Statistical Analysis Plan

A Single-Dose, Open-Label, Randomized, Incomplete Block Design Trial to Characterize the Pharmacokinetics of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and Single Doses of Budesonide Delivered by a Conventional Jet Nebulizer in Pediatric Subjects Aged 4 to 8 Years with Wheezing, Reactive Airway Disease or Mild Asthma

Vectura Study No. VR647/1/002
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Test Product: VR647

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Statistical Analysis Plan Signature Page

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Table of Contents

1. INTRODUCTION 4
2. OBJECTIVES AND ENDPOINTS 4
2.1 Primary Objectives 4
2.2 Secondary Objectives 4
2.3 Endpoints 4
3. STUDY DESIGN 5
4. ANALYSIS POPULATIONS 6
4.1 Analysis Populations 6
4.2 Preliminary Data and Interim Analysis 7
5. TREATMENT DESCRIPTIONS 7
6. PHARMACOKINETIC ANALYSIS 8
6.1 Measurements and Collection Schedule 8
6.2 Bioanalytical Methods 8
6.3 Investigational Product and PK Analyte Information 8
6.3.1 Budesonide 8
6.4 Pharmacokinetic Concentrations 9
6.5 Noncompartmental Pharmacokinetic Analysis and Parameter Calculation 9
6.5.1 Plasma Pharmacokinetic Parameters 9
6.6 Data Summarization and Presentation 11
6.7 Statistical Analysis of PK Parameters 12
6.7.1 Dose Proportionality Analysis of Pharmacokinetic Parameters 12
6.7.2 Analysis of variance 13
6.7.3 Ratios of LSMs 14
7. EFFICACY ANALYSIS 14
7.1 Inhalation Checklist 14
7.2 Duration of Treatment 15
7.3 Modified Patient Satisfaction and Preference Questionnaire (mPASAPQ) 15
8. SAFETY 15
8.1 Subject Discontinuation 16
8.2 Demographics and Baseline Characteristics 16
8.3 Medical, Surgical and Asthma History 16
8.4 Adverse Events and Adverse Device Effects 16
8.5 Vital Signs 17
8.6 Concomitant Medications 18
8.7 Physical Examination 18
9. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS 18
10. SUMMARY TABLES AND FIGURES 19
10.1 In-text Summary Tables and Figures 19
10.2 Section 14 Summary Tables and Figures 21
10.3 Section 16 Data Listings 24
11. TABLE SHELLS 26
11.1 In-Text Table Shells 27
11.2 Post-Text Table Shells 43

1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the summarization of the pharmacokinetic (PK) and safety data from VR647/1/002. This SAP should be read in conjunction with the study protocol (29 September 2017, v1.0) and case report form (CRF) (04 May 2018). The analysis plan may change due to unforeseen circumstances. Any changes made after the locking of the database will be documented in the clinical study report (CSR). Please note that the header for this page will be the one used for the main body of the CSR.

Any additional exploratory analyses not addressed within this SAP and/or driven by the data, or requested by Vectura Limited ("Vectura"), will be considered out of scope.

2. OBJECTIVES AND ENDPOINTS

2.1 Primary Objectives

To characterize the pharmacokinetic (PK) profile of budesonide nebulizer suspension following administration of single oral inhalations of 5, 10 and 20 breaths of VR647 Inhalation Suspension delivered by the VR647 Inhalation System fitted with a mouthpiece and 1 mg/2 mL Pulmicort Respules delivered by the conventional jet nebulizer.

2.2 Secondary Objectives

- To evaluate parent(s')/legal guardian(s') satisfaction with the use of the conventional jet nebulizer and/or the VR647 Inhalation System fitted with a mouthpiece.
- To evaluate the safety and tolerability of single doses of VR647 Inhalation Suspension delivered by the VR647 Inhalation System fitted with a mouthpiece in subjects with wheezing, reactive airway disease or mild asthma.

2.3 Endpoints

Primary Endpoints (Pharmacokinetics):

The following PK parameters for plasma budesonide for VR647 Inhalation Suspension and Pulmicort Respules will be computed, as appropriate, and their descriptive statistics will be presented $AUC_{last,}$ AUC_{inf}, C_{max}, t_{max}, t_{last}, and $t_{½}$.

Secondary Endpoints (Efficacy and Safety):

Efficacy:

- Overall duration of treatment
- Summary of inhalation checklist
- Mean modified patient satisfaction and preference questionnaire (PASAPQ) total score.
- Mean modified PASAPQ satisfaction score.
- Mean modified PASAPQ score indicating willingness to continue with the device.

Safety:

- Changes in vital signs.
- Changes in physical examination.
- Adverse events (AEs) and serious adverse events (SAEs).
- Adverse device effects (ADEs) and serious adverse device effects (SADEs).
- Use of concomitant medications.

3. STUDY DESIGN

This is an open-label, randomized, balanced, incomplete block design trial to characterize the PK of single doses of VR647 Inhalation Suspension delivered by the VR647 Inhalation System fitted with a mouthpiece and single doses of budesonide delivered by a conventional jet nebulizer in pediatric subjects aged 4 to 8 years with wheezing, reactive airway disease or mild asthma.

There will be a screening period of up to 30 days to confirm eligibility. Subjects who fulfill the enrollment criteria will be randomized to one of 12 treatment sequences (AB), (AC), (AD), (BA), (BC), (BD), (CA), (CB), (CD), (DA), (DB) or (DC), corresponding to the following treatment regimens:

Treatment regimen	Treatment description
A	5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
B	10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
C	20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
D	1 mg/2 mL Pulmicort Respules via conventional jet nebulizer

Randomization of approximately 12 subjects to the trial is considered achievable. The trial aims to randomize one third of subjects < 7 years.

The Treatment Period will comprise two dosing visits, with a washout period of 4 to 10 days between each dose. The PK of budesonide will be assessed at each dosing visit, with blood samples collected at the following time points: pre-dose, and at 20 minutes, 40 minutes, 1.5, 3, 4, 6 and 8 hours after the start of nebulization.

To aid with travel logistics due to early morning procedures on the day of dosing, sites may provide subjects and their parent(s)/legal guardian(s) the option of an overnight stay the day before dosing, until completion of procedures 8 hours after start of nebulization. Subjects will return to the clinic approximately 7 days after their last dose (second nebulization) for a follow-up assessment, which may instead be conducted by telephone interview with the parent(s)/legal guardian(s).

On each dosing day, the site staff will record on the inhalation checklist the overall quality of the inhalation maneuvers. Parent(s')/legal guardian(s') satisfaction with the use of the conventional jet nebulizer and/or the VR647 Inhalation System and willingness to continue with the device(s) will be assessed by the modified Patient Satisfaction and Preference Questionnaire (PASAPQ).

Safety and tolerability will be assessed by measurement/recording of vital signs, physical examinations, adverse events (AEs), adverse device effects (ADEs), and concomitant medications.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

Analysis Sets

- **Safety Set:** The Safety Set will be based on all randomized subjects (as treated) who receive at least one dose of trial medication. Subjects with documented failure to take at least one dose of trial medication after randomization will be excluded from the Safety Set.

- **PK Analysis Set:** The PK set will be consisting of all subjects who received at least one dose of study medication and are without any major protocol deviation. All subjects who comply sufficiently with the protocol and display an evaluable PK profile (e.g., exposure to treatment, availability of measurements and absence of major protocol violations) will be included in the PK analysis.

4.2 Preliminary Data and Interim Analysis

No interim analysis is planned for this study.

5. TREATMENT DESCRIPTIONS

The Investigational Medicinal Product is VR647 Inhalation Suspension (budesonide) 1 mg/2 mL, which is delivered by the VR647 Inhalation System. The VR647 Inhalation System comprises the VR647 Inhalation System 1 control unit that has an inspiration flow rate of 6 L/min, a nebulizer handset, a mouthpiece and a VR647 Smart Card designed specifically for this trial.

The VR647 Inhalation System is breath-actuated after a negative pressure is created at the mouthpiece on inhalation. Nebulization will continue until the target inhalation volume (i.e. the target number of breaths) is reached.

The dose of VR647 Inhalation Suspension administered to the subject will be controlled by individual study-specific VR647 Smart Cards configured to deliver 5, 10 or 20 breaths of VR647 Inhalation Suspension according to the following settings:

No. of breaths	Inspiration time (sec)	Predicted delivered dose (µg)[a]
5	4.0	16.2
10	4.0	29.4
20	4.0	53.6

[a] The predicted delivered dose represents the delivered (ex-mouthpiece) dose calculated according to the International Commission on Radiological Protection deposition model for orally inhaled particles.[1] The specific model used for the deposition calculation was published by Köbrich et al 1994. The actual delivered dose (assessed in vitro) will be included in the clinical study report.

The Commercial Pulmicort Respules (budesonide inhalation suspension) 1 mg/2 mL will be delivered by the conventional jet nebulizer (PARI Vios Aerosol Delivery System) and administered until 1 minute after the nebulizer starts to sputter.

In the PK and safety tables, figures, and listings (TFLs), treatments will be referred to as:

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System

Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System

Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System

Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer

The treatments will be referred in the main text of the CSR as “VR647 5 breaths”, “VR647 10 breaths”, “VR647 20 breaths”, and “1.0 mg/2 mL Pulmicort Respules”.

The active ingredient will be referred to in the CSR as “budesonide”.

6. PHARMACOKINETIC ANALYSIS

6.1 Measurements and Collection Schedule

Blood samples for the analysis of plasma budesonide levels will be collected at both dosing visits at pre-dose (Hour 0) and at 20, 40 minutes, 1.5, 3, 4, 6, and 8 hours after the start of nebulization.

Blood samples collected outside of the windows presented in Table 6:1 are to be considered a time deviation. Data from these samples will be included in the calculation of the PK parameters and the individual concentration-time plots (based on actual sample times), as well as in the mean concentration-time plots (based on nominal sample times); however, if there are any significant deviations, additional concentration-time plots of the mean data may be provided.

Table 6:1. Blood Sampling Deviation Windows

Scheduled Blood Sampling Time	Deviation Window
> 0 hour to ≤ 4.0 hours	± 5 minutes
> 4.0 hours to ≤ 8 hours	± 10 minutes

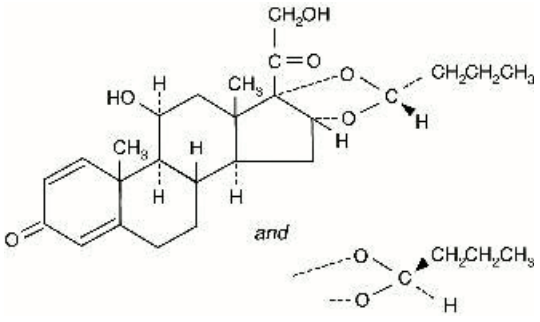
6.2 Bioanalytical Methods

Plasma concentrations of budesonide will be determined using validated bioanalytical methods at York Bioanalytical Solutions Limited (UK).

6.3 Investigational Product and PK Analyte Information

6.3.1 Budesonide

Budesonide is known chemically as (C-22*RS*)-16α,17-[(1RS)-butylidenebis(oxy)]-11β,21-dihydroxypregna-1,4-diene-3,20-dione with a molecular weight of 430.5 g/mol and a molecular formula of $C_{25}H_{34}O_6$. Budesonide is a 1:1 mixture of two epimers (22R and 22S). The two forms do not interconvert. Structure of budesonide is in the following figure:



6.4 Pharmacokinetic Concentrations

Plasma concentrations of budesonide as determined at the collection times and as per the bioanalytical method described in Section 6.1 and Section 6.2, respectively, will be used for the calculation of the plasma budesonide PK parameters.

6.5 Noncompartmental Pharmacokinetic Analysis and Parameter Calculation

6.5.1 Plasma Pharmacokinetic Parameters

The appropriate noncompartmental PK parameters will be calculated from the plasma budesonide concentration-time data using Phoenix® WinNonlin® Version 6.3 or higher. Actual sample times will be used in the calculations. All PK parameters included in the protocol are listed in Table 6:2 below, and are defined as appropriate for study design.

Table 6:2 Noncompartmental Pharmacokinetic Parameters to be Calculated

Parameter	Label to be Used	Definition	Method of Determination
AUC_{last}	AUC_{last}	The area under the plasma concentration-time curve from time 0 to time t, where t is the time of the last measurable concentration (C_{last}).	Calculated using linear-log Trapezoidal method
AUC_{inf}	AUC_{inf}	The area under the plasma concentration-time curve from time 0 extrapolated to infinity. AUC_{inf} is calculated as the sum of AUC_{last} plus the ratio of the last measurable plasma concentration (C_{last}) to the elimination rate constant (λz).	$AUC_{inf} = AUC_{last} + (C_{last}/\lambda z)$
$AUC_{\%extrap}$	$AUC_{\%extrap}$	Percent of AUC_{inf} extrapolated	$AUC_{\%extrap} = (1 - AUC_{last}/AUC_{inf})*100$
C_{max}	C_{max}	Maximum observed concentration	Taken directly from bioanalytical data
t_{max}	t_{max}	Time to reach C_{max}. If the maximum value occurs at more than one time point, t_{max} is defined as the first time point with this value	Taken directly from bioanalytical data

Parameter	Label to be Used	Definition	Method of Determination
t_{last}	tlast	Time of the last measurable concentration (C_{last})	Taken directly from bioanalytical data
λz	λz	Apparent first-order terminal elimination rate constant	Calculated from a semi-log plot of the plasma concentration versus time curve. The parameter will be calculated by linear least-squares regression analysis using the maximum number of points in the terminal log-linear phase (e.g., three or more non-zero plasma concentrations)
$t_{½}$	$t_{½}$	Apparent first-order terminal elimination half-life	Calculated as ln(2)/ λz
Additional PK parameters may be computed if deemed appropriate.			

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 and statistical analysis.

For the calculation of the PK parameters and summary statistics, plasma concentrations below the limit of quantitation (BLQ) will be treated as follows:

- BLQ concentrations prior to the first quantifiable concentration will be imputed with a value of zero.
- If a BLQ value falls between two quantifiable concentrations the value will be set equal to the lower limit of quantitation (LLOQ), unless it's exclusion can be justified (e.g. implausibility given the profile observed and known PK properties).
- Terminal BLQ values will be disregarded in the calculation of the PK parameters and summary statistics.

For the individual and mean figures, plasma concentrations BLQ will be treated as follows:

- For linear concentration scale plots of individual concentration-time data BLQ will be set to 0. For logarithmic concentration scale plots BLQ values will be set equal to the LLOQ.

The λz will be determined using ln-linear regressions composed of at least 3 data points. The λz will not be assigned if 1) the terminal elimination phase is not apparent, 2) if t_{max} is one of the 3 last data points, 3) if the R^2 value is less than 0.8. In

cases where the λz interval is not assigned, the values of AUC_{inf}, $AUC_{\%extrap}$, and $t_{½}$ are considered not calculable and will not be reported. AUC_{inf} will be reported only if R^2 is ≥ 0.80 and $AUC_{\%extrap}$ is not greater than 20% of AUC_{inf}. Wherever the resulting $t_{½}$ is more than half as long as the actual sampling interval, the λz values and associated parameters (AUC_{inf}, $AUC_{\%extrap}$, and $t_{½}$) may not be presented as judged appropriate and in accordance with Celerion SOPs.

6.6 Data Summarization and Presentation

All budesonide PK concentrations and PK parameters descriptive statistics will be generated using SAS Version 9.3 or higher.

Plasma Budesonide Concentrations

Plasma budesonide concentrations will be presented with the same number of decimals/significant figures as provided by the analytical laboratory. They will be listed by nominal sample time for each subject, tabulated by treatment, and summarized using descriptive statistics, including sample size (n), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), Minimum, Maximum, and Median. Concentrations from excluded subjects will be included in the plasma 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 plasma concentration table listings and footnoted accordingly.

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

Plasma Budesonide Pharmacokinetic Parameters

Plasma budesonide PK parameters listed in Table 6:2 will be listed by subject, tabulated by treatment, and summarized using descriptive statistics (n, Mean, SD, CV%, SEM, Minimum, Maximum, and Median). In addition, geometric mean (Geom Mean) and geometric CV% (Geom CV%) will be calculated for the AUC and C_{max}. PK parameter values for excluded subjects will be included in the PK parameter tables, but will be excluded from the summary and inferential statistics and noted as such in the tables. Individual PK parameter values will be presented with 3 significant digits.

Descriptive statistics will be presented as follows:

- n: no decimal
- Minimum, Maximum: same precision as in individual values
- Mean, Geom Mean, Median: one more significant figure than the individual values
- SD, SEM: one more significant figure than arithmetic mean

- Geom CV% and CV%: one decimal

Additional analyses may be performed as deemed necessary upon review of the data and requested by the Sponsor.

6.7 Statistical Analysis of PK Parameters

6.7.1 Dose Proportionality Analysis of Pharmacokinetic Parameters

Dose proportionality will be evaluated for VR647 AUC_{last}, AUC_{inf}, and C_{max} following administration of single oral inhalations of 5, 10 and 20 breaths of VR647 Inhalation Suspension using the power model. Dose proportionality will be assessed based on the number of inhalations and the predicted delivered dose. Due to the complex nature of the association between the systemic exposure and the dose, the assessment of the dose proportionality will not be based solely on a strict statistical rule given the small sample size for each dose level. Rather, several considerations will be taken into account for assessing dose proportionality such as: results derived from the power model statistical analysis (e.g., the slope estimate and width of the 95% CIs) and qualitative assessment specific to the PK of each drug and clinical relevance will be also taken into account.

Power Model: To evaluate dose proportionality, a regression approach will be used. A statistical linear relationship between the ln-transformed PK parameters AUC_{last}, AUC_{inf}, and C_{max} and the ln-transformed dose will be fitted by using a regression model with ln-transformed dose as a covariate.

$$Ln(Y) = \beta_0 + \beta \text{ Ln Dose} + \varepsilon \quad (1)$$

where Y represents the PK parameter AUC_{last}, AUC_{inf}, and C_{max}.

This approach is usually referred to as a power model because after exponentiation:

$$Y = \alpha (\text{Dose})^{\beta}$$

where α only depends on β_0 and error.

Dose proportionality requires that $\beta = 1$ for dose-dependent parameters.

As a first step, the statistical linear relationship between the ln-transformed PK parameters AUC_{last}, AUC_{inf}, and C_{max} and ln-transformed dose will be verified by including the quadratic effect $(\ln \text{Dose})^2$ in model (1). A 5% level of significance will be used to test the quadratic effect. The statistical linear relationship will be concluded if the quadratic effect is not statistically significant. If the statistical linear relationship is established in step 1, a second step will be performed. As a second step, model (1) will be used to calculate the 95% CIs for the slope of the ln-transformed PK parameters AUC_{last}, AUC_{inf}, and C_{max}.

Dose proportionality will be established if a statistical linear relationship is demonstrated and if the 95% CIs around the slope estimate parameters include the value of 1 for dose-dependent parameters (AUC_{last}, AUC_{inf}, and C_{max}).

The above statistical analyses will be done using SAS® Proc Mixed. The following SAS® code will be used:

```
Proc Mixed;
   Model <ln_ Pk Param> = ln_dose;
   Estimate ln_dose/cl alpha=0.05;
Run;
```

Programmer Note: ***For the purpose of the analysis, dose will be represented by 1) the preset number of breaths and 2) the predicted delivered dose.*** *The model <LN_ PK PARAM> = LDOSE LDOSE2 /HTYPE=1 will first be used to test if the quadratic effect is significant where LDOSE = Ln (Dose) and LDOSE2 = [LDOSE]* ^{2}.

The relationship between ln-transformed PK parameter values versus ln-transformed dose will also be displayed graphically.

6.7.2 Analysis of variance

Analyses of variance (ANOVA) will be performed on the natural log (ln)-transformed PK parameters AUC_{last}, AUC_{inf}, and C_{max} using PROC MIXED of SAS® (Version 9.3 or higher). The ANOVA model will include sequence, treatment, and 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 at a 10% level of significance. Each ANOVA will include calculation of least-squares means (LSMs), differences between treatment LSMs, the standard error (SE) associated with this difference.

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

```
Proc Mixed data=<data>;
Class sequence period treatment subject;
Model <ln_PK parm>= sequence period treatment /ddfm=KR;
Random subject(sequence);
Estimate “Test A vs. Reference D” treatment 1 0 0 -1 /cl alpha=0.10 e;
Estimate “Test B vs. Reference D” treatment 0 1 0 -1 /cl alpha=0.10 e;
Estimate “Test C vs. Reference D” treatment 0 0 1 -1 /cl alpha=0.10 e;
Lsmeans treatment/cl;
Run;
```

Programmer Note: Sequence will not be included in the model if there is only one subject assigned to each sequence. In this case, the following SAS code will be used:

Proc Mixed data=<data>;
Class period treatment subject;
Model <ln_PK parm>= period treatment /ddfm=KR;
Random subject;
Estimate "Test A vs. Reference D" treatment 1 0 0 -1 /cl alpha=0.10 e;
Estimate "Test B vs. Reference D" treatment 0 1 0 -1 /cl alpha=0.10 e;
Estimate "Test C vs. Reference D" treatment 0 0 1 -1 /cl alpha=0.10 e;
Lsmeans treatment/cl;
Run;

6.7.3 Ratios of LSMs

Ratios of LSMs will be calculated using the exponentiation of the difference between treatment LSMs from the analyses on the ln-transformed AUC_{last}, AUC_{inf}, and C_{max}. These ratios will be expressed as a percentage relative to 1.0 mg/2 mL Pulmicort Respules.

The comparisons of interest are as follows:

- Treatments A, B, C versus Treatment D

7. EFFICACY ANALYSIS

7.1 Inhalation Checklist

On each dosing day, the site staff will record on the inhalation checklist the overall quality of the inhalation maneuvers.

Data from the inhalation checklist will include, but is not restricted to information regarding the following items:

- Did the subject inhale all the preset number of breaths / Did the subject complete nebulization for a duration of up to one minute?
- Number of Completed Breaths / Proportion of completed intended treatment time
- During each inhalation, did the subject inhale the whole time the compressor was operating?
- Quality of inhalation maneuvers (i.e., good seal between mouthpiece and mouth, proper start of nebulizer, comfortable inhalation).
- Effective use of inhalation system after training

The inhalation checklist data will be summarized on the Safety Set by treatment and overall. Frequency counts and percentages (i.e., of subjects included dosed by treatment) will be provided for categorical responses (i.e. Yes/No) and descriptive statistics (n, arithmetic mean, SD, minimum, median, and maximum) for continuous responses (i.e., number of breaths completed).

7.2 Duration of Treatment

The duration of inhalation will be summarized by treatment and overall using descriptive statistics (number of observations (n), arithmetic mean, standard deviation (SD), minimum, median, and maximum) for subjects included in the Safety Set. Duration of inhalation will be defined as the difference between the end and start time of inhalation and expressed in minutes. Duration will be presented in the listings with 2 decimal places in order to account for the seconds.

7.3 Modified Patient Satisfaction and Preference Questionnaire (mPASAPQ)

After each dosing, parent(s)/legal guardians will complete a modified Patient Satisfaction and Preference Questionnaire. The modified PASAPQ is based on the original 15-item validated version of the PASAPQ and has been adapted to assess nebulizer use (and for this trial excludes assessment of set-up and handling, as this is performed by trial staff). The answers are measured using a 7-point scale for questions 1 to 9 (1 means very dissatisfied and 7 means very satisfied) and a 100-point scale for Question 10. The first 8 questions generate the Total Score domain. Question 9 asks for the overall satisfaction with the device(s) used in the trial and Question 10 asks for willingness to continue with the device(s) used in the trial. Data from this questionnaire will be listed by subject and summarized by treatment. The results from questions 1 through 8 will be added for each subject to generate the Total Score (n = Q1+Q2+Q3+Q4+Q5+Q6+Q7+Q8) and expressed as percentage of maximum total score (i.e., (n/56)*100). The satisfaction and willingness scores will be defined as the results of Questions 9 and 10, respectively. Descriptive statistics will be provided for the total score, satisfaction score, willingness score, and the remaining individual questions by treatment for subjects included in the safety set.

8. SAFETY

All clinical safety data recorded in the case report form (CRF) data will be listed by subject and chronologically by visit. This will include rechecks, unscheduled assessments, and early termination.

Applicable continuous variables will be summarized using n, arithmetic mean, SD, minimum, median, and maximum. Frequency counts will be reported for categorical data when appropriate.

The level of precision will be presented as follows: minimum/maximum in the same precision as in the database, mean/median in one more precision level than

minimum/maximum, SD in one more precision level than mean/median, and n will be presented as an integer.

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

8.1 Subject Discontinuation

Subjects will be summarized by number of subjects dosed, completed, and discontinued the study with discontinuation reasons overall. Individual subject's dosing status for each treatment will be provided along with their study completion status and date.

8.2 Demographics and Baseline Characteristics

Descriptive statistics will be calculated for continuous variables (age (months), weight, height, and body mass index obtained at Screening) overall for subjects included in the Safety Set. In addition to the continuous summary, age will also be summarized categorically by age (years).

Frequency counts will be provided for categorical variables (race, ethnicity, and sex) overall for subjects included in the Safety Set.

Note: If BMI is not recorded in the source dataset, it will be computed for analysis using the following formula: weight (kg) / [height (m)]^2.

8.3 Medical, Surgical and Asthma History

All medical and surgical history collected during the study will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 20.0 and listed.

Asthma related histories recorded during the study will also be listed.

8.4 Adverse Events and Adverse Device Effects

All adverse events (AEs) and adverse device effects (ADEs) occurring during this clinical trial will be coded using MedDRA®, Version 20.0. An ADE is an AE that is considered related to the medical device by the Investigator. An AE of special interest (AESI) is an AE of scientific and medical concern specific to the sponsor's product. AESIs applicable to this study have been defined in the Investigator's Brochure. Vectura Limited ("Vectura") will review coding and identify AESIs at or prior to database lock.

All AEs (including ADEs and AESIs) captured in the database will be listed in by-subject data listings including verbatim term, coded term (system organ class [SOC] and preferred term [PT], treatment, severity, relationship to study drug, relationship to

study procedure, relationship to medical device and action; however, only treatment-emergent AEs (TEAEs) will be summarized for subject included in the Safety Set.

A TEAE is defined as an AE or ADE that is starting or worsening at the time of or after the start of study drug administration. An AE that occurs during the washout period between treatments will be considered treatment-emergent to the last treatment given. If an AE increases in severity, that AE will be given a resolution date and time and a new record will be initiated with the new severity. If the severity of an AE remains the same or decreases, the AE will be kept open through to resolution.

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

TEAEs will be tabulated by SOC and PT. Summary tables will include number of subjects reporting the TEAE and as percent of number of subjects dosed by treatment. The number of TEAEs will be tabulated in a similar manner. Tables which tabulate the number of TEAEs by severity, relationship to study drug and relationship to medical device will also be included.

AESIs will be summarized separately. AEs of special interests are:

- Infections: upper and lower respiratory tract infections; oropharyngeal candidiasis
- Upper respiratory tract: hoarseness, cough, throat irritation
- Eye disorders: media opacities including cataract, glaucoma, increased intraocular pressure
- Endocrine disorders: hypothalamic-pituitary-adrenal (HPA)-axis suppression

Serious adverse events (SAEs) and serious device effects (SADEs), if present will also be tabulated by SOC and PT with relationship to study treatment and medical device. Applicable narratives for SAEs, SADEs, and AESIs will be included in the CSR.

8.5 Vital Signs

Single measurements of blood pressure (systolic and diastolic), heart rate, respiratory rate, and temperature will be performed with subjects in a supine, semi-recumbent, or

seated position at Screening, pre-dose and 30 minutes after the start of nebulization on Days 1 (Treatment period 1) and 8 (± 3 days) (Treatment period 2).

All vital signs data will be listed by subject. Descriptive statistics will be reported for all vital signs measurements by treatment and time point. Change from baseline will be summarized in a similar way. Baseline is defined as the result closest and prior to first dosing in each treatment period, which may include unscheduled or recheck results. This will typically be the pre-dose measurement collected prior to dosing in each treatment period. Post-dose unscheduled events, rechecks, or early termination records will not be included in summaries.

8.6 Concomitant Medications

Concomitant medications will be distinguished between 'concomitant medications at randomization' and 'medications starting after randomization'. Concomitant medications at randomization are medications that started before the date of randomization and stopped after the date of randomization or remained ongoing at the end of the trial and medications starting after randomization are medications that started on or after the date of randomization.

All concomitant medications recorded during the study will be coded with the WHO Dictionary Version 01MAR2017 and listed.

8.7 Physical Examination

Full physical examinations will be performed at Screening and on Day 8 (± 3 days). Individual physical examination records will be listed by subject.

9. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

- The Total Set for analysis population will not be used because data for screening failures are not captured in the database. The number of screened subjects will be presented in the tables summarizing subject disposition. In the current study, all randomized subjects are to receive study drug.
- The Full Analysis Set (FAS), defined in the protocol as all subjects who provide evaluable data for the total score of the modified PASAPQ data will not be used for analysis. Summarization of the efficacy data will be based on the safety set instead.
- Although specified in the protocol, the modified PASAPQ performance score, defined as the summation of results from questions 1, 2, 6, and 7 will not be summarized in the efficacy analysis. The PASAPQ is originally a 15-item questionnaire with the performance domain assessed over 7 items. The mPASAPQ has 10 questions including only 4 from the performance domain of the PASAPQ, therefore it is not appropriate to define or analyze a performance domain. The 3 questions not included in the performance domain were dropped from mPASAPQ as not applicable to patient population & device under study.
- Although not specified in the protocol, the inhalation checklist and duration of treatment were added as efficacy endpoints and will be summarized by treatment.

- Although specified in the protocol, concomitant medications will not be summarized by treatment and overall.
- An additional PK parameter (t_{last}) was added that was not listed in the protocol.

10. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Council for Harmonization (ICH) structure but may be renumbered as appropriate during the compilation of the tables and figures for the report. All PK summary tables and figures will be generated using SAS® Version 9.3 or higher and/or using Phoenix® WinNonlin® Version 6.3 or higher for summary PK TFLs, as appropriate.

The following are lists of Safety and PK TFL numbers and titles that will be included within the report.

10.1 In-text Summary Tables and Figures

The following is a list of table and figure titles that will be included in the text of the report. Tables and figures will be numbered appropriately during compilation of the report.

Section 10:

Table 10-1 Disposition Summary

Section 11:

Table 11-1 Demographic Characteristics (Safety Set)

Table 11-2 Summary of Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer

Table 11-3 Dose Proportionality Assessment (Power Model) of Budesonide Pharmacokinetic Parameters with Dose Expressed as Number of Breaths Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System

Table 11-4 Dose Proportionality Assessment (Power Model) of Budesonide Pharmacokinetic Parameters with Predicted Doses of 16.2 µg, 29.4 µg, and 53.6 µg Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System

Table 11-5 Summary of Statistical Comparisons of Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System Versus 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer

Table 11-6 Summary of Inhalation Checklist (Treatments A – C) (Safety Set)

Table 11-7 Summary of Inhalation Checklist (Treatment D) (Safety Set)

Table 11-8 Summary of Treatment Duration (Safety Set)

Table 11-9 Summary of Modified Patient Satisfaction and Preference Questionnaire (Safety Set)

Figure 11-1 Arithmetic Mean Plasma Budesonide Concentration-Time Profiles Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer (Linear Scale)

Figure 11-2 Scatter Plot of Individual and Mean Plasma Budesonide ln(AUC_{last}) Versus ln(VR647 Dose) Expressed as Number of Breaths (Power Model)

Figure 11-3 Scatter Plot of Individual and Mean Plasma Budesonide ln(AUC_{last}) Versus ln(VR647 Dose) Expressed as Predicted Doses (Power Model)

Figure 11-4 Scatter Plot of Individual and Mean Plasma Budesonide ln(AUC_{inf}) Versus ln(VR647 Dose) Expressed as Number of Breaths (Power Model)

Figure 11-5 Scatter Plot of Individual and Mean Plasma Budesonide ln(AUC_{inf}) Versus ln(VR647 Dose) Expressed as Predicted Doses (Power Model)

Figure 11-6 Scatter Plot of Individual and Mean Plasma Budesonide ln(C_{max}) Versus ln(VR647 Dose) Expressed as Number of Breaths (Power Model)

Figure 11-7 Scatter Plot of Individual and Mean Plasma Budesonide ln(C_{max}) Versus ln(VR647 Dose) Expressed as Predicted Doses (Power Model)

Section 12:

Table 12-1 Overall Summary of Adverse Events (Safety Set)

Table 12-2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Set)

10.2 Section 14 Summary Tables and Figures

The following is a list of table and figure titles that will be included in Section 14 of the report.

14.1 Demographic Data Summary Tables

Table 14.1.1 Disposition Summary
Table 14.1.2 Subject Disposition and Analysis Set
Table 14.1.3 Demographic Characteristics (Safety Set)

14.2 Pharmacokinetic and Efficacy Data Summary Tables and Figures

14.2.1.1 Budesonide Concentration Tables

Table 14.2.1.1.1 Plasma Budesonide Concentrations (pg/mL) Following Single Oral Inhalations of 5 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System (Treatment A)
Table 14.2.1.1.2 Plasma Budesonide Concentrations (pg/mL) Following Single Oral Inhalations of 10 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System (Treatment B)
Table 14.2.1.1.3 Plasma Budesonide Concentrations (pg/mL) Following Single Oral Inhalations of 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System (Treatment C)
Table 14.2.1.1.4 Plasma Budesonide Concentrations (pg/mL) Following a Single Dose of 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer (Treatment D)

14.2.1.2 Budesonide PK Tables

Table 14.2.1.2.1 Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 5 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System (Treatment A)
Table 14.2.1.2.2 Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 10 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System (Treatment B)
Table 14.2.1.2.3 Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 20 Breaths of VR647 Inhalation

Suspension Delivered by the VR647 Inhalation System (Treatment C)

Table 14.2.1.2.4 Plasma Budesonide Pharmacokinetic Parameters Following a Single Dose of 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer (Treatment D)

Table 14.2.1.2.5 Intervals (Hours) Used for Determination of Plasma Budesonide Lambda z Values Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer

Table 14.2.1.2.6 Dose Proportionality Assessment (Power Model) of Budesonide Pharmacokinetic Parameters with Dose Expressed as Number of Breaths Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System

Table 14.2.1.2.7 Dose Proportionality Assessment (Power Model) of Budesonide Pharmacokinetic Parameters with Predicted Doses of 16.2 µg, 29.4 µg, and 53.6 µg Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System

Table 14.2.1.2.8 Summary of Statistical Comparisons of Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System Versus 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer

14.2.2 Budesonide Figures

Figure 14.2.2.1 Arithmetic Mean (±SD) Plasma Budesonide Concentration-Time Profiles Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer (Linear Scale)

Figure 14.2.2.2 Arithmetic Mean Plasma Budesonide Concentration-Time Profiles Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer (Linear Scale)

Figure 14.2.2.3 Arithmetic Mean Plasma Budesonide Concentration-Time Profiles Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer (Semi-Log Scale)

Figure 14.2.2.4 Scatter Plot of Individual and Mean Plasma Budesonide ln(AUC_{last}) Versus ln(VR647 Dose) Expressed as Number of Breaths (Power Model)

Figure 14.2.2.5 Scatter Plot of Individual and Mean Plasma Budesonide ln(AUC_{last}) Versus ln(VR647 Dose) Expressed as Predicted Doses (Power Model)

Figure 14.2.2.6 Scatter Plot of Individual and Mean Plasma Budesonide ln(AUC_{inf}) Versus ln(VR647 Dose) Expressed as Number of Breaths (Power Model)

Figure 14.2.2.7 Scatter Plot of Individual and Mean Plasma Budesonide ln(AUC_{inf}) Versus ln(VR647 Dose) Expressed as Predicted Doses (Power Model)

Figure 14.2.2.8 Scatter Plot of Individual and Mean Plasma Budesonide ln(C_{max}) Versus ln(VR647 Dose) Expressed as Number of Breaths (Power Model)

Figure 14.2.2.9 Scatter Plot of Individual and Mean Plasma Budesonide ln(C_{max}) Versus ln(VR647 Dose) Expressed as Predicted Doses (Power Model)

14.2.3 Efficacy Tables

Table 14.2.3.1.1 Summary of Inhalation Checklist (Treatments A – C) (Safety Set)

Table 14.2.3.1.2 Summary of Inhalation Checklist (Treatment D) (Safety Set)

Table 14.2.3.2 Summary of Treatment Duration (Safety Set)

Table 14.2.3.3 Summary of Modified Patient Satisfaction and Preference Questionnaire (Safety Set)

14.3 Safety Data Summary Tables

14.3.1 Displays of Adverse Events

Table 14.3.1.1 Overall Summary of Adverse Events (Safety Set)

Table 14.3.1.2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Set)

Table 14.3.1.3 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Safety Set)

Table 14.3.1.4 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Device (Safety Set)

Table 14.3.1.5 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Safety Set)

Table 14.3.1.6 Treatment-Emergent Adverse Events of Special Interest by System Organ Class and Preferred Term (Safety Set)

Table 14.3.1.7 Treatment-Emergent Adverse Events of Special Interest by System Organ Class, Preferred Term and Relationship to Study Drug (Safety Set)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Table 14.3.2.1 Serious Adverse Events (Safety Set) <if no serious adverse event occurred, a statement 'No serious adverse events were reported.>

Table 14.3.2.2 Serious Adverse Device Effects (Safety Set) <if no serious adverse device effects occurred, a statement 'No serious adverse device effects were reported.>

Table 14.3.2.3 Adverse Events Leading to Withdrawal (Safety Set) <if no adverse events leading to withdrawal occurred, a statement 'No adverse events leading to withdrawal were reported.>

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

14.3.4. Displays of Vital Signs and Other Safety Data

Table 14.3.4.1 Vital Signs Results by Time-point (Safety Set)

10.3 Section 16 Data Listings

Data listings are numbered following the ICH structure but may be renumbered as appropriate during the compilation of the tables and figures for the report. The following is a list of appendix numbers and titles that will be included as data listings:

16.2. Subject Data Listings

16.2.1. Subject Discontinuation

Appendix 16.2.1 Subject Disposition

16.2.2. Protocol Deviations

Appendix 16.2.2 Protocol Deviations

16.2.3. Subjects Excluded from Pharmacokinetic/Efficacy Analysis

Appendix 16.2.3.1 Subjects Excluded from Pharmacokinetic Analysis

Appendix 16.2.3.2 Subjects Excluded from Efficacy Analysis

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

16.2.4. Demographic Data

Appendix 16.2.4.1 Demographics

Appendix 16.2.4.2 Medical and Surgical History

Appendix 16.2.4.3 Asthma History

16.2.5. Compliance and Drug Concentration Data

Appendix 16.2.5.1.1 Inclusion Criteria

Appendix 16.2.5.1.2 Inclusion Responses

Appendix 16.2.5.2.1 Exclusion Criteria

Appendix 16.2.5.2.1 Exclusion Responses

Appendix 16.2.5.3 Randomization

Appendix 16.2.5.4.1 Nebulization

Appendix 16.2.5.4.2 Dosing

Appendix 16.2.5.4.3 Inhalation Checklist

Appendix 16.2.5.5 Modified Patient Satisfaction and Preference Questionnaire (mPASAPQ)

Appendix 16.2.5.6 Prior and Concomitant Medications

Appendix 16.2.5.7 Overnight Stay and Discharge From Site

Appendix 16.2.5.8 Follow-Up

16.2.6. Individual Concentration Versus Time Data

Appendix 16.2.6.1 PK Blood Sampling

Appendix 16.2.6.2 Individual Plasma Budesonide Concentration Versus Time for Subject # (Linear and Semi-log Scale) – Sequence ##

16.2.7. Individual Adverse Event Listings

Appendix 16.2.7.1.1 Adverse Events (I of II)
Appendix 16.2.7.1.2 Adverse Events (II of II)
Appendix 16.2.7.2 Adverse Event Preferred Term Classification

16.2.8. Individual Laboratory Measurements and Other Safety Observations

Appendix 16.2.8.1 Physical Examination
Appendix 16.2.8.2 Vital Signs
Appendix 16.2.8.3 Vital Signs Change From Baseline

11. TABLE SHELLS

The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables that will be presented and included in the final report. Unless otherwise noted, all tables will be presented in Times New Roman font size 8. These tables will be generated off of the Celerion ADaM Model 2.1 and ADaM Implementation Guide 1.1.

11.1 In-Text Table Shells

Table 10-1 Disposition Summary

.

Disposition	Overall
Screened	XX
Randomized	XX
Treated	XX
Safety Set	XX (XX%)
PK Set	XX (XX%)
Completed Study	XX (XX%)
Discontinued Study	XX (XX%)
Reason 1	X (X%)
Reason 2	X (X%)
Etc.	X (X%)

Percentages are based on the number of subjects that were randomized in the trial.
Safety Set: All randomized and treated subjects who received at least one dose of study medication.
PK Set: All subjects who received at least one dose of study medication, complied sufficiently with the protocol, and displayed an evaluable PK profile.

Source: Table 14.1.1, Appendix 16.2.1

Table 11-1 Demographic Characteristics (Safety Set)

Trait	Category/Statistics	A N=XX	B N=XX	C N=XX	D N=XX	Overall N=XX
Sex [n (%)]	Female	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Male	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Race [n (%)]	Asian	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Black or African American	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	White	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Ethnicity [n (%)]	Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Not Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Age (years) [n (%)]	4	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	5	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	6	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	7	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	8	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Age (months)	n	XX	XX	XX	XX	XX
	Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer
N= Number of subjects dosed. Percentages are based on the number of subjects dosed per treatment.
Age is recorded in the CRF.

Source: Table 14.1.3, Appendix 16.2.4.1

Programmer Note: Weight (kg), Height (cm), and BMI (kg/m²) will be also summarized in the table above. If BMI is not recorded in the source dataset, it will be computed for analysis using the following formula: weight (kg) / [height (m)] 2. A categorical summary of age (in years) will also be included in the table. Given that this study is a crossover study, the same subjects may be counted within two different treatment columns.

Table 11-2 Summary of Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer

	Mean ± SD			
	Treatment A VR647 5 breaths (n=X)[a]	**Treatment B VR647 10 breaths (n=X)**	**Treatment C VR647 20 breaths (n=X)**	**Treatment D 1.0 mg/2 mL Pulmicort Respules (n=X)**
Param1 (units)	XXX ± XX.X	XXX ± XX.X	XXX ± XX.X	XXX ± XX.X
Param1 (units)	XX (XX, XX)	XX (XX, XX)	XX (XX, XX)	XX (XX, XX)
Param1 (units)	XXX (XXX, XXX)	XXX (XXX, XXX)	XXX (XXX, XXX)	XXX (XXX, XXX)
Param1 (units)	XXX ± XX.X	XXX ± XX.X	XXX ± XX.X	XXX ± XX.X
Param1 (units)	XXX ± XX.X	XXX ± XX.X	XXX ± XX.X	XXX ± XX.X
Param1 (units)	XXX ± XX.X	XXX ± XX.X	XXX ± XX.X	XXX ± XX.X

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer

NC = Not calculated
t_{max} is presented as median (minimum, maximum). Otherwise, values are presented as mean ± SD.
[a] n = <X> for <parameters>.

Source: Tables 14.2.1.2.1 through 14.2.1.2.4
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

Notes for Generating the Actual Table:

Programmer's note:

- The following PK parameters will be presented in the following order: AUC_{last}(pg*hr/mL) AUC_{inf}(pg*hr/mL), $AUC_{\%extrap}$, C_{max}(pg/mL) , t_{max}(hr), t_{last} (hr), and $t_{½}$(hr). Additional PK parameters might be presented if deemed necessary (ask the PKist)
- Summary statistics will be presented with same precision as defined in post-text shells
- Please use ITPar1 internal template
- The following changes are made to this table relative to Celerion standard: 4 treatments (for Treatments A through D) will be presented in Table 11-2. In addition, if "n" column as per the template can be added for all treatments and the table can fit one page then that is a better option, else report "n" as reported in this table.

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

Tables 11-3 and 11-4 will be similar to this format.

Table 11-3 Dose Proportionality Assessment (Power Model) of Budesonide Pharmacokinetic Parameters with Dose Expressed as Number of Breaths Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System

Pharmacokinetic Parameter	Slope (b)	Standard Error	95% Confidence Interval for Slope
AUC_{last} (pg*hr/mL)	XXXX	XXXX	(XXXX , XXXX)
AUC_{inf} (pg*hr/mL)	XXXX	XXXX	(XXXX , XXXX)
C_{max} (pg/mL)	XXXX	XXXX	(XXXX , XXXX)
Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System Parameters were ln-transformed prior to analysis. The following statistical model using PROC MIXED of SAS was used to test dose proportionality: Parameter = a * Dose^b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)] Dose proportionality was not rejected if the 95% confidence interval for the slope included the value of 1 Source: Table 14.2.1.2.7 Program: /CAXXXXX/sas_prg/pksas/adam_intext_<program name> DDMMMYYYY HH:MM			

Programmer's Note:

- Slope will be presented to 4 decimal places
- Standard error will be presented to 4 decimal places
- 95% CI will be presented to 4 decimal places

The PK parameters will be AUC_{last}, AUC_{inf}, and C_{max}.

Table 11-5 Summary of Statistical Comparisons of Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System Versus 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer

Parameter	Geometric LSMs				Geometric Mean Ratio (%)	Intra-Subject CV%
	Treatment A	n	Treatment D	n		
AUC_{last} (pg*hr/mL)	XXXX	x	XXXX	x	XX.XX	X.XX
AUC_{inf} (pg*hr/mL)	XXXX	x	XXXX	x	XX.XX	X.XX
C_{max} (pg/mL)	XXXX	x	XXXX	x	XX.XX	X.XX
	Treatment B		**Treatment D**			
AUC_{last} (pg*hr/mL)	XXXX	x	XXXX	x	XX.XX	X.XX
AUC_{inf} (pg*hr/mL)	XXXX	x	XXXX	x	XX.XX	X.XX
C_{max} (pg/mL)	XXXX	x	XXXX	x	XX.XX	X.XX
	Treatment C		**Treatment D**			
AUC_{last} (pg*hr/mL)	XXXX	x	XXXX	x	XX.XX	X.XX
AUC_{inf} (pg*hr/mL)	XXXX	x	XXXX	x	XX.XX	X.XX
C_{max} (pg/mL)	XXXX	x	XXXX	x	XX.XX	X.XX

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer

Parameters were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from the ANOVA.
% Geometric Mean Ratio (GMR) = 100*(test/reference)
Intra-subject CV% was calculated as 100 x square root(exp[MSE-1]). MSE = Residual variance from ANOVA.

Subject X was removed for the statistical analysis because <insert reason>

Source: Table 14.2.1.2.6
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

Notes for Generating the Actual Table:

Presentation of Data:

- The PK parameters will be as per the one presented in the above table
- n will be presented as an integer (with no decimal)
- Please use ITPStat1 internal template
- All statistics will be presented with same precision as defined in post-text shells
- Please use ITPStat1 internal template

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

Table 11-6 Summary of Inhalation Checklist (Treatments A – C) (Safety Set)

Quality Assessment*	Response/ Statistic	Treatment			Overall N=XX
		A N=XX	B N=XX	C N=XX	
Q1	Yes	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	No	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Q1A	n	XX	XX	XX	XX
	Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
	Median	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX
Q2	Yes	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	No	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Q3	Yes	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	No	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Q4	Yes	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	No	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Q5	Yes	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	No	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
N = Number of subjects dosed. Percentages are based on the number of subjects dosed per treatment.
* Quality Assessment:
Q1 = Did the subject inhale all the present number of breaths?
Q1A = If no, number of breaths completed?
Q2 = During each inhalation, did the subject inhale the whole time the compressor was operating?
Q3 = Did the subject achieve a good seal between the mouthpiece and the mouth while they were inhaling?
Q4 = On each inhalation, was the subject able to start the nebulizer correctly?
Q5 = Was the subject able to inhale comfortably during nebulization?

Source: Table 14.2.3.1.1, Appendix 16.2.5.4.2, 16.2.5.4.3

Table 11-7 Summary of Inhalation Checklist (Treatment D) (Safety Set)

Quality Assessment*	Response	Treatment D N=XX
Q1	Yes	XX (XX%)
	No	XX (XX%)
Q1A	≤25%	XX (XX%)
	>25 - ≤50%	XX (XX%)
	>75% - ≤100%	XX (XX%)
Q3	Yes	XX (XX%)
	No	XX (XX%)
Q5	Yes	XX (XX%)
	No	XX (XX%)

Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer
N = Number of subjects dosed. Percentages are based on the number of subjects dosed per treatment.
* Quality Assessment:
Q1 = Did the subject complete dosing?
Q1A = If no, proportion of the intended treatment time completed?
Q3 = Did the subject achieve a good seal between the mouthpiece and the mouth while they were inhaling?
Q5 = Was the subject able to inhale comfortably during nebulization?

Source: Table 14.2.3.1.2, Appendix 16.2.5.4.2, 16.2.5.4.3

Table 11-8 Summary of Treatment Duration (Safety Set)

Assessment	Statistic	Treatment				Overall N=XX
		A N=XX	B N=XX	C N=XX	D N=XX	
Duration (min)	n	XX	XX	XX	XX	XX
	Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer
N = Number of subjects dosed.
Duration is computed as the difference between the end and start time of inhalation and is summarized in minutes and reported with 2 decimal places.

Source: Table 14.2.3.2, Appendix 16.2.5.4.1

Table 11-9 Summary of Modified Patient Satisfaction and Preference Questionnaire (Safety Set)

Assessment*	Statistic	Treatment				
		A N=XX	A N=XX	A N=XX	A N=XX	Treatment
Total Score (%)	n	XX	XX	XX	XX	XX
	Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Satisfaction Score	n	XX	XX	XX	XX	XX
	Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Willingness Score	n	XX	XX	XX	XX	XX
	Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
…	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer
N = Number of subjects dosed.
* As a parent/legal guardian observing your child in the trial, how satisfied are you: Q1. That the nebulizer works correctly? ; Q2. With the ease of inhaling a dose form the nebulizer? ; Q3. With the training provided? ; Q4. With the size of the nebulizer control unit and handset? ; Q5. That the nebulizer looks durable (hard wearing)? ; Q6. With using the nebulizer? ; Q7. With the overall treatment time? ; Q8. With the ease of holding the nebulizer during use? ; Q9. Overall, how satisfied are you with the nebulizer (i.e. satisfaction score)? ; Q10. Please indicate how willing you would be for your child to use the nebulizer used during the study by providing a number between 0 and 100 (i.e., Willingness score).
Questions 1 to 9 were answered using scores from 1 (i.e., very dissatisfied) to 7 (i.e., very satisfied).
Total Score = (Q1+Q2+Q3+Q4+Q5+Q6+Q7+Q8)/56)*100

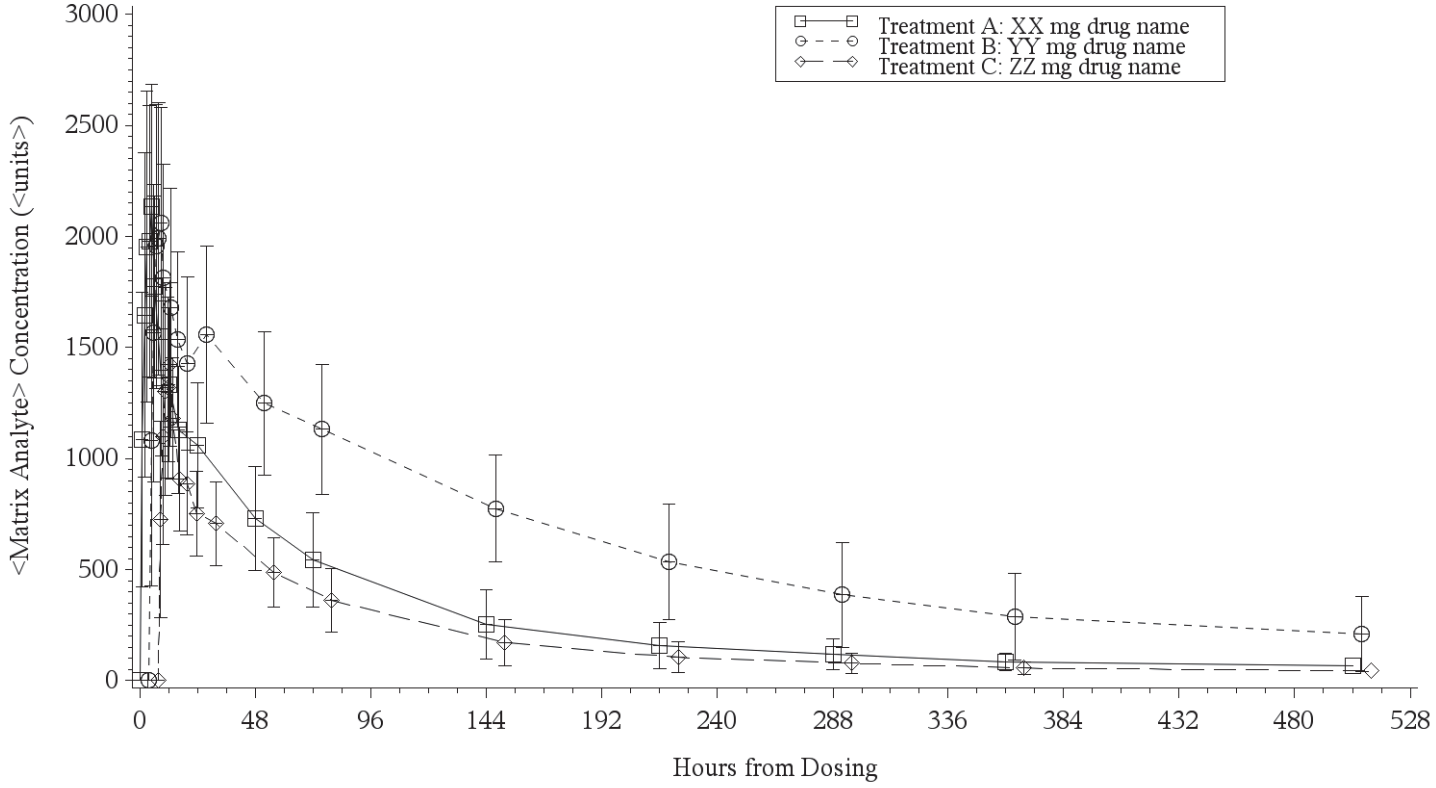
Source: Table 14.2.3.3, Appendix 16.2.5.5

Programmer Note: Questions 1 through 8 will also be summarized individually in this table.

Example of Standard PK Figure Shells

Figure PFPConc1

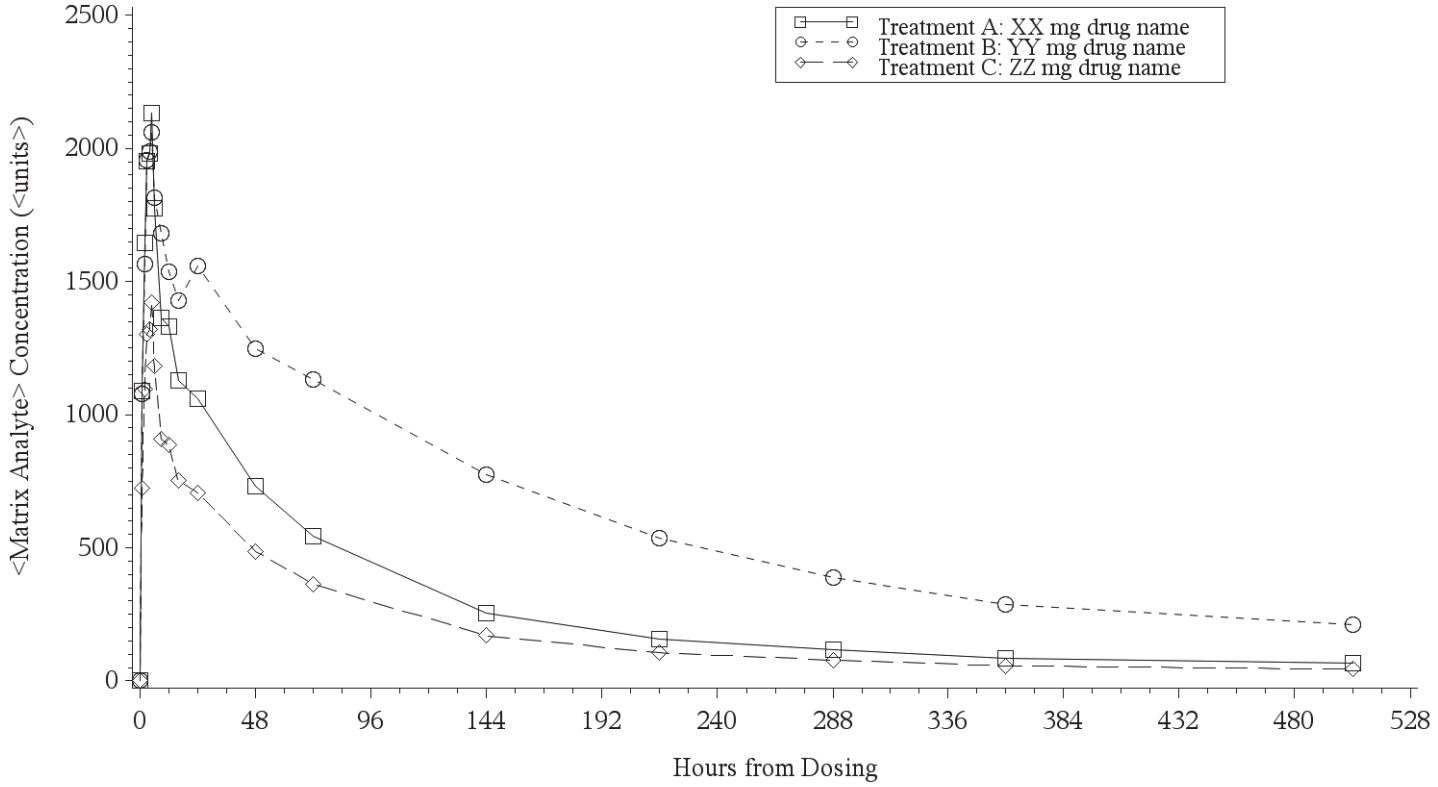
Figure 14.2.2.1 Arithmetic Mean (±SD) Plasma Budesonide Concentration-Time Profiles Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer (Linear Scale)



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

Figure PFPConc2

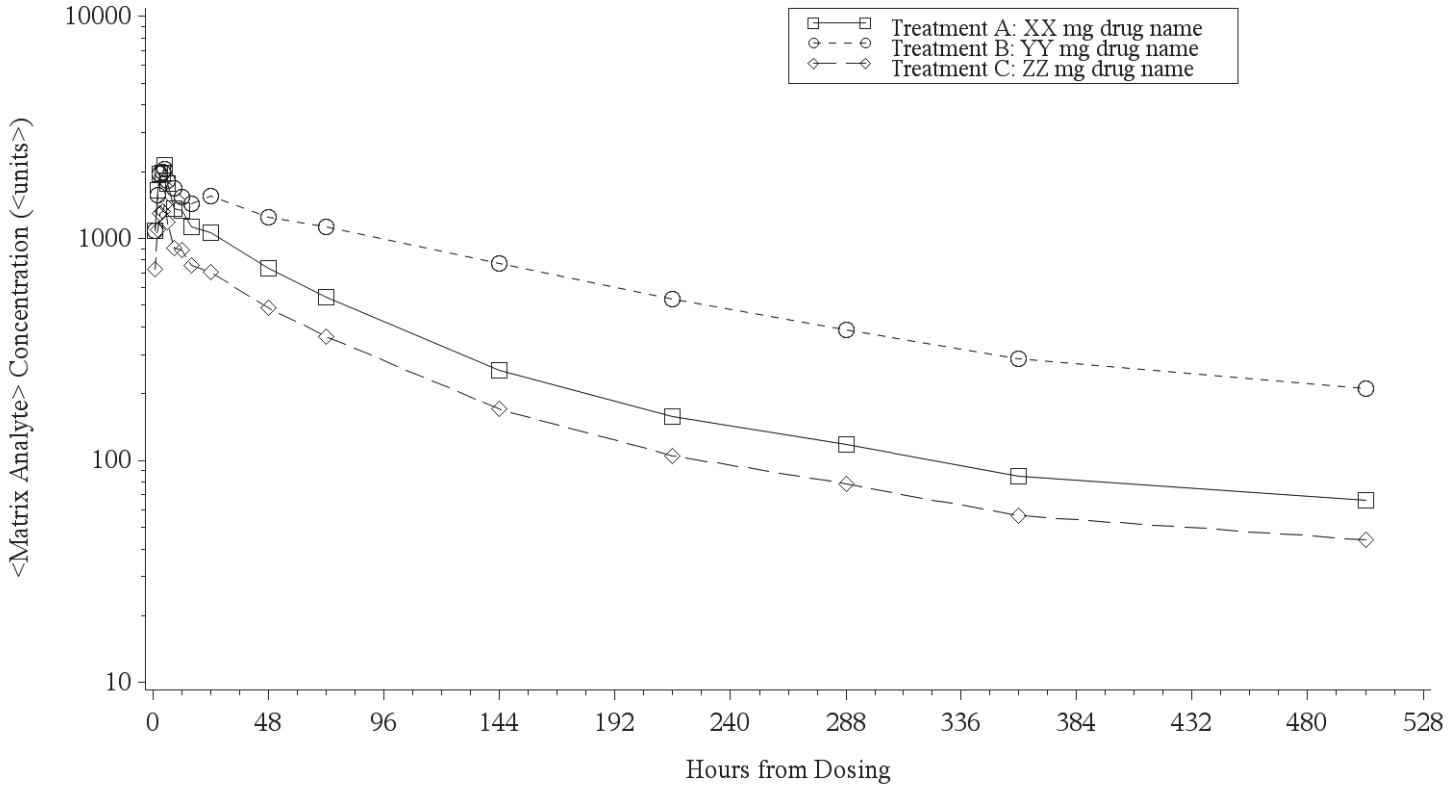
Figure 14.2.2.2 Arithmetic Mean Plasma Budesonide Concentration-Time Profiles Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer (Linear Scale)



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

Figure PFPConc3

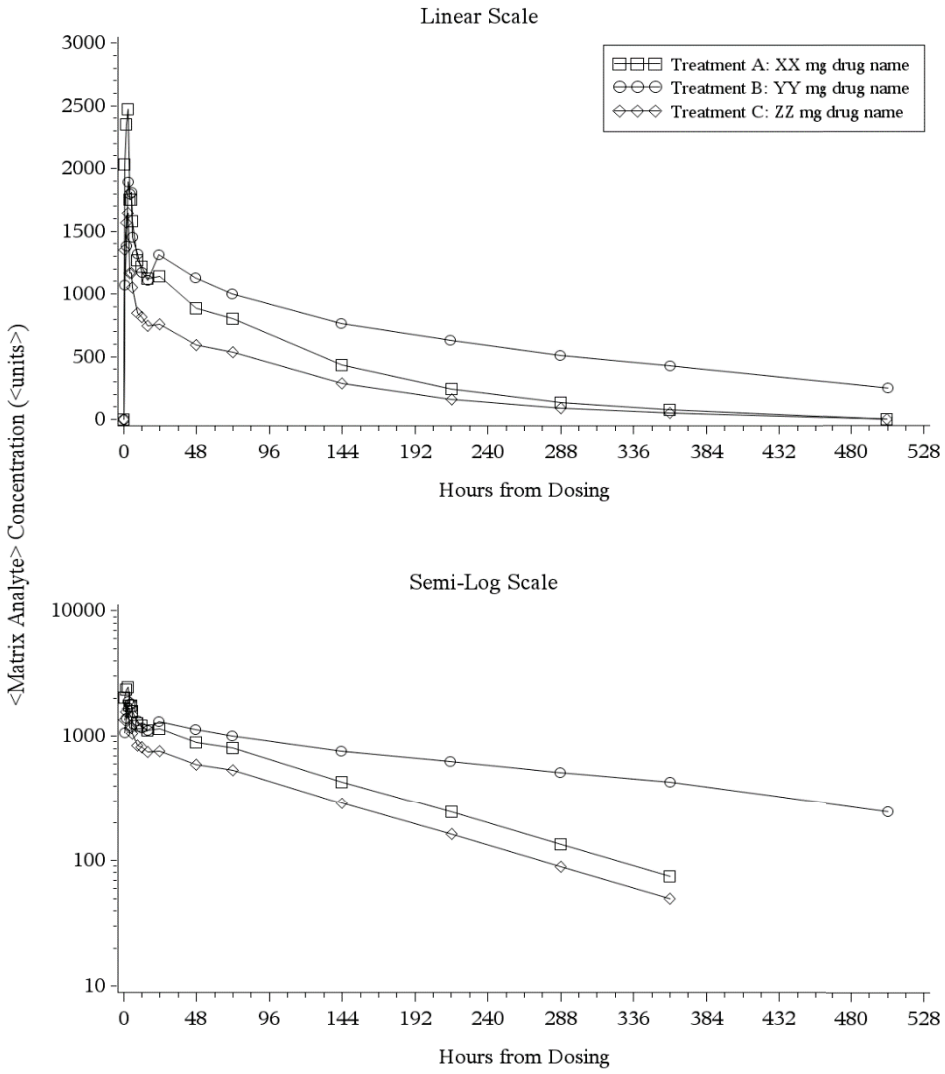
Figure 14.2.2.3 Arithmetic Mean Plasma Budesonide Concentration-Time Profiles Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer (Semi-Log Scale)



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

Figure PFPConc5

Appendix 16.2.6.2 Individual Plasma Budesonide Concentration Versus Time for Subject # (Linear and Semi-log Scale) – Sequence xx



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

Table 12-1 Overall Summary of Adverse Events (Safety Set)

Adverse Event Category [n (%) m]	Treatment				Total (N=XX)
	A (N=XX)	B (N=XX)	C (N=XX)	D (N=XX)	
Any AEs	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any TEAEs	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Drug-Related TEAEs	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Device-Related TEAEs	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Serious AEs	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Serious TEAEs	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Serious Drug-Related TEAEs	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Serious Device-Related TEAEs	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any TEAEs Leading to Withdrawal	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Serious TEAEs Leading to Withdrawal	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Drug-Related TEAEs Leading to Withdrawal	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Device-Related TEAEs Leading to Withdrawal	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any TEAEs of Special Interest	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Serious TEAEs of Special Interest	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Any Drug-Related TEAEs of Special Interest	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer
n = Number of subjects with TEAE, m= Number of events, N= Number of dosed subjects, TEAE = Treatment-emergent adverse event
For each category, subjects are included only once, even if they experienced multiple events in that category.

Source: Table 14..3.1.1

Table 12-2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Set)

System Organ Class Preferred Term [n (%) m]	Treatment				Total (N=XX)
	A (N=XX)	B (N=XX)	C (N=XX)	D (N=XX)	
System Organ Class 1	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Preferred term 1	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX
Etc.	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX	X (X%) XX

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer
n = Number of subjects with treatment-emergent adverse events, m= Number of events, N= Number of dosed subjects
Adverse events are classified according to MedDRA Version 20.0.
For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term.

Source: Table 14..3.1.2

Programmer Note: Sort by decreasing frequency in the total arm for SOC and preferred term within SOC.

11.2 Post-Text Table Shells

Programmer Note:

1. All post-text tables need to be in rtf format.
2. AEs of special interests are:
   Infections: upper and lower respiratory tract infections; oropharyngeal candidiasis
   Upper respiratory tract: hoarseness, cough, throat irritation
   Eye disorders: media opacities including cataract, glaucoma, increased intraocular pressure
   Endocrine disorders: hypothalamic-pituitary-adrenal (HPA)-axis suppression

Table 14.1.1 Disposition Summary

Disposition	Overall
Screened	XX
Randomized	XX
Treated	XX
Safety Set	XX (XX%)
PK Set	XX (XX%)
Completed Study	XX (XX%)
Discontinued Early	XX (XX%)
<Reason 1>	XX (XX%)
<Reason 2>	XX (XX%)

Percentages are based on the number of subjects that were randomized in the trial.
Safety Set: All randomized and treated subjects who received at least one dose of study medication.
PK Set: All subjects who received at least one dose of study medication, complied sufficiently with the protocol, and displayed an evaluable PK profile.

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.1.2 Subject Disposition and Analysis Set

Subject Number	Product Sequence	Treatment Administered A	B	C	D	Study Completion Status	Date	Set PK	Safety
X	XXXXXX	Yes	No	No	No	Terminated Study Prematurely	DDMMMYYYY	Yes	Yes
X	XXXXXX	Yes	Yes	Yes	Yes	Completed Study	DDMMMYYYY	Yes	Yes
X	XXXXXX	Yes	No	No	Yes	Completed Study	DDMMMYYYY	Yes	Yes
X	XXXXXX	Yes	No	Yes	No	Completed Study	DDMMMYYYY	Yes	Yes
X	XXXXXX	Yes	Yes	No	No	Completed Study	DDMMMYYYY	Yes	Yes
X	XXXXXX	No	Yes	Yes	No	Completed Study	DDMMMYYYY	Yes	Yes
X	XXXXXX	No	Yes	No	Yes	Completed Study	DDMMMYYYY	Yes	Yes
X	XXXXXX	Yes	No	Yes	No	Completed Study	DDMMMYYYY	Yes	Yes
X	XXXXXX	No	Yes	Yes	No	Completed Study	DDMMMYYYY	Yes	Yes
XX	XXXXXX	No	Yes	No	Yes	Completed Study	DDMMMYYYY	Yes	Yes
		XX	XX	XX	XX				

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer
Safety Set: All randomized and treated subjects who received at least one dose of study medication.
PK Set: All subjects who received at least one dose of study medication, complied sufficiently with the protocol, and displayed an evaluable PK profile.

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.1.3 Demographic Characteristics (Safety Set)

Trait	Category/ Statistics	Treatment A N=XX	B N=XX	C N=XX	D N=XX	Overall N=XX
Sex [n (%)]	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Male	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Race [n (%)]	Asian	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Black or African American	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	White	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Ethnicity [n (%)]	Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Not Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Age (years) [n (%)]	4	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	5	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	6	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	7	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	8	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Age (months)	n	X	X	X	X	X
	Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Programmer Note: Also include Weight (kg), Height (cm), and BMI (kg/m²) in the table above. If BMI is not recorded in the source dataset, it will be computed for analysis using the following formula: weight (kg) / [height (m)] 2. A categorical summary of age (in years) will also be included in the table. Given that this study is a crossover study, the same subjects may be counted in two different treatment columns.

<Add treatment descriptions>
N = Number of subjects dosed
Age is recorded in the CRF.

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Tables 14.2.1.1.1 through 14.2.1.1.4 will be formatted according to the following shell.

Table 14.2.1.1.1 Plasma Budesonide Concentrations (pg/mL) Following Single Oral Inhalations of 5 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System (Treatment A)

			Sampling Time (hr)								
Subject Number	Treatment Sequence	Study Period	Pre-dose	XX	XX	XX	XX	XX	XX	XX	XX
X	XX	X	BLQ	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
X	XX	X	BLQ	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
X	XX	X	BLQ	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
X	XX	X	BLQ	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
X	XX	X	BLQ	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
X	XX	X	BLQ	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
n			XX	XX	XX	XX	XX	XX	XX	XX	XX
Mean			XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
SD			XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX
CV%			.	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX
Minimum			XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
Median			XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X	XXX.X
Maximum			XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 0 before the first quantifiable concentration. BLQ values were set equal to the lower limit of quantitation (LLOQ) of <xx> if falls between two quantifiable concentrations and to missing thereafter.
. = Value missing or not reportable.
* = Subject excluded from summary statistics due to not completing the study.

Notes for Generating the Actual Table:

PK Time points are presented in Section 6.1.
Please see text (Section 6.6) for description of significant figures/decimals to be used for descriptive statistics.
Template to be used CPConc1.

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

Client has request the following format to present:
Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Tables 14.2.1.2.1 through 14.2.1.2.4 will be formatted according to the following shell.

Table 14.2.1.2.1 Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 5 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System (Treatment A)

			Parameters					
Subject Number	Treatment Sequence	Study Period	Param1 (units)	Param2 (units)	Param3 (units)	Param4 (units)	Param5 (units)	Param6 (units)
X	XX	X	XXXX	X.XX	XXX	XXXX	XX.X	X.XXXX
X	XX	X	XXXX	X.XX	XXX	XXXX	XX.X	X.XXXX
X	XX	X	XXXX	X.XX	XXX	XXXX	XX.X	X.XXXX
X	XX	X	XXXX	X.XX	XXX	XXXX	XX.X	X.XXXX
n			XX	XX	XX	XX	XX	XX
Mean			XXXX.X	X.XXX	XXXX.X	XXXX.X	XX.XX	X.XXXXX
SD			XX.XXXX	X.XXXX	XX.XXXX	XX.XXXX	XX.XXX	X.XXXXXX
CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XX.XXXX	X.XX	XX.XXXX	XX.XXXX	XX.XXX	X.XXXXXX
Minimum			XXXX	X.XXX	XXXX	XXXX	XX.X	X.XXXX
Median			XXXX.X	X.XX	XXXX.X	XXXX.X	XX.XX	X.XXXXX
Maximum			XXXX	X.XXX	XXXX	XXXX	XX.X	X.XXXX
Geom Mean			XXXX.X	XXXX.X	XXXX.X	XXXX.X	XXXX.X	XXXX.X
Geom CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

NC = Not calculated.
. = Value missing or not reportable.

Notes for Generating the Actual Table:

The following PK parameters will be presented in the following order: A AUC_{last}(pg*hr/mL) AUC_{inf}(pg*hr/mL), $AUC_{\%extrap}$, C_{max}(pg/mL), t_{max}(hr), t_{last} (hr), and $t_{½}$(hr). Additional PK parameters might be presented if deemed necessary (ask the PKist)
See Section 6.6 for the precision of the individual and summary statistics.

Template to be used CPPar1

Program: /CAXXXXX/sas prg/pksas/pk-tables.sas
Program: /CAXXXXX/sas prg/pksas/adam pkparam.sas

Client has request the follow format to present:
Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.2.1.2.5 Intervals (Hours) Used for Determination of Plasma Budesonide Lambda z Values Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System and 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer

Subject Number	Treatment	Interval	R2	n
X	A	XX.X - XX.X	X.XXX	X
X	B	XX.X - XX.X	X.XXX	X
X	C	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer

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

Notes for Generating the Actual Table:

Presentation of Data:
Interval start and stop times will be presented to 1 decimal or 3 sig figures;
R^2 will be presented to 3 decimals;
n will be presented as an integer (with no decimal)

Template to be used CPKel2
Program: /CAXXXXX/sas_prg/pksas/kel-tables-parallel.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_kel.sas DDMMMYYYY HH:MM
Client has request the follow format to present:
Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Tables 14.2.1.2.6 and 14.2.1.2.7 will be formatted according to the following shell.

Table 14.2.1.2.6 Dose Proportionality Assessment (Power Model) of Budesonide Pharmacokinetic Parameters with Dose Expressed as Number of Breaths Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System

Pharmacokinetic Parameters	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
Param1	X.XXXX	X.XXXX	X.XXXX - X.XXXX
Param2	X.XXXX	X.XXXX	X.XXXX - X.XXXX
Param3	X.XXXX	X.XXXX	X.XXXX - X.XXXX

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System

Presentation of Data:

- Slope will be presented to 4 decimal places
- Standard error will be presented to 4 decimal places
- 95% CI will be presented to 4 decimal places

Notes for Generating the Actual Table:

Programmers Note:
PK Parameters are AUC_{last}, AUC_{inf}, and C_{max}.

Biostat Note:
Please use the footnote below if it is power model:
Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality: Parameter = a * Dose^b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b included the value of 1.

Program: **/CAXXXXX/sas_prg/pksas/**doseprop-mixed.sas DDMMMYYYY HH:MM
Program: **/CAXXXXX/sas_prg/pksas/**adam_dosepropmixed.sas DDMMMYYYY HH:MM

Page x of y

Table 14.2.1.2.8 will be formatted according to the following shell.

Table 14.2.1.2.8 Summary of Statistical Comparisons of Plasma Budesonide Pharmacokinetic Parameters Following Single Oral Inhalations of 5, 10 and 20 Breaths of VR647 Inhalation Suspension Delivered by the VR647 Inhalation System Versus 1 mg/2 mL Pulmicort Respules Delivered by the Conventional Jet Nebulizer

		Treatment ------- Geometric LSMs -------				Geometric Mean Ratio	Intra-subject
Parameter	(unit)	Treatment A (Test)	(n)	Treatment D (reference)	(n)	(%)	CV%
Param1	(unit)	X.XX	(n)	X.XX	(n)	X.XX	X.XX
Param2	(unit)	X.XX	(n)	X.XX	(n)	X.XX	X.XX
Param3	(unit)	X.XX	(n)	X.XX	(n)	X.XX	X.XX
		Treatment B (Test)	(n)	Treatment D (reference)	(n)		
Param1	(unit)	X.XX	(n)	X.XX	(n)	X.XX	X.XX
Param2	(unit)	X.XX	(n)	X.XX	(n)	X.XX	X.XX
Param3	(unit)	X.XX	(n)	X.XX	(n)	X.XX	X.XX
		Treatment C (Test)	(n)	Treatment D (reference)	(n)		
Param1	(unit)	X.XX	(n)	X.XX	(n)	X.XX	X.XX
Param2	(unit)	X.XX	(n)	X.XX	(n)	X.XX	X.XX
Param3	(unit)	X.XX	(n)	X.XX	(n)	X.XX	X.XX

Parameters were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from the ANOVA.
% Geometric Mean Ratio (GMR) = 100*(test/reference)
Intra-subject CV% was calculated as 100 x square root(exp[MSE-1]). MSE = Residual variance from ANOVA.

Subject X was removed for the statistical analysis because <insert reason>

Notes for Generating the Actual Table:

Presentation of Data:

- Geometric Mean Ratios will be presented to 2 decimal places and n will be presented as an integer.
- Geometric LSMs be presented to same precision as Mean in the PK parameter table CPPar1,

Programmers Note: PK parameters are AUC_{last}, AUC_{inf}, and C_{max}.

PKist Note:
List parameter names exactly as to be presented and in order of presentation in Programmers Note above.

Program: /CAXXXXX/sas_prg/pksas/stats-tables-mixed.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_statsmixed.sas DDMMMYYYY HH:MM

Client has request the follow format to present:
Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Table 14.2.3.1.1 Summary of Inhalation Checklist (Treatments A-C)(Safety Set)

Quality Assessment*	Response/ Statistic	Treatment A N=XX	B N=XX	C N=XX	Overall N=XX
Q1	Yes	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	No	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Q1A	n	XX	XX	XX	XX
	Mean (SD)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)	XX.X (X.XX)
	Median	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX
Q2	Yes	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	No	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Q3	Yes	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	No	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Q4	Yes	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	No	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Q5	Yes	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	No	X (XX%)	X (XX%)	X (XX%)	X (XX%)

<Add treatment descriptions>
N = Number of subjects dosed. Percentages are based on the number of subjects dosed per treatment.
* Quality Assessment:
Q1 = Did the subject inhale all the present number of breaths?
Q1A = If no, number of breaths completed?
Q2 = During each inhalation, did the subject inhale the whole time the compressor was operating?
Q3 = Did the subject achieve a good seal between the mouthpiece and the mouth while they were inhaling?
Q4 = On each inhalation, was the subject able to start the nebulizer correctly?
Q5 = Was the subject able to inhale comfortably during nebulization?

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.2.3.1.2 Summary of Inhalation Checklist (Treatment D)(Safety Set)

Quality Assessment*	Response	Treatment D N=XX
Q1	Yes	X (XX%)
	No	X (XX%)
Q1A	≤25%	X (XX%)
	>25 - ≤50%	X (XX%)
	>75% - ≤100%	X (XX%)
Q3	Yes	X (XX%)
	No	X (XX%)
Q5	Yes	X (XX%)
	No	X (XX%)

<Add treatment descriptions>
N = Number of subjects dosed. Percentages are based on the number of subjects dosed per treatment.
* Quality Assessment:
Q1 = Did the subject complete dosing?
Q1A = If no, proportion of the intended treatment time completed?
Q3 = Did the subject achieve a good seal between the mouthpiece and the mouth while they were inhaling?
Q5 = Was the subject able to inhale comfortably during nebulization?

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.2.3.2 Summary of Treatment Duration (Safety Set)

Assessment	Statistic	Treatment				
		A (N=XX)	B (N=XX)	C (N=XX)	D (N=XX)	Overall (N=XX)
Duration (min)	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX

<Add treatment descriptions>
N = Number of subjects dosed.
Duration is computed as the difference between the end and start time of inhalation and is summarized in minutes and reported with 2 decimal places.

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.2.3.3 Summary of Modified Patient Satisfaction and Preference Questionnaire (mPASAPQ)
(Safety Set)

Question*	Statistic	Treatment A (N=XX)	B (N=XX)	C (N=XX)	D (N=XX)	Overall (N=XX)
Total Score (%)	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX
Satisfaction Score	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX
Willingness Score	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX

Programmer Note: Questions 1 through 8 will also be summarized individually in this table.
<Add treatment descriptions>
N = Number of subjects dosed.
* As a parent/legal guardian observing your child in the trial, how satisfied are you: Q1. That the nebulizer works correctly? ; Q2. With the ease of inhaling a dose form the nebulizer? ; Q3. With the training provided? ; Q4. With the size of the nebulizer control unit and handset? ; Q5. That the nebulizer looks durable (hard wearing)? ; Q6. With using the nebulizer? ; Q7. With the overall treatment time? ; Q8. With the ease of holding the nebulizer during use? ; Q9. Overall, how satisfied are you with the nebulizer (i.e. satisfaction score)? ; Q10. Please indicate how willing you would be for your child to use the nebulizer used during the study by providing a number between 0 and 100 (i.e., Willingness score).
Questions 1 to 9 were answered using scores from 1 (i.e., very dissatisfied) to 7 (i.e., very satisfied).
Total Score = (Q1+Q2+Q3+Q4+Q5+Q6+Q7+Q8)/56)*100

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.3.1.1 Overall Summary of Adverse Events
(Safety Set)

Adverse Event Category [n (%) m]	Treatment A (N=XX)	B (N=XX)	C (N=XX)	D (N=XX)	Total (N=XX)
Any AEs	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any TEAEs	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Drug-Related TEAEs	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Device-Related TEAEs	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Serious AEs	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Serious TEAEs	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Serious Drug-Related TEAEs	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Serious Device-Related TEAEs	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any TEAEs Leading to Withdrawal	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Serious TEAEs Leading to Withdrawal	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Drug-Related TEAEs Leading to Withdrawal	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Device-Related TEAEs Leading to Withdrawal	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any TEAEs of Special Interest	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Serious TEAEs of Special Interest	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
Any Drug-Related TEAEs of Special Interest	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX

Treatment A: 5 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment B: 10 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment C: 20 breaths of VR647 Inhalation Suspension via VR647 Inhalation System
Treatment D: 1 mg/2 mL Pulmicort Respules via conventional jet nebulizer

n = Number of subjects, m = Number of events, N = Number of dosed subjects, TEAE = Treatment-emergent adverse event
* Adverse events are classified according to MedDRA Version 20.0.
For each category, subjects are included only once, even if they experienced multiple events in that category.

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.3.1.2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Set)

	Treatment				
System Organ Class Preferred Term [n (%) m]	A (N=XX)	B (N=XX)	C (N=XX)	D (N=XX)	Total (N=XX)
Any TEAEs	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
System Organ Class 1	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
Preferred term 1	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
Preferred term 2	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
System Organ Class 2	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
Preferred term 1	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
System Organ Class 3	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
Preferred term 1	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX	X (XX %) XX
System Organ Class 4	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
Preferred term 1	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
System Organ Class 5	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
Preferred term 1	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX
Preferred term 2	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX	X (X %) XX

etc.

<Add treatment descriptions>
n = Number of subjects, m = Number of events, N = Number of dosed subjects, TEAE = Treatment-emergent adverse event
* Adverse events are classified according to MedDRA Version 20.0.
For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term.

Programmer note: Sort by decreasing frequency in the total arm for SOC and preferred term within SOC. The first row of this table should match the counts of the Any TEAEs category on Table 14.3.1.1.

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Note: Table 14.3.1.4 and 14.3.1.7 will appear similar to Table 14.3.1.3

Table 14.3.1.3 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Safety Set)

System Organ Class Preferred Term [n (%)]	Relationship to Study Drug	Treatment A (N=XX)	 B (N=XX)	 C (N=XX)	 D (N=XX)	 Total N=XX)
Any TEAEs	Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Not Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
System Organ Class 1	Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Not Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
Preferred term 1	Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Not Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
System Organ Class 2	Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Not Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
Preferred term 1	Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Not Related	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)

etc.

<Add treatment descriptions>
n = Number of subjects, N = Number of dosed subjects, TEAE = Treatment-emergent adverse event
* Adverse events are classified according to MedDRA Version 20.0.
For each system organ class and preferred term, subjects may be counted more than once according to the relationship of the TEAEs. Adverse events with missing relationship are assumed to be 'Related'.

Programmer Note: For Table 14.3.1.4, the column 'Relationship to Study Drug' will be replaced by 'Relationship to Device'. If there are no AEs related to device, the following null banner will be added:

Null banner: No Treatment-emergent Adverse Events related to the device

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.3.1.5 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
(Safety Set)

System Organ Class Preferred Term [n (%)]	Maximum Severity	Treatment A (N=XX)	 B (N=XX)	 C (N=XX)	 D (N=XX)	 Total (N=XX)
Any TEAEs	Mild	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Moderate	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Severe	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
System Organ Class 1	Mild	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Moderate	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Severe	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
Preferred term 1	Mild	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Moderate	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Severe	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
System Organ Class 2	Mild	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Moderate	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Severe	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
Preferred term 1	Mild	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Moderate	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)
	Severe	X (XX %)	X (XX %)	X (XX %)	X (XX %)	X (XX %)

etc.

<Add treatment descriptions>
n = Number of subjects, N = Number of dosed subjects, TEAE = Treatment-emergent adverse event
* Adverse events are classified according to MedDRA Version 20.0.
For each system organ class and preferred term, subjects are included only once, at the maximum severity. Adverse events with missing severity are assumed to be 'Severe'.

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.3.1.6 Treatment-Emergent Adverse Events of Special Interest by System Organ Class and Preferred Term (Safety Set)

Match format of Table 14.3.1.2

First line text: Any Treatment-emergent Adverse Events of Special Interest

Null banner: No Treatment-emergent Adverse Events of Special Interest

Table 14.3.2.1 Serious Adverse Events (Safety Set)

Programmer Note: Tables 14.3.2.1, 14.3.2.2 and 14.3.2.3 will match the format of Listing 16.2.7 in the event of SAEs, SADEs or AEs leading to withdrawal.

Null banner for Table 14.3.2.1: No serious adverse events were reported.
Null banner for Table 14.3.2.2: No serious adverse device effects were reported.
Null Banner for Table 14.3.2.3: No adverse events leading to withdrawal were reported.

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

Table 14.3.4.1 Vital Sign Results by Time-point (Safety Set)

Vital Sign Parameter (unit) Time-point	Treatment A (N=XX)	 B (N=XX)	 C (N=XX)	 D (N=XX)
Vital sign parameter 1 (unit)				
Day 1 Pre-dose (Baseline)				
n	XX.X	XX.X	XX.X	XX.X
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Day 1 0.5 Hour Post-dose				
n	XX.X	XX.X	XX.X	XX.X
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Change from Baseline to Day 1 0.5 Hour Post-dose				
n	XX.X	XX.X	XX.X	XX.X
Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
Median	XX.X	XX.X	XX.X	XX.X
Min, Max	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Etc.				

<Add treatment descriptions>
Note: Baseline is Day 1 pre-dose of each period and is the last non-missing measurement prior to dosing.

<Measurement includes for systolic and diastolic BP, heart and respiratory rate, and temperature. Time points are Day 1 pre-dose and Hour 0.5.>

Source: Listing xx.x.xx, Dataset: xxxx, Program: xxxxxx.sas, Output: xxxx.rtf, Generated on: DDMMMYYYY HH:MM
Page x of y

12. LISTING SHELLS

The following listing shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the listings that will be presented and included in the final report. These listings will be generated off of the Celerion SDTM Tabulation Model 1.4 mapped in accordance with SDTM Implementation Guide 3.2. All listings will be presented in Courrier New size font 9.

Listing 16.2.1 Subject Disposition

Site/ Subject Number	Informed Consent Date	Completion/ Discontinuation Date	Completed Study?	Primary Reason for Discontinuation	Comments
X/X	DDMMMYYYY	DDMMMYYYY	Yes		
X/X	DDMMMYYYY	DDMMMYYYY	Yes		
X/X	DDMMMYYYY	DDMMMYYYY	No	Personal Reason	
X/X	DDMMMYYYY	DDMMMYYYY	Yes		

Programmer Note: Please also include treatment sequence, Informed Re-Consent date, Informed Assent date and protocol amendment version, if present, in this listing.

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

Listing 16.2.4.1 Demographics

Site/ Subject Number	Age (years)	Age (months)	Gender	Race	Ethnicity	Weight (kg)	Height (cm)
X/X	XX	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XX.XX	XXX
X/X	XX	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XX.XX	XXX
X/X	XX	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XX.XX	XXX
X/X	XX	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XX.XX	XXX

Programmer Note: BMI will also be included in this listing. If BMI is not recorded in the source dataset, it will be computed for analysis using the following formula: weight (kg) / [height (m)] 2.

Note: BMI = Body mass index

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

Listing 16.2.4.2 Medical and Surgical History

Site/ Subject Number	Any History?	MH Number	System Organ Class/ Preferred Term/ Verbatim Term	Diagnosis/Surgery Date Start	End
X/X	XXX	X	XXXXXX/XXXXX/XXXXXX	DDMMMYYYY	Ongoing
		X	XXXXXX/XXXXX/XXXXXX	DDMMMYYYY	DDMMMYYYY
X/X	XXX	X	XXXXXX/XXXXX/XXXXXX	DDMMMYYYY	DDMMMYYYY

Medical history events are coded using MedDRA Version 20.0.

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

Listing 16.2.4.3.1 Asthma History (I of III)

Site/ Subject Number	Does Subject Have? Wheezing	Reactive Airway Disease	Mild Asthma	Age at which Symptoms Appeared (years)
X/X	XXX	XXXX	XXXXX	XXX
X/X	XXX	XXXX	XXXXX	XXX

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

Listing 16.2.4.3.2 Asthma History (II of III)

Site/ Subject Number	Typical Symptoms	If Other, Specify	More than 3 Symptom episodes Per year?	Are any Symptoms Severe?	Are any Symptoms Worse at night?	Does subject Exhibit airflow Limitation?
X/X	XXXXXXXX		XXXX	XXX	XXX	XXX
X/X	XXXXXXXX	XXXXX	XXXX	XXX	XXX	XXX

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

Listing 16.2.4.3.3 Asthma History (III of III)

Site/ Subject Number	Family History of Atopy?	Date of Last asthma Symptoms	Medication Used?	Drug Name	Route	If Other Route, Specify	Total Daily Dose	Unit	If Other Unit, Specify	Start Date	End Date	Ongoing?
X/X	XXXXXXXX	XXXXX	XXXX	XXXX	XXXX	XXXXX	XXXXXXX	XXXXXX	XXXXXX	XXXXX	XXXXX	No
X/X	XXXXXXXX	XXXXX	XXXX									

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

Listing 16.2.5.1.1 Inclusion Criteria

X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.

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

Listing 16.2.5.1.2 Inclusion Responses

Site/ Subject Number	Visit	Date	Inclusion Criteria* 1	2	3	4	5
X/X	XX	DDMMMYYYY	Yes	Yes	Yes	Yes	Yes
X/X	XX	DDMMMYYYY	Yes	Yes	Yes	Yes	Yes

* = Please refer to Listing 16.2.5.1.1 for specific inclusion criteria.

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

Listing 16.2.5.2.1 Exclusion Criteria

X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.

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

Listing 16.2.5.2.2 Exclusion Responses

Site/ Subject Number	Visit	Date	Exclusion Criteria* 1	2	3	4	5	6
X/X	XX	DDMMMYYYY	Yes	Yes	Yes	Yes	Yes	Yes
X/X	XX	DDMMMYYYY	Yes	Yes	Yes	Yes	Yes	Yes

* = Please refer to Listing 16.2.5.2.1 for specific exclusion criteria.

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

Listing 16.2.5.3 Randomization

Site/ Subject Number	Has subject Been Randomized?	If Yes, Randomization			If no, Specify
		Date	Number	Treatment Sequence	
X/X	XXXXXXXX	XXXXXXX	XXXX	XXXX	
X/X	XXXXXXXX	XXXXXXX	XXXX	XXXX	

<Add treatment descriptions>

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

Listing 16.2.5.4.1 Nebulization

Site/ Subject Number	Visit	Treatment	Demonstration And Training?	Nebulization Performed?	If yes: Device Serial Number	If yes: Date of Nebulization	If yes: Start Time	If yes: End Time	If yes: Dur* (min)	Use of Albuterol Prior to Dosing?	If yes: 6 hours Prior?	If yes: Date	If yes: Time
X/X	X		XX	XXX									
	X	X	XX	XXX	XXXX	DDMMMYYYY	X:XX:XX	X:XX:XX	X.XX	XXX	XXX	DDMMMYYY	XX:XX

<Add treatment descriptions>
* Duration is computed as the difference between the end and start time of inhalation and will be expressed in minutes and reported with 2 decimal places.

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

Listing 16.2.5.4.2 Dosing

Site/ Subject Number	Visit	Treat-ment	Preset Number of Breaths	Inhale all preset number of breaths? / Did subject Complete dosing?	If no, Number of Breaths completed? / Proportion of intended Treatment time completed?	Comments
X/X	X	X	XX	XXX	XXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXX

<Add treatment descriptions>

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

Listing 16.2.5.4.3 Inhalation Checklist

Site/ Subject Number	Visit	Treat-ment	Did subject inhale The whole time The compressor Was operating?	Did the subject Achieve a good seal Between the mouth-piece and the mouth?	Was the subject Able to start The nebulizer Correctly?	Was the subject Able to inhale Correctly?	Overall, did the subject Demonstrate their ability To use the VR647 Inhalation System effectively after Training?
X/X	X	X	XX	XXX	XXX	XXXXX	XXXX

<Add treatment descriptions>
Responses will only be presented if data is collected for that treatment.

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

Listing 16.2.5.5 Modified Patient Satisfaction and Preference Questionnaire (mPASAPQ)

Site/ Subject Number	Visit	Treat-ment	Relationship to Subject	Question*										Total Score**
				Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	n (%)
X/X	X	X	XXXXXXXXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX (XX%)

<Add treatment descriptions>
* As a parent/legal guardian observing your child in the trial, how satisfied are you: Q1. That the nebulizer works correctly? ; Q2. With the ease of inhaling a dose from the nebulizer? ; Q3. With the training provided? ; Q4. With the size of the nebulizer control unit and handset? ; Q5. That the nebulizer looks durable (hard wearing)? ; Q6. With using the nebulizer? ; Q7. With the overall treatment time? ; Q8. With the ease of holding the nebulizer during use? ; Q9. Overall, how satisfied are you with the nebulizer? ; Q10. Please indicate how willing you would be for your child to use the nebulizer used during the study by providing a value between 0 (not willing) and 100 (willing).
Questions 1 to 9 were answered using scores from 1 (i.e., very dissatisfied) to 7 (i.e., very satisfied).
** Total Score: n = Q1+Q2+Q3+Q4+Q5+Q6+Q7+Q8 ; % = (n/56)*100

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

Listing 16.2.5.6 Prior and Concomitant Medications

Site/ Subject Number	Any Med?	Treat- Ment	Medication (WHO* Term)	Indication	Start Date	Start Time	Stop Date	Stop Time	Dose and Unit	Route	Frequency	Ongoing?	Prior to Rando$?
X/X	Yes	X	ACETAMINOPHEN (ACETAMINOPHEN)	Toothache	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	620 mg	ORAL	Once	No	X

Programmer Note: Please also include columns for primary medical history term and primary adverse event term. In order to populate the 'Prior to Rando*'column, the start date of the medication will be compared to the date of randomization. If the start date of the medication is prior to the randomization date, please populate the column with 'Yes'. If the start date of the medication is on or after the randomization date, please populate the column with 'No'.

<Add treatment descriptions>
* Concomitant medications are coded with WHO dictionary version 01MAR2017.
$ Rando = Randomization: Yes if start date of medication is prior to randomization date, No if start date of medication is on or after the randomization date.

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

Listing 16.2.5.7 Overnight Stay and Discharge From Site

Site/ Subject Number	Visit	Did subject utilize The option of an Overnight stay?	If Yes			
			Date of Admission	Time of Admission	Date of Discharge	Time of Discharge
X/X	XXXX	XXXXXXXX	XXXXXXX	XXXXX	XXXXXXXXX	XXXXXXXX
	XXXX	XXXXXXXX				

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

Listing 16.2.5.8 Follow-Up

Site/ Subject Number	Visit Type	Any AEs or ADEs starting Or ending since last visit?	Any concomitant medications starting Or ending since last visit?
X/X	XXXXX	XXXXXXX	XXXXX

AE = Adverse event, ADE = Adverse device effect

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

Listing 16.2.6.1 PK Blood Sampling

Site/ Subject Number	Visit	Treat-ment	Day	Time Point	Date	Actual Time	Comments
X/X	XXXX	X	X	Pre-dose	DDMMMYYYY	XX:XX	
				20 Minutes	DDMMMYYYY	XX:XX	
				40 Minutes	DDMMMYYYY	XX:XX	
				1.5 Hours	DDMMMYYYY	XX:XX	
				3 Hours	DDMMMYYYY	XX:XX	
				4 Hours	DDMMMYYYY	XX:XX	
				6 Hours	DDMMMYYYY	XX:XX	
				8 Hours	DDMMMYYYY	XX:XX	

Programmer Note: Please also include 'Not done' column if populated by 'Yes' in the database.

<Add treatment descriptions>

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

Listing 16.2.7.1.1 Adverse Events (I of II)

Site/ Subject Number	Treatment	TE?#	Adverse Event*	Preferred Term	Time from Last Dose (DD:HH:MM)	Onset Date	Onset Time	Resolved Date	Resolved Time	Duration (DD:HH:MM)	Ongoing?
X/X	X	Yes	XXXXXXXXXXXX	XXXXXXXXX XXXXXXX	XX:XX:XX	DDMMMYYYY	X:XX	DDMMMYYYY	X:XX	XX:XX:XX	No

<Add treatment descriptions>
= Abbreviation for treatment-emergent, * = Adverse events are classified according to MedDRA® Version 20.0.

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

Listing 16.2.7.1.2 Adverse Events (II of II)

Site/ Subject Number	Treatment	Adverse Event	Onset Date	Onset Time	Onset Freq	Severity	Ser*	Outcome	Relationship to Study Drug/ Medical Device	Relationship to Study Procedure	Action Taken
X/X	X	XXXXXXXXXXXXXXXXX	DDMMMYYYY	XX:XX	Inter.	Mild	NS	Recovered/ Resolved	Not Related/ Not Related	Not Related	None

<Add treatment descriptions>
Ser* represents Serious: NS = Not Serious
Freq represents Frequency: SE = Single Episode, Inter. = Intermittent, Cont. = Continuous

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

Listing 16.2.7.2 Adverse Event Preferred Term Classification

Site/ Subject Number	Treat-ment	Adverse Event	Preferred Term	System Organ Class	Onset Date	Onset Time
X/X	X	XXXXXXX XXXXX XXXX XXXXXX	XXXXXXXXXX XXXXXXX	XXXXXXXXXXXXXXXXXXXX	DDMMMYYYY	XX:XX

<Add treatment descriptions>
Adverse events are classified according to MedDRA® Version 20.0.

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

Listing 16.2.8.1 Physical Examination

Site/ Subject Number	Visit	Date	Was Physical Exam Performed?	Reason Not Done	Body System	Result	Clinical Significance	Comment or Description
X/X	X	DDMMMYYYY	Yes		XXXX	XXXXXXXXX	XXXXX	XXXXXXXXXXXXXX
	X	DDMMMYYYY	Yes		XXXX	XXXXXXXXX		

Note: NCS = Not clinically significant CS = Clinically significant

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

Listing 16.2.8.2 Vital Signs

Site/ Subject Number	Visit	Treat-ment	Time Point	Date	Time	Blood Pressure (mmHg) Position	Blood Pressure (mmHg) Sys/Dia	Heart Rate (bpm)	Respir-ation (rpm)	Temper-ature (°C)	Comments
X/X	XXX			DDMMMYYYY	XX:XX	SEM	XXX/ XX	XX	XX	XX.X	XXXXXX
	XXX	X	XXXXXX	DDMMMYYYY	XX:XX	SEM	XXX/ XX	XX	XX	XX.X	
			XXXXXX	DDMMMYYYY	XX:XX	SEM	XXX/ XX	XX	XX	XX.X	
			XXXXXX	DDMMMYYYY	XX:XX	SEM	XXX/ XX	XX	XX	XX.X	

Programmer note: Sort unscheduled assessment with other scheduled assessments. Please also include 'Not done' column if populated by 'Yes' in the database. Please do not present weight in this listing.

<Add treatment descriptions>
SIT = sitting, SEM = semi-recumbent, SUP = supine, STD = standing, Sys/Dia = systolic/diastolic

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

Listing 16.2.8.3 Vital Signs Change From Baseline

Site/ Subject Number	Visit	Treat-ment	Time Point	Blood Pressure (mmHg) Systolic/Diastolic	Heart Rate (bpm)	Respir-ation (rpm)	Temper-ature (°C)
X/X	XXX	X	XXXXXX	XXX/ XX	XX	XX	XX.X
	XXX		XXXXXX	XXX/ XX	XX	XX	XX.X
			XXXXXX	XXX/ XX	XX	XX	XX.X
			XXXXXX	XXX/ XX	XX	XX	XX.X

Programmer note: This listing will be generated of the ADVS ADaM dataset.

<Add treatment descriptions>
Baseline is Day 1 pre-dose of each period and is the last non-missing measurement prior to dosing.

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