Ranges

16.2 Subject Data Listings

16.2.1 Subject Discontinuation

Number	Title
Appendix 16.2.1.1	Subject Disposition (Safety Population)

16.2.2 Protocol Deviations

Number	Title
Appendix 16.2.2	Protocol Deviations

16.2.3 Subjects Excluded from Pharmacokinetic, Subjective Effects, Topography, and Product Use Behaviour Analysis

Number	Title
Appendix 16.2.3	Subjects Excluded from Pharmacokinetic, Subjective Effects, Topography, and Product Use Behaviour Analysis

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

16.2.4 Demographic Data

Number	Title
Appendix 16.2.4.1	Demographics (Safety Population)
Appendix 16.2.4.2	Oral/Physical Examination (I of II) (Safety Population)

Number	Title
Appendix 16.2.4.3	Oral/Physical Examination (II of II) (Safety Population)
Appendix 16.2.4.4	Oral/Physical Examination Descriptions (Safety Population)
Appendix 16.2.4.5	Medical History (Safety Population)
Appendix 16.2.4.6	Smoking History and Usual Brand Attributes (Safety Population)

16.2.5 Compliance and/or Product Use and Nicotine Concentration Data

Number	Title
Appendix 16.2.5.1	Subject Eligibility (Safety Population)
Appendix 16.2.5.2	Product Trial (Safety Population)
Appendix 16.2.5.2	Product Description
Appendix 16.2.5.3	Controlled Product Use Administration Times (Safety Population)
Appendix 16.2.5.4	Ad Libitum Product Use Administration Times (Safety Population)
Appendix 16.2.5.5	Ad Libitum Smoking (Safety Population)
Appendix 16.2.5.6	Prior and Concomitant Medications (Safety Population)
Appendix 16.2.5.7	Pharmacokinetic Blood Draw Times and Concentration Data (Safety Population)

16.2.6 Individual Pharmacokinetic, Subjective Measures, Topography, and Product Use Behaviour Data

Number	Title	Shell
Appendix 16.2.6.1	Individual Unadjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Linear and Semi-Log Scales) (Outcomes Population)	PFPConc5
Appendix 16.2.6.2	Individual Baseline-Adjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Linear and Semi-Log Scales) (Outcomes Population	PFPConc5
Appendix 16.2.6.3	Intervals (Minutes) Used for Determination of Baseline-Adjusted Plasma Nicotine Kel Values (Outcomes Population)	CPKel2
Appendix 16.2.6.4	Urge to Smoke (Safety Population)	
Appendix 16.2.6.5	Urge to Smoke Parameters (Safety Population)	

Number	Title	Shell
Appendix 16.2.6.6	Product Evaluation Scale Collection (Safety Population)	
Appendix 16.2.6.7	Product Evaluation Scale Item Score (Safety Population)	
Appendix 16.2.6.8	Product Evaluation Scale Factor Score (Safety Population)	
Appendix 16.2.6.9	Intent to Use (Safety Population)	
Appendix 16.2.6.10	Puff Topography (Safety Population)	
Appendix 16.2.6.11	Puff Topography Parameters – Per-Puff (Safety Population)	
Appendix 16.2.6.12	Puff Topography Parameters – Per-Product (Safety Population)	
Appendix 16.2.6.13	Product Use Behaviour During Ad Libitum Product Use (Safety Population)	

16.2.7 Adverse Events Listings

Number	Title
Appendix 16.2.7.1	Adverse Events (Safety Population)
Appendix 16.2.7.2	Details for Serious Adverse Events (Safety Population) *This listing will be removed if no serious adverse events are reported.*
Appendix 16.2.7.3	Device Malfunction (Safety Population)

16.2.8 Clinical Laboratory Reports

Number	Title
Appendix 16.2.8.1	Clinical Laboratory Report - Chemistry (Safety Population)
Appendix 16.2.8.2	Clinical Laboratory Report - Haematology (Safety Population)
Appendix 16.2.8.3	Clinical Laboratory Report - Urinalysis (Safety Population)
Appendix 16.2.8.4	Clinical Laboratory Report - Urine Drug Screening (Safety Population)
Appendix 16.2.8.5	Clinical Laboratory Report - Virology (Safety Population)
Appendix 16.2.8.6	Carbon Monoxide Breath Test (Safety Population)

Number	Title
Appendix 16.2.8.7	Vital Signs (Safety Population)
Appendix 16.2.8.8	12-Lead Electrocardiogram (Safety Population)

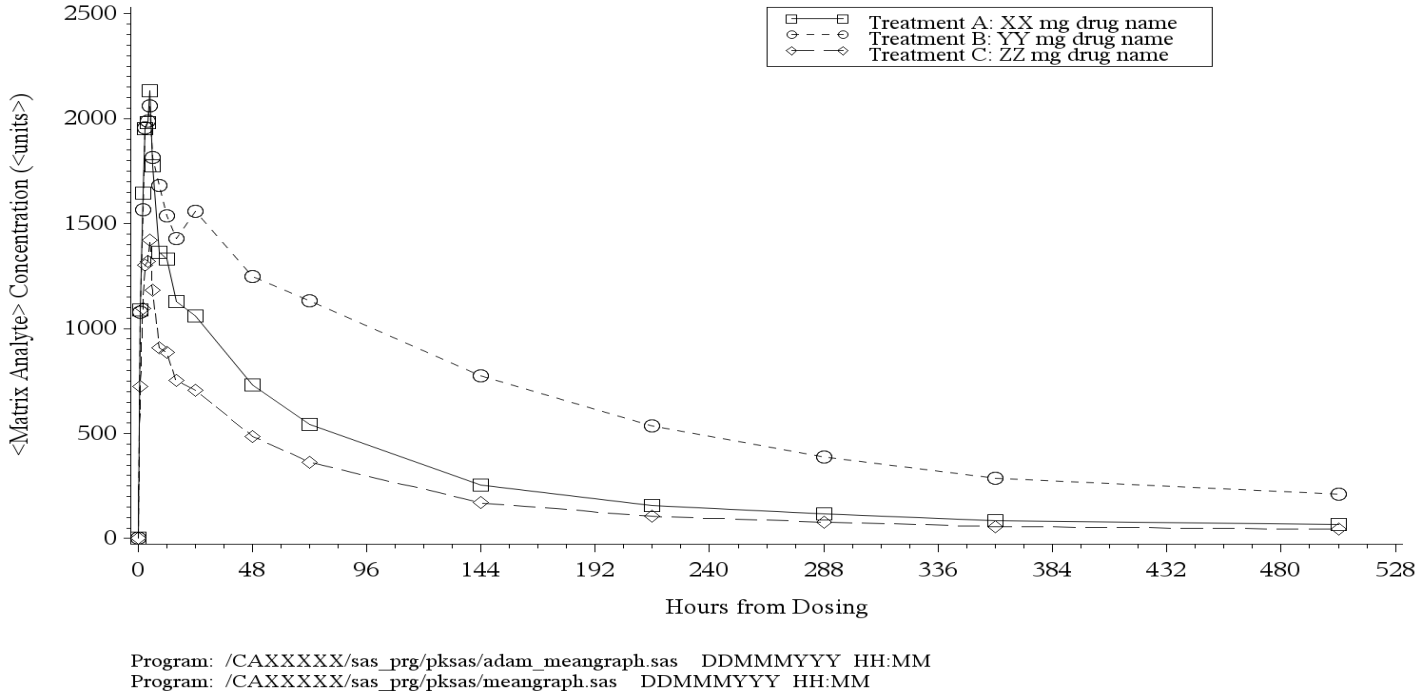
15. TABLE, FIGURE, AND LISTING SHELLS

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, post-text tables will be presented in Courier New font size 9. Figures will be generated as RTF and tables and listings will be generated as SAS® LST format and converted to MS Word for inclusion in the CSR. In compliance with Celerion PGs/SOPs, SAS® outputs will not be manually edited. Tables and figures will be generated from ADaM datasets created in accordance with CDISC guidance (ADaM Model 2.1 and ADaM implementation Guide 1.1).

15.1 Figure Shells

Internal template: Figure PFPConc2

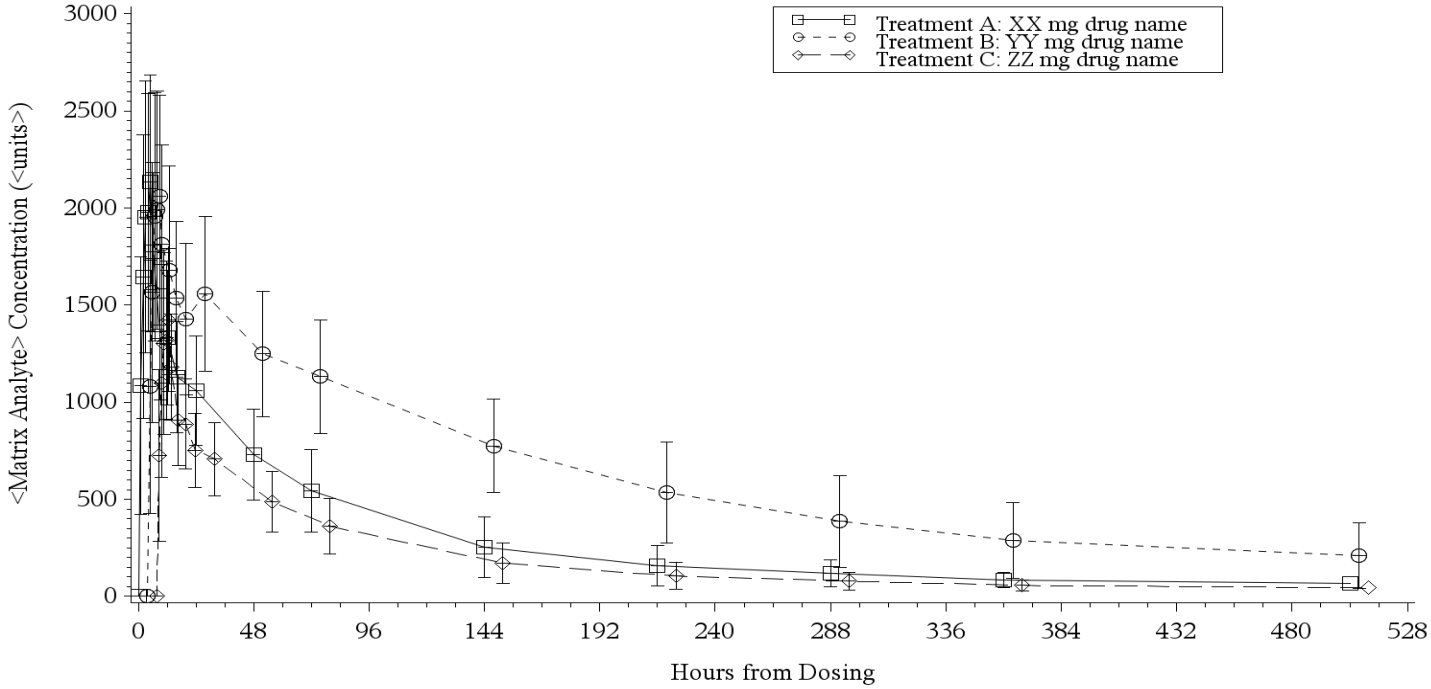
Figure 14.2.2.2 Mean Unadjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Linear Scale) (Outcomes Population)



Programming note : the legend will present the 5 products ‘Product X: Product Description’
The x-axis title will be: ‘Time From Start of Product Use (min)’.

Internal template: Figure PFPConc1

Figure 14.2.2.1 Mean (SD) Unadjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Linear Scale) (Outcomes Population)

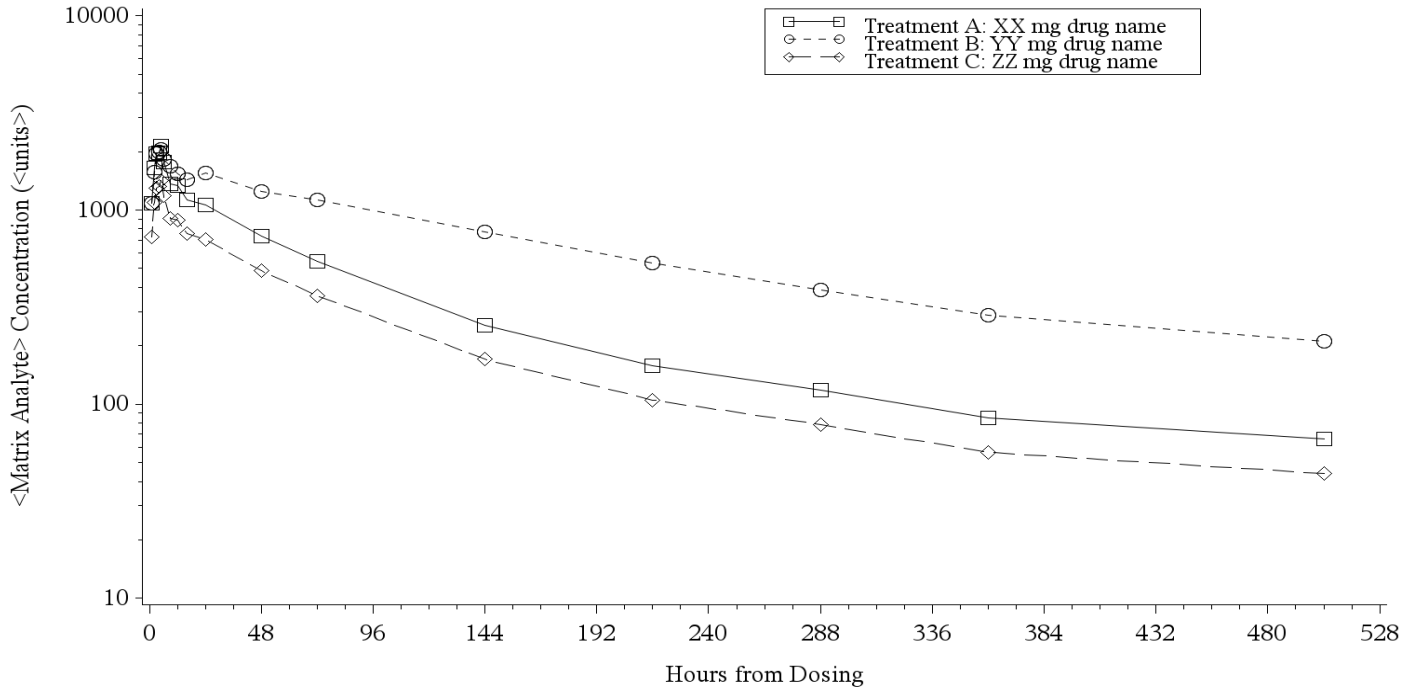


Treatments B and C are shifted to the right for ease of reading
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYY HH:MM

Programming note : the legend will present the 5 products 'Product X: Product Description'
The x-axis title will be: 'Time From Start of Product Use (min)'.

Internal template: Figure PFPConc3

Figure 14.2.2.3 Mean Unadjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Semi-Log Scale) (Outcomes Population)



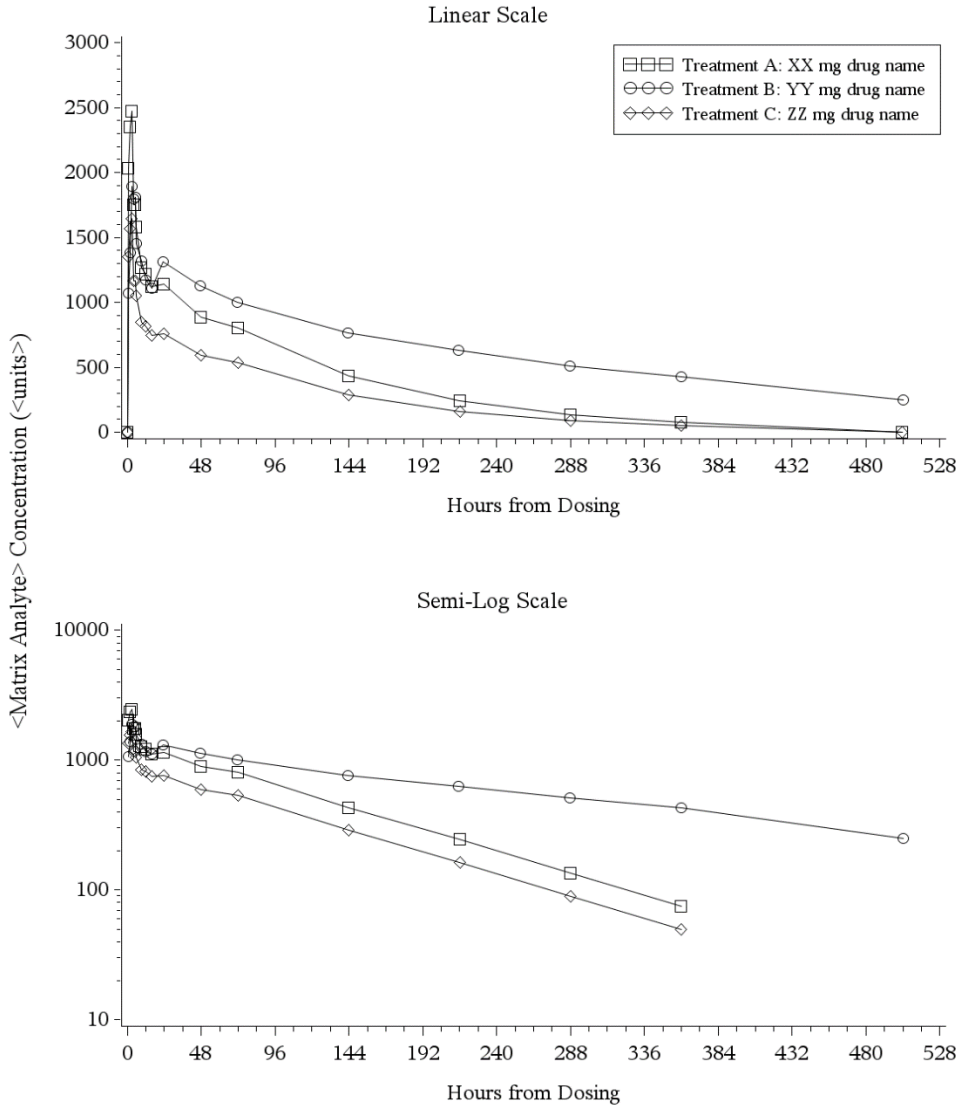
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYY HH:MM

Programming note : the legend will present the 5 products 'Time From Start of Product Use (min)'
The x-axis title will be: 'Time From Start of Product Use (min)'

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

Appendix 16.2.6.1.1

Individual Unadjusted Plasma Nicotine Concentrations Versus Time Following Controlled Product Use (Linear and Semi-Log Scales) (Outcomes Population)



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

Programming note : the legend will present the 4 products 'Time From Start of Product Use (min)'
The x-axis title will be: 'Time From Start of Product Use (min)'

15.2 Section 14 Summary Tables Shells

Table CDS Disposition Summary (Safety Population)

		Randomized Product Sequence					
Category	Product Trial*	ABECD	BCADE	CDBEA	DECAB	EADBC	Overall#
Enrolled	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)
Randomised	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)
Completed Study	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)
Discontinued From Study	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
<Reason>	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

Product A: Pulze 2.0 device with iD Balanced Blue stick
Product B: Pulze 2.0 device with iD Rich Bronze stick
Product C: Pulze 2.0 device with iSenzia Forest Berry stick
Product D: Pulze 2.0 device with iSenzia Summer Watermelon stick
Product E: Subject's own brand combustible cigarette (OBCC)
*Only includes subjects that enrolled in the Product Trial period and dropped prior to randomisation.
#Subjects who only participated in the Product Trial period are not included in the Overall summary.

Source: ADaM.ADSL
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1programname2022Q1.sas DDMMMYYYY HH:MM

Table SDS Subject Dosing Status and Study Disposition (Safety Population)

Subject Number	Randomised Product Sequence	Product Trial	Product Administered					Study Completion	
			A	B	C	D	E	Status	Date
00X	XXXXX	Yes	Yes	No	No	No	No	Discontinued From Study: <Reason>	DDMONYYYY
00X	XXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMONYYYY
00X	XXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMONYYYY
00X	XXXXX	Yes	Yes	Yes	Yes	Yes	Yes	Completed Study	DDMONYYYY
00X^		Yes	No	No	No	No	No	Dropped Prior to Randomisation	DDMMMYYYY
			XX	XX	XX	XX	XX		

Programmer Note: Please refer to Section 7 for the product description.

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
^Subject enrolled in the Product Trial and dropped prior to randomisation.
Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CDEM Demographic Summary (Safety Population)

			Randomised Product Sequence					
Trait	Category/Statistic	Product Trial*	ABECD	BCADE	CDBEA	DECAB	EADBC	Overall#
Sex	Male	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Race	Asian	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Black or African American	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	White	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Ethnicity	Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Not Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Age (yr)	n	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX	XX

Programmer note: Include Body Mass Index (kg/m^2), Height (cm), and Weight (kg).

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
*Only includes subjects that enrolled in the Product Trial period and dropped prior to randomisation.
#Subjects who only participated in the Product Trial period are not included in the Overall summary.

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CSHUB Smoking History and Usual Brand Attributes Summary (Safety Population)

			Randomised Product Sequence					
Trait	Category/Statistic	Product Trial*	ABECD	BCADE	CDBEA	DECAB	EADBC	Overall#
Brand	XXXXXXXXXX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	XXXXXXXXXX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Brand Style	XXXXXXXXXX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	XXXXXXXXXX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Flavour	XXXXXXXXXX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	XXXXXXXXXX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Cigarette Length	XXXXXXXXXX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	XXXXXXXXXX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Number of Cigarettes Smoked (per day)	n	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX	XX

Programmer note: Include Number of Years Smoking Cigarettes.

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
*Only includes subjects that enrolled in the Product Trial period and dropped prior to randomisation.
#Subjects who only participated in the Product Trial period are not included in the Overall summary.

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Note: Plasma Nicotine Concentration Tables (CPCONC1) will have the following format:

Page 1 of X

Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Product Use of iD Balanced Blue Stick
(Outcomes Population)

Subject Number	Product Sequence	Study Period	Sex	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
XX	XXXXXX	X	XX	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
n			Male**	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

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

Programming Notes: 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: < For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 1/2 LLOQ.>

**There will also be summary statistics for female and overall
The following footnote will only be included in the baseline-adjusted plasma nicotine tables: < Prior to baseline adjustment, concentration values that are below the limit of quantitation (BLQ) of <XX> were set to 1/2 the LLOQ.
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 <xx> ng/mL) for the calculation of the descriptive statistics.>
For baseline-adjusted table, Pre-use will be replaced with 0.
Concentrations will be presented to same precision as in bioanalytical data.
Summary statistics presentation with respect to the precision of the bioanalytical data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal.
PK Time points are: pre-use and 2, 4, 6, 8, 10, 15, 30, 45, 60, 120 and 240 minutes following the start of product use.

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

Note: Plasma Nicotine Pharmacokinetic Parameter Tables (CPPAR1) will be in the following format:

Page 1 of X

Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Controlled Product Use of iD Balanced Blue Stick
(Outcomes Population)

Subject Number	Product Sequence	Study Period	Sex	Parameters: Parm 1 <unit>	Parm 2 <unit>	Parm 3 <unit>	Parm 4 <unit>	Parm X <unit>
XX	XXXXXX	X	XXXX	X.XX	X.XX	X.XX	X.XX	X.XX
XX	XXXXXX	X	XXXX	X.XX	X.XX	X.XX	X.XX	X.XX
XX	XXXXXX	X	XXXX	X.XX	X.XX	X.XX	X.XX	X.XX
n	Male**			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
Geom. Mean				X.X	X.X	X.X	X.X	X.X
Geom. CV%				XX.X	XX.X	XX.X	XX.X	XX.X

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 summary statistics for female and overall in the baseline-adjusted PK tables.
The plasma nicotine PK Parameters are AUC0-90 (ng*min/mL), AUC0-240 (ng*min/mL), AUCt (ng*min/mL), AUC0-inf (ng*min/mL), AUC%extrap (%), Cmax (ng/mL), Clast (ng/mL), Tmax (min), T½ (min), and kel (1/min). Geometric mean and geometric CV% will be calculated only for Cmax amd AUCs.

Descriptive statistics precision is specified in Section 8.5.

Note: Statistical summary of plasma nicotine PK parameters by product (CPStatSum) will have the following format:

Page 1 of X

Statistical Summary of Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Cmax and AUCt Following Controlled Product Use (Outcomes Population)

Product	Parameter	n	Geometric LS Mean	95% Confidence Interval
A	Cmax	x	X.XX	XX.XX – XXX.XX
	AUCt	x	X.XX	XX.XX – XXX.XX
B	Cmax	x	X.XX	XX.XX – XXX.XX
	AUCt	x	X.XX	XX.XX – XXX.XX

n = Number of observations used in the analysis
Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >

The mixed model includes sequence, product, and study period as fixed effects and subject-nested-within-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.

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 tables. 95% confidence intervals will be presented to 2 decimal places.
The table will additionally present Products C, D, and E.

Note: Statistical comparison table of PK parameters (CPStat1) will have the following format:

Page 1 of X

Statistical Comparison of Baseline-Adjusted Plasma Nicotine Pharmacokinetic Parameters Cmax and AUCt
Following Controlled Product Use (Outcomes Population)

Comparison	Parameter	Geometric LS Means: Test (n)	Geometric LS Means: Reference (n)	% Geometric LS Mean Ratio (Test/Reference)	95% Confidence Interval	p-value
Product A vs Product E	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	AUCt	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
	AUCt	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
	AUCt	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
	AUCt	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Test = The first product in the comparison
Reference = The second product in the comparison
n = Number of observation used in the analysis
Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >

The mixed model includes sequence, product, and study period as fixed effects and subject-nested-within-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)

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 95% confidence intervals will be presented to 2 decimal places; p-value will be presented to 4 decimals.

The table should include all the comparisons of interest listed in Section 8.6.

Note: **Statistical comparison table of PK parameter Tmax (CPStat2) will have the following format:**

Page X of X

Nonparametric Statistical Comparison of Plasma Nicotine Pharmacokinetic Parameter Tmax Following Controlled Product Use (Outcomes Population)

Comparison	Difference <X> - <Y> Median	95% Confidence Interval	p-value
Product A vs Product E	X.XX	-X.XXXX - X.XXXX	X.XXXX
Product B vs Product E	X.XX	-X.XXXX - X.XXXX	X.XXXX
Product C vs Product E	X.XX	-X.XXXX - X.XXXX	X.XXXX
Product D vs Product E	X.XX	-X.XXXX - X.XXXX	X.XXXX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
The 95% confidence interval is constructed using Walsh Averages and appropriate quantile of the Wilcoxon Signed Rank test statistic.

Notes for Generating the Actual Table:

Presentation of Data:

- Median difference will be presented to 2 decimals or 3 significant figures.
- 95% CI will be presented to 4 decimals.
- p-value will be presented to 4 decimals.

The table should include all the comparisons of interest listed in Section 8.6.

Table UTSS Summary of Urge to Smoke VAS Scores Following Controlled Product Use by Sex and Product (Outcomes Population)

			Sample Times (Minutes)							
Product	Sex	Statistics	Pre-use	4	8	15	45	60	120	240
A	Male	n	X	X	X	X	X	X	X	X
		n missing	X	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX	XX
		Q1	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Q3	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX	XX
		95% 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	X.X-X.X	X.X-X.X

<Similar to above for all products and Sex = Female and Overall>

Programmer note: Table 14.2.3.1.2 will resemble the shell above but the Pre-use column will not be included.

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

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table UTSP Summary of Urge to Smoke VAS Parameters Following Controlled Product Use by Sex and Product (Outcomes Population)

			Product				
Parameter	Sex	Statistics	A	B	C	D	E
Emax	Male	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
		95% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

<Similar to above for Temax, AUCEC0-240 and Sex = Female and Overall>

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

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table SUTSP Statistical Summary of Urge to Smoke VAS Parameters Emax and AUEC0-240 Following Controlled Product Use (Outcomes Population)

Product	Parameter	n	------- LS Mean -------	95% Confidence Interval
A	Emax	X	X.XXX	XX.XX - XXX.XX
	AUCE0-240	X	X.XXX	XX.XX - XXX.XX
B	Emax	X	X.XXX	XX.XX - XXX.XX
	AUCE0-240	X	X.XXX	XX.XX - XXX.XX
C	Emax	X	X.XXX	XX.XX - XXX.XX
	AUCE0-240	X	X.XXX	XX.XX - XXX.XX
D	Emax	X	X.XXX	XX.XX - XXX.XX
	AUCE0-240	X	X.XXX	XX.XX - XXX.XX
E	Emax	X	X.XXX	XX.XX - XXX.XX
	AUCE0-240	X	X.XXX	XX.XX - XXX.XX

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
n = Number of observations used in analysis
The mixed model includes sequence, product, and study period as fixed effects and subject-nested-within-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.

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table SCUTS Statistical Comparison of Urge to Smoke VAS Parameters Emax and AUEC0-240 Following Controlled Product Use
(Outcomes Population)

Comparison	Parameter	LS Mean Test (n)	LS Mean Reference (n)	LS Mean Difference (Test - Reference)	95% Confidence Interval	p-value
Product A vs Product E	Emax	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	AUCE0-240	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
Product B vs Product E	Emax	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	AUCE0-240	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
Product C vs Product E	Emax	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	AUCE0-240	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
Product D vs Product E	Emax	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	AUCE0-240	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
Product A vs Product D	Emax	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	AUCE0-240	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX

Programmer note: The table should include all the comparisons of interest listed in Section 8.6.

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Test = The first product in the comparison; Reference = The second product in the comparison; n = Number of observations used in analysis
The mixed model includes sequence, product, and study period as fixed effects and subject-nested-within-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.

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table PESS Summary of PES Factor Scores Following Controlled Product Use by Sex and Product (Outcomes Population)

			Product				
Subscale	Sex	Statistics	A	B	C	D	E
Satisfaction	Male	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
		95% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

<Similar to above for all subscales and Sex = Female and Overall>

Programmer note: The table should include all the Subscales listed in Section 9.2.

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

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table ITUS Summary of Intent to Use VAS Raw Scores Following Controlled Product Use by Sex and Product (Outcomes Population)

		Product				
Sex	Statistics	A	B	C	D	E
Male	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
	95% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

<Similar to above for Sex = Female and Overall>

Programmer note: Table 14.2.3.3.2 will resemble the shell above with bipolar scores.

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

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table ITUF Frequency of Intent to Use VAS Bipolar Scores in Each Category Following Controlled Product Use by Sex and Product
(Outcomes Population)

Bipolar Score Category	Sex	Product A (N = X)	B (N = X)	C (N = X)	D (N = X)	E (N = X)
-50 to <0	Male	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Overall	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
0	Male	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Overall	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
>0 to 50	Male	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Overall	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

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

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table PUFS Summary of Per-Product Puff Topography Parameters by Sex and Product (Outcomes Population)

			Product				
Parameter (units)	Sex	Statistics	A	B	C	D	E
Total Puff Number	Male	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
		95% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

<Similar to above for all Parameters and Sex = Female and Overall>

Programmer note: The table should include all the per-product parameters listed in Section 10.
Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table SPUFS Statistical Summary of Per-Product Puff Topography Parameters Following Ad Libitum Product Use (Outcomes Population)

Product	Parameter (Units)	n	------- LS Mean -------	95% Confidence Interval
A	Total Puff Number	X	X.XXX	XX.XX - XXX.XX
	Total Puff Duration (s)	X	X.XXX	XX.XX - XXX.XX
	Average Puff Duration (s)	X	X.XXX	XX.XX - XXX.XX
	Total Puff Volume (mL)	X	X.XXX	XX.XX - XXX.XX
	Average Puff Volume (mL)	X	X.XXX	XX.XX - XXX.XX
	Average Peak Flow Rate (mL/s)	X	X.XXX	XX.XX - XXX.XX
	Average Flow Rate (mL/s)	X	X.XXX	XX.XX - XXX.XX
	Total Inter-puff Interval (s)	X	X.XXX	XX.XX - XXX.XX
	Average Inter-puff Interval (s)	X	X.XXX	XX.XX - XXX.XX

<Similar to above for Products>

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
n = Number of observations used in analysis
The mixed model includes sequence, product, and study period as fixed effects and subject-nested-within-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.

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table SCUFS Statistical Comparison of Urge to Smoke VAS Parameters Emax and AUEC0-240 Following Controlled Product Use
(Outcomes Population)

Comparison	Parameter (Units)	LS Mean Test (n)	LS Mean Reference (n)	LS Mean Difference (Test - Reference)	95% Confidence Interval	p-value
Product A vs Product E	Total Puff Number	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	Total Puff Duration (s)	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	Average Puff Duration (s)	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	Total Puff Volume (mL)	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	Average Puff Volume (mL)	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	Average Peak Flow Rate (mL/s)	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	Average Flow Rate (mL/s)	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	Total Inter-puff Interval (s)	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX
	Average Inter-puff Interval (s)	X.XX (X)	X.XX (X)	X.XXX	XX.XX - XXX.XX	X.XXXX

Programmer note: The table should include all the comparisons of interest listed in Section 8.6.

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Test = The first product in the comparison; Reference = The second product in the comparison; n = Number of observations used in analysis
The mixed model includes sequence, product, and study period as fixed effects and subject-nested-within-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.

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table PUBS Summary of Total Number of HTP/HHP Sticks Used During the Ad Libitum Product Use by Sex and Product (Outcomes Population)

		Product			
Sex	Statistics	A	B	C	D
Male	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
	95% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

<Similar to above for Sex = Female and Overall>

Product A: < >
Product B: < >
Product C: < >
Product D: < >
HTP = Heated tobacco product; HHP = Heated herbal product

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table SPUBS Summary of Total Number of OBCCs on Days -1 through 5 During the Ad Libitum Product Use by Sex and Study Period
(Outcomes Population)

		Study Period					
Sex	Statistics	Check-in	1	2	3	4	Overall
Male	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
	95% 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

<Similar to above for Sex = Female and Overall>

OBCC = Subject's Own Brand Combustible cigarette

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table SCPUB Summary of Total Number of Puffs During the Controlled Product Use by Sex and Product (Outcomes Population)

		Product				
Sex	Statistics	A	B	C	D	E
Male	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
	95% CI	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X	X.X-X.X

<Similar to above for Sex = Female and Overall>

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

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CAES Product Use-Emergent Adverse Event Frequency by Product –
Number of Subjects Reporting the Event (% of Subjects Who Received Study Product) (Safety Population)

		Product					
Adverse Event	Product Trial* (N = X)	A (N = X)	B (N = X)	C (N = X)	D (N = X)	E (N = X)	Overall# (N = X)
Number of Subjects With PUEAEs	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Number of Subjects Without PUEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	X (XX%)
Eye disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Vision blurred	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Gastrointestinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Dyspepsia	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Nausea	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Musculoskeletal and connective tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Back pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Muscle cramps	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Musculoskeletal pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Nervous system disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)
Headache	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (XX%)

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Although a subject may have had 2 or more adverse events, the subject is counted only once within a category. The same subject may appear in different categories.
Adverse events are classified according to MedDRA Version 26.1.
*Only includes subjects that enrolled in the Product Trial period and dropped prior to randomisation.
#Subjects who only participated in the Product Trial period are not included in the Overall summary.
PUEAEs = Product use-emergent adverse event

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CAEE Product Use-Emergent Adverse Event Frequency by Product –
Number of Adverse Events (% of Total Adverse Events) (Safety Population)

		Product					
Adverse Event	Product Trial*	A	B	C	D	E	Overall#
Number of PUEAEs	X	X	X	X	X	X	X
Eye disorders	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%)
Gastrointestinal disorders	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%)
Nausea	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%)
Back pain	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%)
Musculoskeletal pain	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%)
Headache	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%)
Vaginal discharge	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Respiratory, thoracic and mediastinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Epistaxis	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Adverse events are classified according to MedDRA Version 26.1.
*Only includes subjects that enrolled in the Product Trial period and dropped prior to randomisation.
#Subjects who only participated in the Product Trial period are not included in the Overall summary.
PUEAEs = Product use-emergent adverse event

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CAESR Product Use-Emergent Adverse Event Frequency by Product, Severity, and Relationship to Study Product - Number of Adverse Events (Safety Population)

Adverse Event	Product	Number of Subjects With PUEAEs	Number of PUEAEs	Severity			Relationship to Study Product				
				Mild	Moderate	Severe	Unrelated	Unlikely	Possibly	Probably	Likely
Abdominal pain	A	X	X	X	X	X	X	X	X	X	X
Constipation	E	X	X	X	X	X	X	X	X	X	X
Dry throat	C	X	X	X	X	X	X	X	X	X	X
Dysmenorrhoea	B	X	X	X	X	X	X	X	X	X	X
Headache	A	X	X	X	X	X	X	X	X	X	X
	D	X	X	X	X	X	X	X	X	X	X
Myalgia	A	X	X	X	X	X	X	X	X	X	X
Nasal congestion	Product Trial*	X	X	X	X	X	X	X	X	X	X
Skin laceration	C	X	X	X	X	X	X	X	X	X	X
	Product Trial*	X	X	X	X	X	X	X	X	X	X
	A	X	X	X	X	X	X	X	X	X	X
	B	X	X	X	X	X	X	X	X	X	X
	C	X	X	X	X	X	X	X	X	X	X
	D	X	X	X	X	X	X	X	X	X	X
	E	X	X	X	X	X	X	X	X	X	X
	Overall#	X	X	X	X	X	X	X	X	X	X

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Adverse events are classified according to MedDRA Version 26.1.
*Only includes subjects that enrolled in the Product Trial period and dropped prior to randomisation.
#Subjects who only participated in the Product Trial period are not included in the Overall summary.
PUEAEs = Product use-emergent adverse event

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table 14.3.2.1 Serious Adverse Events (Safety Population)

Will match format of Appendix 16.2.7

Or contain statement as follows:

"There were no events that met this criteria."

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CLBO Out-of-Range Values and Recheck Results - <Clinical Laboratory Panel> (Safety Population)

Subject Number	Age/ Sex	Study Period	Day	Hour	Date	Time	Parameter1 <Range> (Unit)	Parameter2 <Range> (Unit)	Parameter3 <Range> (Unit)	Parameter4 <Range> (Unit)
001	XX/X	Screen			DDMMMYYYY	HH:MM:SS	XX H		XX L	XX H
		1	1	8.67	DDMMMYYYY	HH:MM:SS	XX L	XX L		XX L

Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early termination chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for. Unscheduled and Early Termination records should only be included if they are out of range or recheck results.

F = Female; M = Male
H = Above reference range; L = Below reference range

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CLBD Clinical Laboratory Summary and Change From Baseline – <Clinical Laboratory Panel> (Safety Population)

Laboratory Test (units)	Reference Range	Time Point	Statistic	Summary (N = X)	Change From Baseline
Testname (unit)	< – >#	Baseline	n	X	
			Mean	X.X*	
			SD	X.XX	
			Minimum	XX	
			Median	X.X	
			Maximum	XX	
		End of study	n	X	X
			Mean	X.X^	X.X
			SD	X.XX	X.XX
			Minimum	XX	XX
			Median	X.X	X.X
			Maximum	XX	XX

Programmer Note: Summaries at specific time points will be flagged (with a *) if they are above or below the reference range. This only applies to the clinical laboratory summary results (i.e., not the change from baseline or any other endpoints). Time Point column will match those found in Clinical Laboratory Tests section 12.6 of the SAP.

Baseline is the last measurement collected prior to first product use on Day 1.
= Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10 for the breakdown.
* = Above reference range; ^ = Below reference range
EOS = End of study

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CVS Vital Sign Summary and Change From Baseline (Safety Population)

Vital Sign (units)	Time Point	Statistic	Summary (N = X)	Change From Baseline
Testname (unit)	Baseline	n	X	
		Mean	X.X	
		SD	X.XX	
		Minimum	XX	
		Median	X.X	
		Maximum	XX	
	Day 2 Preuse	n	X	X
		Mean	X.X	X.X
		SD	X.XX	X.XX
		Minimum	XX	XX
		Median	X.X	X.X
		Maximum	XX	XX
	Day 3 Preuse	n	X	X
		Mean	X.X	X.X
		SD	X.XX	X.XX
		Minimum	XX	XX
		Median	X.X	X.X
		Maximum	XX	XX

Programmer Note: Time Point column will match those found in section of the Vital Signs Section 12.7 of the SAP.

Baseline is the last measurement collected prior to first product use on Day 1.

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CEG 12-Lead Electrocardiogram Summary and Change From Baseline (Safety Population)

Measurement (units)	Time Point	Statistic	Summary (N = X)	Change From Baseline
Testname (unit)	Baseline	n	X	
		Mean	X.X	
		SD	X.XX	
		Minimum	XX	
		Median	X.X	
		Maximum	XX	
	End of Study	n	X	X
		Mean	X.X	X.X
		SD	X.XX	X.XX
		Minimum	XX	XX
		Median	X.X	X.X
		Maximum	XX	XX

Programmer Note: Time Point column will match those found in Electrocardiogram Section 12.8 of the SAP.

Baseline is the last measurement collected prior to first product use on Day 1.

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

Table CDM Incidence of Device Malfunction (Safety Population)

		Product				
Device Malfunction	Product Trial* (N = X)	A (N = X)	B (N = X)	C (N = X)	D (N = X)	Overall# (N = X)
Number of Subjects Who Use the Device	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Number of Subjects Experienced Device Malfunction	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Event Description 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Event Description 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Event Description 3	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Product A: < >
Product B: < >
Product C: < >
Product D: < >
*Only includes subjects that enrolled in the Product Trial period and dropped prior to randomisation.
#Subjects who only participated in the Product Trial period are not included in the Overall summary.

Source: ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/tab/programname2022Q1.sas DDMMMYYYY HH:MM

15.3 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 be generated from data created in accordance with SDTM Model 1.7 with Implementation Guide 3.3 or higher. Listings with derived data (i.e., urge to smoke parameters, product evaluation scale factor scores) may be created from the ADaM data. All listings will be presented in Courier New size font 9. Time point information will match that found in the CRF.

Appendix 16.1.10 Clinical Laboratory Reference Ranges

Laboratory Group	Test Name	Sex	Age Category	Reference Range	Unit
Chemistry	Testname1	MALE		XX - XXX	mEq/L
	Testname2	MALE	0-25	XX - XXX	U/L
			26-99	XX - XXX	U/L
<similar for all other tests, note that age will only be presented when different reference range exists>					
Hematology	<similar to chemistry>				
Urinalysis	Testname	MALE		NEGATIVE	
Urine Drug Screening	Amphetamines	MALE		NOT DETECTED	

Source: SDTM.LB
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.1 Subject Disposition (Safety Population)

		End of Product				End of Study			
Subject Number	Randomised/ Actual Product Sequence	Did Subject Prematurely Discontinue?	Date of Discontinuation	Primary Product Discontinuation Reason	Specify	Did Subject Complete the Study?	Date of Last Contact	Primary Study Discontinuation Reason	Specify
001	ABECD/ABECD	Yes	DDMMMYYYY			Yes	DDMMMYYYY		
002	BCADE/BCADE	No	DDMMMYYYY	Personal Reason	XXXXXXXXXXX	No	DDMMMYYYY	Personal Reason	XXXXXXXX
003	CDBEA/CDB	No	DDMMMYYYY	Other	XXXXXXXXXXX	No	DDMMMYYYY	Other	XXXXXXXX

<similar to above for all subjects>

Product A: Pulze 2.0 device with iD Balanced Blue stick
Product B: Pulze 2.0 device with iD Rich Bronze stick
Product C: Pulze 2.0 device with iSenzia Forest Berry stick
Product D: Pulze 2.0 device with iSenzia Summer Watermelon stick
Product E: Subject's own brand combustible cigarette (OBCC)

Source: SDTM.< >; ADSL.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.4.1 Demographics (Safety Population)

Subject Number	Year of Birth	Age (yr)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	Body Mass Index (kg/m²)	Informed Consent Date
001	YYYY	47	Male	< >	Not Hispanic or Latino	XXX	XX.X	XX.XX	DDMMMYYYY
002	<similar to above.>								

<similar to above for all subjects >

Age is approximated as year of informed consent – year of birth. There will be a subtraction of 1 if the difference in years is 1 more than the age specified in the inclusion criteria.

Source: SDTM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.4.2 Oral/Physical Examination (I of II) (Safety Population)

Subject Number	Study Period	Date	Was PE Performed?	System1	System2	System3	System4	System5	System6
001	Screen	DDMMMYYYY	Yes	NORMAL	ABNORMAL*	NORMAL	NORMAL	NORMAL	NORMAL

<similar to above for Appendix 16.2.4.3>

* = See Appendix 16.2.4.4 Oral/Physical Examination Description
HEENT = Head, eyes, ears, nose, throat; PE = Physical examination

Source: SDTM.< >
Program: /CAXXXX/sas_prg/stsas/programname2022Q1.sas DDMMMYYYY HH:MM

Appendix 16.2.4.4 Oral/Physical Examination Descriptions (Safety Population)

Subject Number	Study Period	Date	System	Result	Description or Comment
001	Screen	DDMMMYYYY	Skin	ABNORMAL	RIGHT CHEST SCAR-NCS

Source: SDTM.< >
Program: /CAXXXX/sas_prg/stsas/programname2022Q1.sas DDMMMYYYY HH:MM

Appendix 16.2.4.5 Medical History (Safety Population)

Subject Number	Any History?	Condition or Event	Date		
			Start	End	Ongoing?
001	No				
002	Yes	< >	YYYY		Yes

<note date can be YYYY, MONYYYY, or DDMONYYYY based on individual subject data>

<similar to above for all subjects >

Source: SDTM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.4.6 Smoking History and Usual Brand Attributes (Safety Population)

Subject Number	Substance	Start Date	Stop Date	Amount	Brand	Brand Style	Flavour	Cigarette Length
001	Tobacco Use	DDMONYYYY	DDMONYYYY	XXXXXXXX	XXXXXXXX	XXXXXXX	XXXXXXXX	XXXXXXXXX
		DDMONYYYY		XXXXXXXX	XXXXXXXX	XXXXXXX	XXXXXXXX	XXXXXXXXX
002	Tobacco Use	DDMONYYYY		XXXXXXXX	XXXXXXXX	XXXXXXX	XXXXXXXX	XXXXXXXXX

<similar to above for all subjects >

Source: SDTM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.5.1 Subject Eligibility (Safety Population)

Subject Number	Study Period	Did subject meet all eligibility criteria?	Criterion Not Met
001	Screen	Yes	
002	Screen	No	Exclusion 5

<similar to above for all subjects>

Source: SDTM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.5.2 Product Trial (Safety Population)

Subject Number	Study Period	Day	Interval	Product Use Date	Product Use Start Time	Product Use End Time	Planned Product	Route	Form	Comments
001	Check-in	-1	-18.00 TO -17.92	DDMONYYYY	HH:MM:SS	HH:MM:SS	< >	INHALATION	HTP	
					HH:MM:SS	HH:MM:SS	< >	INHALATION	HHP	<This column prints only if data is present>

<similar to above for all subjects >

HHP = Heated herbal product; HTP = Heated tobacco product

Source: SDTM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.5.3 Product Description

CRF Product Description	Form	Route
< >	HEATED TOBACCO PRODUCT	INHALATION
< >	HEATED HERBAL PRODUCT	INHALATION
< >	CIGARETTE	INHALATION

Source: SDTM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.5.4 Controlled Product Use Administration Times (Safety Population)

Subject Number	Study Period	Product	Day	Interval	Product Use Date	Product Use Start Time	Product Use End Time	Puff Count	Comments
001	1	A	1	0.00 TO 0.10	DDMONYYYY	HH:MM:SS	HH:MM:SS	XX	
	2	B	1	0.00 TO 0.10	DDMONYYYY	HH:MM:SS	HH:MM:SS	XX	
	3	E	1	0.00 TO 0.10	DDMONYYYY	HH:MM:SS	HH:MM:SS	XX	
	4	C	1	0.00 TO 0.10	DDMONYYYY	HH:MM:SS	HH:MM:SS	XX	
	5	D	1	0.00 TO 0.10	DDMONYYYY	HH:MM:SS	HH:MM:SS	XX	<This column prints only if data is present>

<similar to above for all subjects/time points>

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

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

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Appendix 16.2.5.5 Ad Libitum Product Use Administration Times (Safety Population)

Subject Number	Study Period	Product	Day	Interval	Product Use Date	Product Use Start Time	Product Use End Time	Comments
001	1	A	1	4.03 TO 8.03	DDMONYYYY	HH:MM:SS	HH:MM:SS	
	2	B	1	4.03 TO 8.03	DDMONYYYY	HH:MM:SS	HH:MM:SS	
	3	E	1	4.03 TO 8.03	DDMONYYYY	HH:MM:SS	HH:MM:SS	
	4	C	1	4.03 TO 8.03	DDMONYYYY	HH:MM:SS	HH:MM:SS	
	5	D	1	4.03 TO 8.03	DDMONYYYY	HH:MM:SS	HH:MM:SS	<This column prints only if data is present>

<similar to above for all subjects/time points>

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

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

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Appendix 16.2.5.6 Ad Libitum Smoking (Safety Population)

Subject Number	Study Period	Product	Day	Hour	Start Date	Start Time	Stop Date	Stop Time	Comments
001	Check-in		-1	-17.75	DDMONYYYY	HH:MM:SS	DDMONYYYY	HH:MM:SS	
	1	A	1	4.03	DDMONYYYY	HH:MM:SS	DDMONYYYY	HH:MM:SS	
				6.03	DDMONYYYY	HH:MM:SS	DDMONYYYY	HH:MM:SS	
				8.05	DDMONYYYY	HH:MM:SS	DDMONYYYY	HH:MM:SS	
	2	B	1	4.03	DDMONYYYY	HH:MM:SS	DDMONYYYY	HH:MM:SS	
				6.03	DDMONYYYY	HH:MM:SS	DDMONYYYY	HH:MM:SS	
				8.05	DDMONYYYY	HH:MM:SS	DDMONYYYY	HH:MM:SS	<This column prints only if data is present>

<similar to above for all subjects/time points>

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
After Hour 8 in each period, subjects will smoke their OBCC.

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.5.7 Prior and Concomitant Medications (Safety Population)

Subject Number	Product	Prior?	Medication (WHO DD)	Dosage	Route	Start Date	Start Time	End Date	End Time	Frequency	Indication	Ongoing?
001			None									
002			None									
003		Yes	CETIRIZINE (CETIRIZINE)	X MG	BY MOUTH	DDMONYYYY		DDMONYYYY	HH:MM	XXXXXXX	XXXXXXX	No
	B	No	PARACETAMOL (PARACETAMOL)	X MG	XXXXXXXXX	DDMONYYYY	HH:MM			XXXXXXX	XXXXXXX	Yes

<similar to above for all subjects>

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Concomitant medications are coded with WHO Drug Dictionary Version 01-Sep-2023_b3.
WHO DD = World Health Organization Drug Dictionary
Prior is defined as a medication administered prior to the first study product administration.

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.5.8 Plasma Nicotine Pharmacokinetic Blood Draw Times and Concentration Data (Safety Population)

Subject Number	Study Period	Product	CRF Day	CRF Hour	Blood Draw Date	Blood Draw Time	Elapsed Time From Last Product Use (units)	Unadjusted Concentration (units)	Baseline-Adjusted Concentration (units)	Comments
1	1	A	1	-0.05	DDMONYYYY	HH:MM:SS	0.0	X.XX	X.XX	
				0.25	DDMONYYYY	HH:MM:SS	0.265	X.XX	X.XX	
				0.50	DDMONYYYY	HH:MM:SS	0.590	X.XX	X.XX	Late Draw
			< >							

<similar for all other time points and subjects>

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

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

- Population: Safety population will be used in this listing.
- Time may be expressed in minutes, as appropriate

Internal template: CPKel1

Appendix 16.2.6.3 Intervals (Minutes) Used for the Determination of Baseline-Adjusted Plasma Nicotine Kel Values (Outcomes Population)

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Table CPKel1. Intervals (Hours) Used for Determination of <Analyte> Kel Values

Subject Number	Product Sequence	<Product A> Interval	<Product A> R2	<Product A> n	<Product B> Interval	<Product B> R2	<Product B> n
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
X	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X

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

R2 = Coefficient of determination
n = Number of points used in Kel calculation
. = Kel value not reportable.

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)

Appendix 16.2.6.4 Urge to Smoke (Safety Population)

Subject Number	Study Period	Product	Day	Hour	Date	Was Event Performed? (Yes/No)	VAS Score*	Change From Baseline	Comments
001	1	A	1	-0.17	DDMONYYYY	Yes	XX	XX	
				0.05	DDMONYYYY	Yes	XX	XX	
				0.12	DDMONYYYY	Yes	XX	XX	
				0.23	DDMONYYYY	Yes	XX	XX	
				0.73	DDMONYYYY	Yes	XX	XX	
				0.98	DDMONYYYY	Yes	XX	XX	
				1.98	DDMONYYYY	Yes	XX	XX	
				3.98	DDMONYYYY	Yes	XX	XX	
	2	B	1	-0.17	DDMONYYYY	No			Not recorded in error
				0.05	DDMONYYYY	Yes	XX	XX	
				0.12	DDMONYYYY	Yes	XX	XX	<This column prints only if data is present>

<similar to above for all subjects/time points>

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Baseline is the last measurement collected prior to product use for the respective product.
*VAS Score for question: Right now, how much would you like to smoke a cigarette?

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.6.5 Urge to Smoke Parameters (Safety Population)

Subject Number	Study Period	Product	Date	Emax	TEmax	AUEC0-240
001	1	A	DDMONYYYY	XX	XX	XX
	2	B	DDMONYYYY	XX	XX	XX
	3	C	DDMONYYYY	XX	XX	XX
	4	D	DDMONYYYY	XX	XX	XX
	5	E	DDMONYYYY	XX	XX	XX

<similar to above for all subjects >

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

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.6.6 Product Evaluation Scale Collection (Safety Population)

Subject Number	Study Period	Product	Date	Timepoint	Was Event Performed? (Yes/No)	Comments
001	1	A	DDMONYYYY	XXXX	Yes	
	2	B	DDMONYYYY	XXXX	Yes	
	3	C	DDMONYYYY	XXXX	Yes	
	4	D	DDMONYYYY	XXXX	Yes	
	5	E	DDMONYYYY	XXXX	Yes	<This column prints only if data is present>

<similar to above for all subjects >

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

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.6.7 Product Evaluation Scale Item Score (Safety Population)

Subject Number	Study Period	Product	Date	Timepoint	Question 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
001	1	A	DDMONYYYY	XXXX	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	2	B	DDMONYYYY	XXXX	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	3	C	DDMONYYYY	XXXX	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	4	D	DDMONYYYY	XXXX	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	5	E	DDMONYYYY	XXXX	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

<similar to above for all subjects >

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Question: 1. Was it satisfying? 2. Did it taste good? 3. Did you enjoy the sensations in your mouth? 4. Did it calm you down?
5. Did it make you feel more awake? 6. Did it make you feel less irritable? 7. Did it help you concentrate?
8. Did it reduce your hunger for food? 9. Did it make you dizzy? 10. Did it make you nauseous?
11. Did it immediately relieve your craving for a cigarette? 12. Did you enjoy it? 13. Did it relieve withdrawal symptoms?
14. Did it relieve the urge to smoke? 15. Was it enough nicotine? 16. Was it too much nicotine? 17. Was it easy to use?
18. Were there bothersome side effects? 19. Were you comfortable using the product in public?
20. Did you still have a craving for a cigarette after using the product?
21. Are you concerned that you would become dependent on this product?
Scale: 1 = not at all; 2 = very little; 3 = a little; 4 = moderately; 5 = a lot; 6 = quite a lot; 7 = extremely

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.6.8 Product Evaluation Scale Factor Score (Safety Population)

Subject Number	Study Period	Product	Date	Timepoint	Factor: Satisfaction	Factor: Psychological Reward	Factor: Aversion	Factor: Relief	Factor: Easy to Use	Factor: Comfortable in Public	Factor: Concern for Becoming Dependent
001	1	A	DDMONYYYY	XXXX	X	X	X	X	X	X	X
	2	B	DDMONYYYY	XXXX	X	X	X	X	X	X	X
	3	C	DDMONYYYY	XXXX	X	X	X	X	X	X	X
	4	D	DDMONYYYY	XXXX	X	X	X	X	X	X	X
	5	E	DDMONYYYY	XXXX	X	X	X	X	X	X	X

<similar to above for all subjects >

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Factor score: Satisfaction = average of items 1, 2, 3, and 12; Psychological Reward = average of items 4 through 8;
Aversion = average of items 9, 10, 16, and 18; Relief = average of items 11, 13, 14, 15, and reversed for item 20; Easy to Use = item 17;
Comfortable in Public = item 19; Concern for Becoming Dependent = item 21
Refer to Appendix 16.2.6.6 for description of items.
Scale: 1 = not at all; 2 = very little; 3 = a little; 4 = moderately; 5 = a lot; 6 = quite a lot; 7 = extremely

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.6.9 Intent to Use (Safety Population)

Subject Number	Study Period	Product	Date	Timepoint	Was Event Performed? (Yes/No)	VAS Score*	Comments
001	1	A	DDMONYYYY	XXXX	Yes	XX	
	2	B	DDMONYYYY	XXXX	Yes	XX	
	3	C	DDMONYYYY	XXXX	Yes	XX	
	4	D	DDMONYYYY	XXXX	Yes	XX	
	5	E	DDMONYYYY	XXXX	Yes	XX	<This column prints only if data is present>

<similar to above for all subjects >

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
*VAS Score for question: If available, how likely are you to buy and use your assigned study product in the future?

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.6.10 Puff Topography (Safety Population)

Subject Number	Study Period	Product	Date	Timepoint	Was Event Performed? (Yes/No)	Comments
001	1	A	DDMONYYYY	XXXX	Yes	
	2	B	DDMONYYYY	XXXX	Yes	
	3	C	DDMONYYYY	XXXX	Yes	
	4	D	DDMONYYYY	XXXX	Yes	
	5	E	DDMONYYYY	XXXX	Yes	<This column prints only if data is present>

<similar to above for all subjects >

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

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.6.11 Puff Topography Parameters – Per-Puff (Safety Population)

Subject Number	Study Period	Product	Date	Timepoint	Puff Count	Puff Duration (s)	Puff Volume (mL)	Peak Puff Flow Rate (mL/s)	Average Puff Flow Rate (mL/s)	Inter-puff Interval (s)
001	1	A	DDMONYYYY	XXXX	XX	XX	XX	XX	XX	XX
				XXXX	XX	XX	XX	XX	XX	XX
				XXXX	XX	XX	XX	XX	XX	XX
				XXXX	XX	XX	XX	XX	XX	XX
				XXXX	XX	XX	XX	XX	XX	XX

<similar to above for all subjects, period and timepoints >

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

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.6.12 Puff Topography Parameters – Per-Product (Safety Population)

Subject Number	Study Period	Product	Total Puff Number	Total Puff Duration (s)	Average Puff Duration (s)	Total Puff Volume (mL)	Average Puff Volume (mL)	Average Peak Flow Rate (mL/s)	Average Flow Rate (mL/s)	Total Inter-puff Interval (s)	Average Inter-puff Interval (s)
001	1	A	XX	XX	XX	XX	XX	XX	XX	XX	XX
	2	B	XX	XX	XX	XX	XX	XX	XX	XX	XX
	3	C	XX	XX	XX	XX	XX	XX	XX	XX	XX
	4	D	XX	XX	XX	XX	XX	XX	XX	XX	XX
	5	E	XX	XX	XX	XX	XX	XX	XX	XX	XX

<similar to above for all subjects>

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

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.6.13 Product Use Behaviour During Ad Libitum Product Use (Safety Population)

Subject Number	Study Period	Product	Number of HTP/HHP Sticks Used	Number of OBCCs Smoked	Number of Puffs
001	1	A	XX	XX	XX
	2	B	XX	XX	XX
	3	C	XX	XX	XX
	4	D	XX	XX	XX
	5	E	XX	XX	XX

<similar to above for all subjects >

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
HTP = Heated tobacco product; HHP = Heated herbal product; OBCC = Combustible cigarette

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.7.1 Adverse Events (Safety Population)

Subject Number	Age/ Sex	Product	PUE?	System Organ Class/ Preferred Term (Verbatim)	Time From Last Product Use (DD:HH:MM)	Date:Time Start/ End Duration (DD:HH:MM)	Serious/ Outcome	Severity/ Frequency	Study Product Relationship/ Action
001	30/F			None					
002	24/M			None					
003	52/M	A	Yes	XXXXXXXXXXXX/ XXXXXXXXXXXXXXXX (XXXXXXXXXXX)	XX:XX:XX	DDMONYYYY:HH:MM/ DDMONYYYY:HH:MM 00:23:15	No/ Resolved	Moderate/ Intermittent	Likely/ Product Withdrawn
		B	Yes	<similar to above>					

Programmer Note: AEs should be presented start date/time order for each subject.

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Adverse events are classified according to MedDRA Version 26.1.
PUE = Product use-emergent
F = Female; M = Male

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.7.2 Details for Serious Adverse Events (Safety Population)

Subject Number	Age/ Sex	Product	PUE?	System Organ Class/ Preferred Term (Verbatim)	Date:Time Start/ End Duration (DD:HH:MM)	Serious Event?	Congenital Anomaly/ Birth Defect?	Persistent or Significant Disability or Incapacity?	Hospital-ization?	Life-Threat?	Important Medical Event?	Death?
003	52/M	A	Yes	XXXXXXXXXXX/ XXXXXXXXXXXXXXXXX (XXXXXXXXXXX)	DDMONYYYY:HH:MM/ DDMONYYYY:HH:MM 00:23:15	Yes	No	No	Yes	No	Yes: < >	No

Programmer Note: If Serious = Yes then present AEs in this listing otherwise please do not include this listing.

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
Adverse events are classified according to MedDRA Version 26.1.
PUE = Product use-emergent
F = Female; M = Male

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.7.3 Device Malfunction (Safety Population)

Subject Number	Study Period	Product	Did the Device Malfunction?	Date	Time	Device Serial Number	Replacement			
							Date	Time	Device Serial Number	Comments
001	1	A	Yes	DDMONYYYY	HH:MM:SS	XXXXXXXXXXX	DDMONYYYY	HH:MM:SS	XXXXXXXXXXX	XXXXXXXX
	2	B	No							

<similar to above for all subjects and periods>

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

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendices 16.2.8.2 – 16.2.8.5 will resemble 16.2.8.1.

Appendix 16.2.8.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Subject Number	Age/ Sex	Study Period	Day	Hour	Date	Time	Chloride M: 97-105 (mEq/L)	Potassium M: 3.7-5.2 (mEq/L)	Phosphorus M: 2.4-4.4 (mg/dL)	Sodium M: 135-143 (mEq/L)
001	XX/M	Screen			DDMONYYYY	HH:MM:SS	XXX	X.X	X.X	XXX H
		Check-in	-1	-22.50	DDMONYYYY	HH:MM:SS	XXX H	X.X	X.X L	XXX H
		Recheck			DDMONYYYY	HH:MM:SS	XXX	X.X	X.X	XXX
		5	1	8.67	DDMONYYYY	HH:MM:SS	XXX	X.X	X.X	XXX

<similar to above for all subjects/time points>

F = Female; M = Male
H = Above reference range; L = Below reference range

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.8.6 Carbon Monoxide Breath Test (Safety Population)

Subject Number	Study Period	Day	Hour	Date	Time	Result (ppm)	Comments
001	Screen			DDMMMYYYY	HH:MM:SS	XX	XXXXXXXXXXXXXXXXXXXXX
	Check-in	-1	-23.00	DDMMMYYYY	HH:MM:SS	XX	XXXXXXXXXXXXXXXXXXXXX

Source: SDTM.< >
Program: /CAXXXX/sas_prg/stsas/programname2022Q1.sas DDMMMYYYY HH:MM

Appendix 16.2.8.7 Vital Signs (Safety Population)

Subject Number	Age/ Sex	Study Period	Product	Day	Hour	Date	Time	Blood Pressure (mmHg) Systolic/Diastolic	Pulse (bpm)	Respiration (brpm)	Temperature (°C)	Weight (kg)
001	30/F	Screen				DDMONYYYY	HH:MM:SS	XXX/XX	XX	XX	XX.X	XX.X
					R		HH:MM:SS	XXX/XX				
					R		HH:MM:SS	XXX/XX				
		Check-in		-1	-22.00	DDMONYYYY	HH:MM:SS	XXX/XX	XX	XX	XX.X	
		1	A	1	-0.50	DDMONYYYY	HH:MM:SS	XXX/XX	XX	XX	XX.X	
		2	B	1	-0.50	DDMONYYYY	HH:MM:SS	XXX/XX	XX	XX	XX.X	
		3	C	1	-0.50	DDMONYYYY	HH:MM:SS	XXX/XX	XX	XX	XX.X	
		4	D	1	-0.50	DDMONYYYY	HH:MM:SS	XXX/XX	XX	XX	XX.X	
		5	E	1	-0.50	DDMONYYYY	HH:MM:SS	XXX/XX	XX	XX	XX.X	
				1	8.50	DDMONYYYY	HH:MM:SS	XXX/XX	XX			

Product A: < >
Product B: < >
Product C: < >
Product D: < >
Product E: < >
F = Female; M = Male
R = Recheck value; bpm = beats/minute; brpm = breaths/minute

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

Appendix 16.2.8.8 12-Lead Electrocardiogram (Safety Population)

Subject Number	Age/ Sex	Study Period	Day	Hour	Date	Time	Result	Heart Rate (bpm)	RR (msec)	PR (msec)	QRS (msec)	QT (msec)	QTcF (msec)	Specify/Comments
001	30/F	Screen			DDMONYYYY	X:XX:XX	WNL	XX	XXX	XX	XX	XXX	XXX	EARLY REPOLARIZATION; LEFT AXIS DEVIATION
		Check-in	-1	-22.25	DDMONYYYY	XX:XX:XX	ANCS	XX	XXX	XX	XX	XXX	410	LEFT AXIS DEVIATION
		5	1	8.33	DDMONYYYY	XX:XX:XX	< >	XX	XXX	XX	XX	XXX	441 @	SINUS BRADYCARDIA
					DDMONYYYY	XX:XX:XX	< >	XX	XXX	XX	XX	XXX	451#@	

F = Female; M = Male
R = Recheck value; WNL = Within normal limits; ANCS = Abnormal, not clinically significant
QTcF = QT corrected for heart rate using Fridericia's correction
# = QTc value greater than 450 msec; @ = QTc change from baseline greater than 30 msec

Source: SDTM.< >; ADaM.< >
Program: /CAXXXXX/sas_prg/stsas/lis/programname2022Q1.sas DDMONYYYY HH:MM

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