NEURELIS, INC.

STATISTICAL ANALYSIS PLAN

Section 14 and 16

Protocol No.: DIAZ.001.04

An Open-Label, Repeat-Dose Pharmacokinetics Study of NRL-1 in Epilepsy Subjects Under Seizure and Normal Conditions (DIAZ.001.04)

CONFIDENTIAL

Version: 1.0

Date: May 25, 2018

SIGNATURE PAGE

Prepared By:

Name: Jaekwan Kim
Manager, Statistics, GSG

Signature: Jaekwan Kim
디지털 서명자Jaekwan Kim
DN: cn=Jaekwan Kim, o=gsg-us.com, ou, email=jaekwan.kim@gsg-us.com, c=US
날짜: 2018.05.25 11:53:42 +09'00'

Date: 2018/05/25
(yyyy/mm/dd)

Reviewed By:

Name: Chaeyong Chang
President, GSG

Signature: chaeyong chang
Digitally signed by chaeyong chang
DN: cn=chaeyong chang, o=gsg-us.com, ou=gsg-us.com, email=chaeyong.chang@gsg-us.com, c=US
Date: 2018.07.02 10:12:06 -04'00'

Date: 2018/05/25
(yyyy/mm/dd)

Name: Richard E. Lowenthal, MSc, MBA
Program Manager, Neurelis, Inc

Signature: Richard Lowenthal
Digitally signed by Richard Lowenthal
DN: cn=Richard Lowenthal, o=Pacific Link Consulting, ou=President, email=richard@pacificlinkconsulting.com, c=US
Date: 2018.07.02 21:13:56 -07'00'

Date: 2018/05/25
(yyyy/mm/dd)

(yyyy/mm/dd)

Approved By:

Enrique Carrazana

Signature: Enrique Carrazana, M.D.
Digitally signed by Enrique Carrazana, M.D.
DN: cn=Enrique Carrazana, M.D., o, ou, email=ecarrazana@aol.com, c=US
Date: 2018.07.03 00:18:20 -04'00'

Date: 2018/07/03
(yyyy/mm/dd)

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AE	adverse event
$AUC_{(0-6)}$	area under the plasma concentration time-curve to 6 hours post dose
BLQ	below the limit of quantization
C-SSRS	Columbia Suicide Severity Rating Scale
C_{max}	Maximum plasma concentration
ECG	Electrocardiogram
EMU	Epilepsy Monitoring Unit
FDA	US Food and Drug Administration
HEENT	head, ears, eyes, nose, and throat
ICH	International Conference on Harmonization
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram(s)
mL	milliliter
NIH	National Institutes of Health
NRL-1	Diazepam nasal spray
PK	pharmacokinetics
QTcF	Corrected QT interval, Fridericia's formula
SAE	serious adverse event
TEAE	treatment-emergent adverse event
t_{max}	time to maximum plasma concentration
VAS	Visual Analog Scale
WHODD	World Health Organization Drug Dictionary

1. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the procedures to be used for analyzing and reporting results for study DIAZ.001.04.

This SAP is based on the final amended protocol version 5 (2-May-2017).

2. STUDY OBJECTIVES AND ENDPOINTS

2.1. Study Objectives

Primary objective

The primary objective of this study is to assess the pharmacokinetics (PK) of diazepam after single intranasal doses of NRL-1 administered to Epilepsy subjects during the ictal or peri-ictal period (defined as either during or immediately following a seizure), where the seizure involved motor activity or alteration of awareness. The primary PK variables to determine absorption will be the maximum plasma concentration (C_{max}) and the area under the curve through 6 hours ($AUC_{(0-6)}$). FDA has requested that analyses be presented by Overall and age group of 6-11; 12-16 and 16+ dosing in the Diastat labeling.

Secondary objective

The secondary objectives of this study include:

- To compare the diazepam C_{max}, time to peak concentration (t_{max}) and $AUC_{(0-6)}$ after single administration of NRL-1 in Epilepsy subjects during the ictal or peri-ictal period to that after administration of NRL-1 to the same subjects under normal conditions.
- To compare the diazepam C_{max}, t_{max}, and $AUC_{(0-6)}$ after single administration of NRL-1 between Epilepsy subjects ages 6 to 11 and those greater than 12 years of age.
- To compare the diazepam C_{max}, t_{max}, and $AUC_{(0-6)}$ after single administration of NRL-1 in Epilepsy subjects during the ictal or peri-ictal period and that of healthy normal subjects from PK data obtained in the DIAZ.001.02 and DIAZ.001.03 studies.
- To assess the safety and tolerability of diazepam after intranasal administration of NRL-1

2.2. Study Endpoints

2.2.1. Efficacy endpoint(s)

There are no efficacy endpoints for this study.

2.2.2. Safety Endpoint(s)

Safety data will be summarized by dose group and based on their initial dose level or treatment group (i.e. if a dose reduction occurs they will be considered in their initial group). Overall and age group of 6-11; 12-16 and 16+ descriptive statistics will be provided for actual values and change from baseline values for physical and neurological examination including HEENT, vital signs, clinical laboratory tests (serum chemistry, hematology, and urinalysis) and C-SSRS assessments (children and adult).

A nasal examination and irritation assessments will be conducted to evaluate any effects of the NRL-1 formulation on the nasal mucosa. The following will be assessed on separate scales: nasal irritation, erythema, edema, nasal discharge, mucosal erythema, mucosal edema, nasal discharge, mucosal crusting, mucosal epistaxis, VAS and NIH toolbox odor identification test.

For the actual incidence of seizure (it can occur period 1 or period 2), start time, stop time, NRL-1 dosing time, phase of seizure, type of seizure, time to seizure stop from dose time to stop time for those subjects dosed in the Ictal Phase will be provided.

The incidence and severity of TEAEs reported during the study and their relationship to study drug will be tabulated. TEAEs will be coded using the MedDRA and will be presented by body system.

The World Health Organization Drug Dictionary (WHODD) will be used to classify prior and concomitant medications by therapeutic class and preferred term. Prior and concomitant medication usage will be summarized by the number and percentage of subjects receiving each medication within each therapeutic class by dose cohort.

2.2.3. Pharmacokinetic Endpoints

The following PK parameters for diazepam will be calculated using non-compartmental analysis: C_{max}, t_{max}, and $AUC_{(0-6)}$.

For the actual time of seizure (it can occur Period 1 or Period 2) onset prior to the first dose of NRL-1, and time of the blood sampling will be recorded. PK parameters will be determined using actual times of sample collection relative to the administration of NRL-1.

Individual subject plasma concentrations, actual sampling times, and PK parameters will be listed by analyte and treatment. Any plasma concentration below the limit of quantitation (BLQ) will be reported as zero prior to t_{max} and as "BLQ" after t_{max}, which essentially treats it as a missing value.

Descriptive statistics will be calculated by analyte and treatment for plasma concentrations and PK parameters. Individual subject and mean plasma concentrations will be displayed on linear and semi-logarithmic axes.

3. STUDY DESIGN

This is a Phase 1, open-label, PK and safety study in Epilepsy subjects under both ictal or peri-ictal (involving motor activity and/or altered awareness) and normal conditions. A single intranasal dose of NRL-1 will be administered at either 5 mg, 10 mg, 15 mg, or 20 mg based on the subject's body weight.

The study consists of a screening period, a baseline period, a post-dose period where dosing is done during the ictal or peri-ictal period (Treatment period 1), a baseline period and a post-dose period after a second single-dose treatment under normal non-seizing conditions approximately 14-days later (Treatment period 2), and follow-up telephone contacts 7-days and 14-days after the last dose of NRL-1. Between doses of NRL-1, subjects and caregivers should avoid the use of other diazepam containing products. For subjects who will roll over to the DIAZ.001.05 long term safety study, the Day 14 (second dosing for NRL-1) assessments can be used as baseline assessments for DIAZ.001.05 to allow subjects to initiate long term treatment under the protocol.

Baseline in period 1 for this study is considered the period within 7 days of admission. The subject will be admitted and observed in the clinical site (i.e. EMU or Clinical Research Center) and dosing will occur at the time of a seizure that is considered suitable for administration of NRL-1. Time point 0 will be defined as the time of dosing of NRL-1 and initiation of PK blood sampling. EEG monitoring was used to determine the seizure start, stop time and assessment of seizure type.

The first treatment with NRL-1 will initially be administered under ictal or peri-ictal conditions in a clinical setting to subjects having partial or generalized Epilepsy with motor seizures or seizures with clear alterations of awareness. Since the primary objective is to obtain diazepam plasma concentrations and PK information when the drug is given in the ictal or peri-ictal period, dosing of NRL-1 will ideally occur during or within 5 minutes after the onset of the seizure.

A 3 mL blood sample for PK will be collected at the baseline and at the post-dose period once admitted to the clinical site. During the post-dose period, 3 mL blood samples will be collected at predetermined times after NRL-1 dosing to determine the diazepam plasma concentration versus time profile. If the baseline pre-dose blood sample is unable to be collected, i.e., subject experiences a seizure prior to collection, then the pre-dose assessment closest to dosing will be included in the analysis.

In treatment period 1, if the subject experiences a seizure after NRL-1 dosing (during the blood sampling period), PK blood draws will be suspended as long as required for the subject's medical care and will resume when clinically feasible. If the subject experiences a seizure after NRL-1 dosing and is administered an exclusionary medication (such as IV, oral or rectal diazepam), PK blood draws will be stopped, time of dosing diazepam recorded, and the Medical Monitor will be notified. All other safety procedures will be performed as per the protocol Schedule of Study Procedures.

The second treatment with NRL-1 will occur on a subsequent visit after at least a 14-day washout period(if subjects are on oral contraceptives (OC) the period between dosing

should be extended to approximately 28-days to ensure that the subject is dosed at the same approximate time of the OC cycle). Subjects will return to the clinical site to receive a single dose of NRL-1 when in a normal state. Please note that it is not anticipated that subjects will need to be admitted or held overnight for the second dosing, and the site will select an appropriate clinical facility for this portion of the study. Subjects should be seizure free for at least 12 hours prior to dosing. A 3 mL blood sample for PK will be collected at the post-dose period in the clinic prior to administration of NRL-1. During the post-dose period, 3 mL blood samples will be collected at predetermined times after NRL-1 dosing to determine the diazepam plasma concentration versus time profile.

Safety assessments include physical and neurological examination including head, ears, eyes, nose, and throat (HEENT), vital signs, laboratories (hematology, serum chemistry, and urinalysis), 12-lead ECGs, and AE assessment. Concomitant medications will be recorded. Columbia-Suicide Severity Rating Scale (C-SSRS for adults or children), nasal irritation assessment, assessment of mucosal erythema, mucosal edema, nasal discharge, mucosal crusting and mucosal epistaxis, sedation score assessment, VAS and smell test (National Institutes of Health [NIH] Toolbox Odor Identification Test).

Appendix A1: Schedule of Study Procedures (Treatment 1): NRL-1 Dose Treatment (During Clinical Site Visit – Seizing Conditions) (Treatment period 1)

Study Procedure	Screening[a]	Baseline[b]	Post-Dose Procedures															
Study Day	Day -21 to Day -1	Day -7 to Day 0	0min	15min	30min	45min	1hr	1.25hrs	1.5hrs	1.75hrs	2hrs	3hrs	4hrs	5hrs	6hrs	8hrs*	12hrs*	Discharge[c]
Signed informed consent	X																	
Inclusion/Exclusion Criteria	X	X																
Admission to Clinical Site		X																
Medical history including seizure history	X	X																
Columbia-Suicide Severity Rating Scale[d]	X	X													X			
Physical and Neurological exam (including HEENT)	X	X																
Vital signs[e]	X	X				X					X		X		X	X*	X*	X
Height and Weight	X	X[f]																
EEG (continuous) [g]		X→																
Hematology, Serum Chemistry and Urinalysis	X	X																
Serum ß-hCG (Pregnancy)[h]	X																	
Urine Pregnancy Test[h]		X																
HIV Antibody and Hepatitis Test[i]	X																	
Urine Drug and Alcohol Screen[j]	X	X																
Prior and Concomitant medication assessment	X	X	X→															
Adverse event assessment[k]			X→															
ECG (12-Lead in triplicate)[l]	X	X																
NRL-1 administration			**X**															
Blood Sample for PK[m,n]		X	X[j]	X	X	X	X	X	X	X	X	X	X	X	X	X*	X*	
Nasal Irritation[o]		X									X		X		X			X
Nasal Examinations[p]		X			X		X				X		X		X			X
Sedation Score[q]		X		X	X		X				X		X		X			X
Smell Test [r]		X					X						X					X
VAS for Pain[s]		X		X	X		X				X		X		X			X

* Optional assessment if feasible

a. Screening evaluations must be performed within 21 days prior to dosing on Day 0. Screening evaluations performed within 7 days (Day -7 to Day 0) of dosing do not need to be repeated if subjects are maintained in house. Screening procedures are performed only once prior to the first dose of study medication (Treatment 1 or 2).
b. Baseline evaluations will be performed upon admission to the clinical site and within 7 days of dosing if maintained in house. Time point 0 will be considered the time of dosing NRL-1 and initiation of PK blood sampling. Subjects may be dosed in either Treatment 1 or Treatment 2 first. The second treatment with NRL-1 will be separated by a minimum 14-day wash out period and baseline evaluation will be repeated for each treatment period (if subjects are on oral contraceptives (OC) the period between dosing should be extended to approximately 28-days to ensure that the subject is dosed at the same approximate time of the OC cycle).
c. Discharge occurs anytime after the PK blood sample is taken at 6 hours post dose (or optional 8 and 12 hours). When discharge occurs after 6 hours post dose, the assessments at discharge that overlap with the assessments at 6 hours post dose do not have to be repeated. In that case, check the check box in the CRF at 6 hours post dose to confirm that the assessments that overlap with the assessments at discharge is not going to be repeated.
d. Suicidal events will be assessed using the C-SSRS (adult or children) at screening, baseline, and at 6 hours post dose. The baseline C-SSRS should be performed within 3 hours prior to dosing of NRL-1 (see APPENDIX C).
e. Vital signs (temperature, pulse, respiratory rate and blood pressure) are to be obtained at screening, baseline, and at 45 (± 5 min) minutes, 2 (± 15 min), 4 (± 30 min), 6 (± 30 min), 8 (± 30 min), and 12 (± 30 min) hours post dosing, and at discharge. Vital signs at 8 and 12 hours are optional.
f. Weight only.
g. Subjects will be monitored for seizure activity with a continuous EEG evaluation. The EEG is considered standard of care when in the EMU setting, but is part of the study procedures if in a CTRC setting. The start time, stop time, and type of seizure will be recorded based on the EEG results. The time of NRL-1 dosing will also be recorded as part of the study database.
h. A serum (ß-hCG) pregnancy test will be administered to females of childbearing potential at screening. Urine pregnancy test is only required for female subjects of child bearing potential. If a serum pregnancy test is done on Day -1, urine pregnancy test does not have to be repeated on Day 0 (baseline). Pregnancy testing does not have to be done on subjects age 6 to 11.
i. Hepatitis B surface antigen (HbSAg), or Hepatitis C
j. When marijuana was used for medical reasons in the opinion of the investigator, it is not considered as drug abuse and the patient can be enrolled even if the marijuana metabolites in the urine revealed as positive. In this case, information about marijuana use should be entered in the CRF page for concomitant medication.
k. Adverse event assessment is continuous from time of first dose of NRL-1.
l. ECG is to be performed in triplicate. Three consecutive ECGs (each approximately 1-2 minutes apart) are performed.
m. Blood samples (3 mL each) are to be obtained before dosing (0, pre-dose) and at 15, 30, and 45 minutes, and 1, 1.25, 1.5, 1.75, 2, 3, 4, 5, and 6 hours. Blood samples should also be obtained if feasible at 8 and 12 hours after dosing. If a blood sample collection is delayed, then the collection will occur as soon as feasible and should not be skipped even if close to the next blood draw. Actual blood collection times can vary as follows: 1) ± 10 minutes for the 15 to 60 minute samples, 2) ± 15 minutes for the 1.25 to 6 hour samples, and 3) ± 30 minutes for the optional 8 and 12 hour samples.
n. If a second dose of NRL-1 is administered due to a subsequent seizure btween 4 and 12 hours after the initial dose, when clinically feasible, PK samples should be collected based on the time of the second dose at 0, 30 minutes, and 1, 2, and 4 hours after dosing.
o. Nasal Irritation assessments are performed prior to dosing (baseline) and at 2 (± 15 min), 4 (± 30 min), and 6 (± 30 min) hours post dose, and at discharge.
p. Nasal examination and scoring for mucosal erythema, mucosal edema, nasal discharge, mucosal crusting and mucosal epistaxis will be performed prior to dosing (baseline) and at 30 (± 10 min) minutes, 1 (± 10 min), 2 (± 15 min), 4 (± 30 min), and 6 (± 30 min) hours post dose, and at discharge.
q. Sedation Scores are just prior to dosing (baseline) and at 15 (± 5 min) and 30 (± 10 min) minutes, 1 (± 10 min), 2 (± 15 min), 4 (± 30 min), and 6 (± 30 min) hours post dose, and at discharge.
r. Smell tests and examination of the nasal mucosa will be conducted at baseline, and at 1 hour (± 15 min), 4 hours (± 30 min) post dose, and at discharge. The NIH Toolbox Odor Identification Test will be used as smell tests (1, 2).
s. VAS Scores are just prior to dosing (baseline) and at 15 (± 5 min) and 30 (± 10 min) minutes, 1(± 10 min), 2 (± 15 min), 4 (± 30 min), 6 (± 30 min) hours post dose, and at discharge.

Appendix A2: Schedule of Study Procedures (Treatment 2): NRL-1 Dose Treatment (Non-Seizing [Normative] Conditions)

Study Procedure	Baseline[a]	Post-Dose Procedures																Follow-up Telephone Contact[m]	
Study Day	Day 14	0 min	15min	30min	45min	1hr	1.25hrs	1.5hrs	1.75hrs	2hrs	3hrs	4hrs	5hrs	6hrs	8hrs[n]	12hrs[n]	Discharge[l]	Day 21	Day 28
Inclusion/Exclusion Criteria	X																		
Admission to Clinical Unit	X																		
Columbia-Suicide Severity Rating Scale[k]	X													X					
Physical and Neurological exam (including HEENT)	X																		
Vital signs[b]	X				X					X		X		X	X*	X*	X		
Weight	X																		
Hematology, Serum Chemistry and Urinalysis	X																		
Urine Pregnancy Test[c]	X																		
Urine Drug, Alcohol and Cotinine Screen[e]	X																		
Prior and Concomitant medication assessment	X	X→																	
Adverse event assessment[d]	X	X→																	
ECG (12-Lead in triplicate)[g] **NRL-1 administration**	X	**X**																	
Blood Sample for PK[f]	X	X[j]	X	X	X	X	X	X	X	X	X	X	X	X	X*	X*			
Nasal Irritation[g]	X									X		X		X			X		
Nasal Examinations[h]	X			X		X				X		X		X			X		
Sedation Score Assessment[i]	X		X	X		X				X		X		X			X		
Smell Test [n]	X					X						X					X		
VAS for Pain[j]	X		X[k]	X		X				X		X		X			X		

* Optional assessment if feasible

a. Baseline evaluations will be performed within 48 hours prior to dosing NRL-1. The Day 14 visit may be between 14 and 28 days after the initial dosing of NRL-1.
b. Follow-up phone calls 7 days (± 2 days) and 14 days (± 3 days) after the second dose of NRL-1 dosing to determine if any AE has occurred and to follow-up on any TEAEs ongoing since last communication with the subject. Subjects who prematurely discontinued will be followed up by phone calls approximately 7 days (± 2 days) after the last dose of NRL-1.
c. Discharge occurs anytime after the PK blood sample is taken at 6 hours post dose (or optional 8 and 12 hours). When discharge occurs after 6 hours post dose, the assessments at discharge that overlap with the assessments at 6 hours post dose do not have to be repeated. In that case, check the check box in the CRF at 6 hours post dose to confirm that the assessments that overlap with the assessments at discharge is not going to be repeated.
d. Suicidal events will be assessed using the C-SSRS (adult or children) at screening and baseline, and at 6 hours post dose. The baseline C-SSRS should be performed within 3 hours of administering the dose (see APPENDIX C).
e. Vital signs (temperature, pulse, respiratory rate and blood pressure) are to be obtained at baseline and at 45 (± 5 min), 2 (± 15 min), 4 (± 30 min), 6 (± 30 min), 8 (± 30 min), and 12 (± 30 min) hours post dosing and at discharge. Vital signs at 8, 12 hours are optional.
f. Pregnancy test is only required for female subjects of child bearing potential. Pregnancy test does not have to be done on subjects age 6 to 11.
g. When marijuana is used for medical reason in the opinion of the investigator, it is not considered as drug abuse and the patient can be enrolled even if the marijuana metabolites in the urine revealed as positive. In this case, information about marijuana use should be entered in the CRF page for concomitant medication.
h. Adverse event assessment is continuous.
i. ECG is to be performed in triplicate. Three consecutive ECGs (each approximately 1-2 minutes apart) are performed as part of the screening process.
j. Blood samples are to be obtained before dosing (0, pre-dose) and at 15, 30, and 45 minutes, and 1, 1.25, 1.5, 1.75, 2, 3, 4, 5, and 6 hours. Blood samples should also be obtained if feasible at 8, 12 hours. Actual blood collection times can vary as follows: 1) ± 10 minutes for the 15 to 60 minute samples, 2) ± 15 minutes for the 1.25 to 8 hour samples, 3) and ± 30 minutes for the 8 and12 hour sample.
k. Nasal Irritation assessments are performed prior to dosing (baseline) and at 2 (± 15 min), 4 (± 30 min), and 6 (± 30 min) hours post dose, and at discharge.
l. Nasal examination and scoring for mucosal erythema, mucosal edema, nasal discharge, mucosal crusting and mucosal epistaxis will be performed prior to dosing (baseline) and at 30 (± 10 min) minutes, 1 (± 10 min), 2 (± 15 min), 4 (± 30 min), and 6 (± 30 min) hours post dose, and at discharge.
m. Sedation Scores are just prior to dosing (baseline) and at 15 (± 5 min) and 30 (± 10 min) minutes, and 1 (± 10 min), 2 (± 15 min), 4 (± 30 min), and 6 (± 30 min) hours post dose, and at discharge.
n. Smell tests and examination of the nasal mucosa will be conducted at baseline, and at 1 hour (± 10 min), 4 hours (± 30 min), and at discharge. The NIH Toolbox Odor Identification Test will be used as smell tests (1, 2).
o. VAS Scores are just prior to dosing (baseline) and at 15 (± 5 min) and 30 (± 10 min) minutes, and 1 (± 10 min), 2 (± 15 min), 4 (± 30 min), and 6 (± 30 min) hours post dose, and at discharge.

4. PLANNED ANALYSES

4.1. Interim Analysis

Total of two interim analysis will be performed. First Interim analysis will be performed using soft lock data (cutoff date : April 30, 2018) for regulatory approval. Second interim analysis will be performed after NDA submission for the 120 day safety update.

4.2. Final Analysis

Final analyses will be completed following database lock in the study. Any changes from the planned analyses described in this section will be stated in the final study report.

5. SAMPLE SIZE CONSIDERATIONS

5.1. Sample Size Determination

Approximately forty-five (45), male and female subjects, 15 age 6 to 11 years and 30 over 12 years of age, are to be dosed as part of this study with dosing during the ictal or peri-ictal period of a seizure. Of these at least 10 adult subjects and 5 pediatric subjects will have PK assessments after dosing during the ictal period.

5.2. Sample Size Re-estimation

A re-estimation of sample size will not be performed on this study.

6. ANALYSIS POPULATIONS

Safety Population

Subjects who receive at least one dose of NRL-1will be included in the safety analyses.

PK Analysis Population

Subjects who complete the study through the 6 hours PK sampling periods on at least one of the dosing days will be included in the primary PK analysis and preliminary efficacy assessment. For the comparative bioavailability assessment, plasma samples from all subjects that complete the two periods of the study will be analyzed.

7. GENERAL CONSIDERATIONS FOR DATA ANALYSES

In general, the sort order for listings will be dose level (ascending dose levels of NRL-1), subject and assessment time, while summaries will be presented by dose level (ascending dose levels of NRL-1) and assessment time. A separate but identical analysis will be performed by age groups (6-11; 12-16 and 16+).

Unless stated otherwise, descriptive summaries will include n (Number of subjects), mean, standard deviation, median, range for continuous variables and n (Number of subjects) and percent for categorical variables. For planned ECG parameter assessments that are done in triplicate, the mean value will be used in the calculation of all descriptive statistics. If there are repeated assessments at a scheduled time point, the assessment closest to the scheduled time will be used in the calculation of all descriptive statistics. Any unscheduled or unplanned readings will be presented within the subject listings, but only the scheduled readings will be used in any summaries. Version 9.4 of the SAS™ system (SAS is a registered trademark of the SAS Institute, Inc., Cary, NC, USA) will be used to analyze the data as well as to generate tables, figures, and listings.

7.1. Multicenter Studies

Multi center will participate in the study.

7.2. Other Strata and Covariates

There are no other strata and covariates.

7.3. Examination of Subgroups

There is subgroup analysis of safety data by age group of 6-11; 12-16 and 16+ will be provided.

7.4. Multiple Comparisons and Multiplicity

No adjustments for multiple comparisons are planned.

8. DATA HANDLING CONVENTIONS

8.1. Premature Withdrawal and Missing Data

All subjects who withdraw from the study prematurely will be documented and the reason for their withdrawal will be reported in the final study report. Subjects who discontinue participation in the study prior to receiving study drug for a given dose level will be replaced, if possible. Missing data will not be imputed.

8.2. Derived and Transformed Data

QTc intervals will be calculated by Fridericia's (QTcF) formulas.

Fridericia's formula is:

$$\text{QTcF interval (msec)} = \text{QT interval (msec)} / (\text{RR interval (sec)})^{1/3}$$

where RR interval (sec) = 1/(heart rate (bpm)/60)

8.3. Values of Clinical Concern

Values that exceed the lower/upper limits of clinical lab values, all abnormal or "not clinically significant", and all changes in vital signs will be reviewed for clinical relevance by the Medical Monitor.

9. STUDY POPULATION

Subjects with a clinical diagnosis of epilepsy who, in the opinion of the Investigator, may need a benzodiazepine for seizure control.

9.1. Disposition of Subjects

All data from enrolled subjects will be summarized to provide the number of subjects who complete the study within each treatment and the number of subjects withdrawn and the reasons for withdrawal will be summarized. Subjects who have not been dosed due to lack of Seizure, will be summarized in the disposition table. Also, subject listing will be provided.

9.2. Protocol Deviations

Protocol deviations will be reported to Neurelis, Inc and will be documented in the clinical study report. Any changes from the analyses described within this statistical analysis plan will be stated in the final study report.

9.3. Demographic and Baseline Characteristics

Demographic and baseline characteristics for the subject population will be listed and summarized using the safety population. Descriptive summaries (n(Number of subjects), mean, standard deviation, minimum, median, and maximum and n(Number of subjects) and percent for categorical variables) will be provided by treatment group.

Subject demographics will be summarized by treatment group. Age, weight and height at screening will be summarized by descriptive statistics (n, mean, standard deviation, median, minimum and maximum). Gender and race will be summarized by number and percentage in each category.

Baseline characteristics such as laboratory evaluations, vital signs, ECGs at screening will be summarized by descriptive statistics (n, mean, standard deviation, median, minimum and maximum). Medical history (number and percentage of subjects with any condition and each condition) will be summarized by treatment group. Seizure types (number and percent of subjects) will be summarized by treatment group.

No statistical tests will be performed on the demographic and baseline characteristics.

10. EFFICACY ANALYSIS

No efficacy measures will be assessed during this study.

Time to seizure stop from dose time (n, mean, standard deviation, median, minimum and maximum) will be summarized by treatment. No formal statistical comparisons will be conducted.

11. SAFETY ANALYSES

Safety assessments include adverse events, vital signs, 12-lead electrocardiograms and clinical laboratory evaluations (hematology, serum chemistry, urinalysis, and serology). In addition, Columbia Suicide Severity Rating Scale (C-SSRS), Nasal Irritation Assessment, Sedation Score Assessment, VAS and Smell Test and examination of nasal mucosa will be conducted.

No formal statistical comparisons of the safety data will be conducted.

11.1. Extent of Exposure

The exposure data will be a by-subject listing, including the treatment administered with the dates and times of treatment administration.

11.2. Adverse Events

All adverse events (AEs) will be coded and classified according to System Organ Class (SOC) and Preferred Term (PT) using MedDRA(Version 16.1or more). TEAE(treatment

emergent Adverse Event) will be populated. All AEs (non-serious and serious) will be listed. A summary, by treatment group, of the number and percent of subjects reporting each event at least once will be generated for all AEs and also for drug-related AEs. Adverse events by System Organ Class, Preferred Term, and Severity will be summarized by Treatment group. A listing of the relationship with study drug by System Organ Class and Preferred Term will also be produced.

11.3. Deaths and Serious Adverse Events

Any deaths and other serious adverse events will be summarized and listed as appropriate to the data.

11.4. Adverse Events Leading to Discontinuation of Investigational Product and/or Withdrawal from the Study and Other Significant Adverse Events

If any subject withdraws due to an AE, then a listing and a summary will be provided for these subject(s).

11.5. Pregnancies (as applicable)

If any female subject becomes pregnant during the course of the study, this information will be tabulated and listed.

11.6. Clinical Laboratory Evaluations

All laboratory data will be listed for each subject. Summary statistics (n(Number of subjects), mean, standard deviation, median, range for continuous variables and n(Number of subjects) and percent for categorical variables) will be displayed for laboratory parameters. Clinically significant abnormalities, if they occur, will also be listed. To assess changes in laboratory parameters occurring during treatment, a shift summary of change from baseline to time-point (visit) and summary of change from baseline will be produced. Urine analysis for categorical variables will be categorized by treatment, class variable (*e.g.,* negative or positive) and visit.

11.7. Other Safety Measures

11.7.1. Concomitant Medication

Prior and concomitant medication will be coded and classified to according Preferred Term (PT) and modified drug name using The World Health Organization Drug Dictionary (WHODRL). Prior and concomitant medication by Preferred Term and modified drug name will be summarized by Treatment group.

11.7.2. Vital Signs

All vital sign data will be listed for each subject. Summary statistics (n(Number of subjects), mean, standard deviation, minimum, median, and maximum)for vital parameter(temperature, breathing rate, radial pulse, systolic blood pressure, diastolic blood pressure, height and weight) will be presented by treatments and visit. And also summary of the change from baseline will be summarized.

11.7.3. Electrocardiograms

In order to assess the effect of treatment on cardiac intervals, triplicate 12-lead digital ECGs will be collected. ECG sign data will be listed for each subject. A descriptive summary (n(Number of subjects), mean, standard deviation, minimum, median, and maximum and n(Number of subjects) and percent for categorical variables)for ECG parameter will be presented by treatments.

11.7.4. Physical examination

All physical examination data will be listed for each subject. Frequency and percent by treatment group will be displayed for physical examination parameters. A shift summary of change from screening to time-point (visit) will be produced.

11.7.5. C-SSRS assessments (children and adult)

C-SSRS assessments (children and adult) data will be listed for each treatment and subject.

11.7.6. Nasal Irritation, Mucosal Erythema, Mucosal Edema, Nasal Discharge, Mucosal Crusting and Mucosal Epistaxis

Nasal examination and irritation assessments (Nasal Irritation, Mucosal Erythema, Mucosal edema, Nasal discharge, Mucosal crusting and Mucosal epistaxis) data will be listed for each subject. Frequency and percent by treatment group will be displayed for Nasal examination and irritation assessments.

Assessment will be dichomized for each assements (Nasal Irritation, Mucosal Erythema, Mucosal edema, Nasal discharge, Mucosal crusting and Mucosal epistaxis). One category will be Grade 0 or Score 0 and other category will be combination of any Non Grade 0 or Non Score 0 assessments. A shift summary of change from screening to time-point (visit) will be produced. A figure showing each assessment (Nasal Irritation, Mucosal Erythema, Mucosal edema, Nasal discharge, Mucosal crusting and Mucosal

epistaxis) mean and standard deviation by visit will be provided. Same tables and figures by age group of 6-11; 12-16 and 16+ will be provided.

11.7.7. Visual Analogue Scale

Visual Analogue Scale will be listed for each subject. Summary statistics (n(Number of subjects), mean, standard deviation, minimum, median, and maximum)for Visual Analogue Scale will be presented by treatments and visit. A figure showing mean and standard deviation by visit will be provided. Same tables and figures by age group of 6-11; 12-16 and 16+ will be provided.

11.7.8. NIH Toolbox Odor Identification Test

NIH Toolbox Odor Identification Test will be listed for each subject. Summary statistics (n(Number of subjects), mean, standard deviation, minimum, median, and maximum)for NIH Toolbox Odor Identification Test will be presented by treatments and visit. A figure showing mean and standard deviation by visit will be provided. Same tables and figures by age group of 6-11; 12-16 and 16+ will be provided.

11.7.9. Sedation Score Assessment

Sedation Score Assessment will be summarized for each subject. Summary statistics (n(Number of subjects), mean, standard deviation, minimum, median, and maximum)for Sedation Score Assessment will be presented by treatments and visit. Assessment will be dichomized. One category will be Score 0 and other category will be combination of any Non Score 0 assessments. A shift summary of change from screening to time-point (visit) will be produced. A figure showing mean and standard deviation by visit will be provided. Same tables and figures by age group of 6-11; 12-16 and 16+ will be provided.

12. TABLES, LISTINGS & FIGURES

12.1.1. Tables

Table No	Title
Table 14.1.1	Subject Disposition-Safety Population
Table 14.1.2.1	Analysis Populations-Safety Population
Table 14.1.2.2.1	Demographics (6-11 years old subject)-Safety Population
Table 14.1.2.2.2	Demographics (12-16 years old subject)-Safety Population
Table 14.1.2.2.3	Demographics (> 16 years old subject)-Safety Population
Table 14.1.2.2.4	Demographics (All subject)-Safety Population
Table 14.1.2.3.1	Seizure Duration by Age group-Safety Population
Table 14.1.2.3.2	Seizure-Safety Population
Table 14.1.3	Inclusion/Exclusion Criteria Fulfilled -Safety Population
Table 14.1.4	Medical History by Body System -Safety Population
Table 14.1.5	Urine Drug Screening-Safety Population

Table 14.1.6	Serology at Screening-Safety Population
Table 14.1.7	Pregnancy Test -Safety Population
Table 14.1.8.1	Incidence of Treatment-Period Concomitant Medications - Safety Population
Table 14.1.8.2	Incidence of Prior Medications-Safety Population
Table 14.2.2.1	Nasal Irritation Assessments by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.2.2	Nasal Irritation Assessments by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.2.3	Nasal Irritation Assessments by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.2.4	Nasal Irritation Assessments by Treatment and Visit (All subject)-Safety Population
Table 14.2.2.5	Nasal Irritation Assessments - Shift Tables by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.2.6	Nasal Irritation Assessments - Shift Tables by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.2.7	Nasal Irritation Assessments - Shift Tables by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.2.8	Nasal Irritation Assessments - Shift Tables by Treatment and Visit (All subject)-Safety Population
Table 14.2.3.1	Visual Analogue Scale by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.3.2	Visual Analogue Scale by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.3.3	Visual Analogue Scale by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.3.4	Visual Analogue Scale by Treatment and Visit (All subject)-Safety Population
Table 14.2.4.1	Mucosal Erythema by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.4.2	Mucosal Erythema by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.4.3	Mucosal Erythema by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.4.4	Mucosal Erythema by Treatment and Visit (All subject)-Safety Population
Table 14.2.4.5	Mucosal Erythema - Shift Tables by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.4.6	Mucosal Erythema - Shift Tables by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.4.7	Mucosal Erythema - Shift Tables by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.4.8	Mucosal Erythema - Shift Tables by Treatment and Visit (All subject)-Safety Population

Table 14.2.5.1	Mucosal Edema by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.5.2	Mucosal Edema by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.5.3	Mucosal Edema by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.5.4	Mucosal Edema by Treatment and Visit (All subject)-Safety Population
Table 14.2.5.5	Mucosal Edema - Shift Tables by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.5.6	Mucosal Edema - Shift Tables by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.5.7	Mucosal Edema - Shift Tables by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.5.8	Mucosal Edema - Shift Tables by Treatment and Visit (All subject)-Safety Population
Table 14.2.6.1	Nasal Discharge by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.6.2	Nasal Discharge by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.6.3	Nasal Discharge by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.6.4	Nasal Discharge by Treatment and Visit (All subject)-Safety Population
Table 14.2.6.5	Nasal Discharge - Shift Tables by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.6.6	Nasal Discharge - Shift Tables by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.6.7	Nasal Discharge - Shift Tables by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.6.8	Nasal Discharge - Shift Tables by Treatment and Visit (All subject)-Safety Population
Table 14.2.7.1	Mucosal Crusting by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.7.2	Mucosal Crusting by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.7.3	Mucosal Crusting by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.7.4	Mucosal Crusting by Treatment and Visit (All subject)-Safety Population
Table 14.2.7.5	Mucosal Crusting - Shift Tables by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.7.6	Mucosal Crusting - Shift Tables by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.7.7	Mucosal Crusting - Shift Tables by Treatment and Visit (> 16 years old subject)-Safety Population

Table 14.2.7.8	Mucosal Crusting - Shift Tables by Treatment and Visit (All subject)-Safety Population
Table 14.2.8.1	Mucosal Epistaxis by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.8.2	Mucosal Epistaxis by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.8.3	Mucosal Epistaxis by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.8.4	Mucosal Epistaxis by Treatment and Visit (All subject)-Safety Population
Table 14.2.8.5	Mucosal Epistaxis - Shift Tables by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.8.6	Mucosal Epistaxis - Shift Tables by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.8.7	Mucosal Epistaxis - Shift Tables by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.8.8	Mucosal Epistaxis - Shift Tables by Treatment and Visit (All subject)-Safety Population
Table 14.2.9.1	NIH TOOLBOX ODOR IDENTIFICATION TEST by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.9.2	NIH TOOLBOX ODOR IDENTIFICATION TEST by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.9.3	NIH TOOLBOX ODOR IDENTIFICATION TEST by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.9.4	NIH TOOLBOX ODOR IDENTIFICATION TEST by Treatment and Visit (All subject)-Safety Population
Table 14.2.10.1	Sedation Score Assessment by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.10.2	Sedation Score Assessment by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.10.3	Sedation Score Assessment by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.10.4	Sedation Score Assessment by Treatment and Visit (All subject)-Safety Population
Table 14.2.10.5	Sedation Score Assessment - Shift Tables by Treatment and Visit (6-11 years old subject)-Safety Population
Table 14.2.10.6	Sedation Score Assessment - Shift Tables by Treatment and Visit (12-16 years old subject)-Safety Population
Table 14.2.10.7	Sedation Score Assessment - Shift Tables by Treatment and Visit (> 16 years old subject)-Safety Population
Table 14.2.10.8	Sedation Score Assessment - Shift Tables by Treatment and Visit (All subject)-Safety Population
Table 14.3.1.1	Summary of Treatment-Emergent Adverse Events by Treatment -Safety Population

Table 14.3.1.2	Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term and Treatment -Safety Population
Table 14.3.1.3	Treatment-Emergent Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term and Treatment-Safety Population
Table 14.3.1.4	Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, Strongest Relationship to Study Drug and Treatment -Safety Population
Table 14.3.1.5	Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, Maximum Severity and Treatment -Safety Population
Table 14.3.1.6	Treatment-Emergent Treatment-Related Serious Adverse Events by MedDRA System Organ Class, Preferred Term and Treatment -Safety Population
Table 14.3.1.7	Treatment-Emergent Serious Adverse Events by MedDRA System Organ Class, Preferred Term, Strongest Relationship to Study Drug and Treatment -Safety Population
Table 14.3.1.8	Treatment-Emergent Serious Adverse Events by MedDRA System Organ Class, Preferred Term, Maximum Severity and Treatment -Safety Population
Table 14.3.1.9	Treatment-Emergent Adverse Events leading to Discontinuation by MedDRA System Organ Class, Preferred Term and Treatment -Safety Population
Table 14.3.2.1	Serious Adverse Events -Safety Population
Table 14.3.2.2	Adverse Event leading to Discontinuation - Safety Population
Table 14.3.2.3	Adverse Event leading to Death -Safety Population
Table 14.3.4.1	Listing of Abnormal values of the Laboratory Test -Safety Population
Table 14.3.4.2	Listing of Abnormal values of the Laboratory Test - Urinalysis -Safety Population
Table 14.3.5.1.1.1	Laboratory: Hematology by Treatment and Visit (6-11 years old subject) -Safety Population
Table 14.3.5.1.1.2	Laboratory: Hematology by Treatment and Visit (12 -16 years old subject) -Safety Population
Table 14.3.5.1.1.3	Laboratory: Hematology by Treatment and Visit (> 16 years old subject) -Safety Population
Table 14.3.5.1.1.4	Laboratory: Hematology by Treatment and Visit (All subject) -Safety Population
Table 14.3.5.2.1.1	Laboratory: Chemistry by Treatment and Visit (6-11 years old subject) -Safety Population
Table 14.3.5.2.1.2	Laboratory: Chemistry by Treatment and Visit (12 -16 years old subject) -Safety Population

Table 14.3.5.2.1.3	Laboratory: Chemistry by Treatment and Visit (> 16 years old subject) -Safety Population
Table 14.3.5.2.1.4	Laboratory: Chemistry by Treatment and Visit (All subject) -Safety Population
Table 14.3.5.3.1.1	Laboratory: Urinalysis by Treatment and Visit (6-11 years old subject) -Safety Population
Table 14.3.5.3.1.2	Laboratory: Urinalysis by Treatment and Visit (12 -16 years old subject) -Safety Population
Table 14.3.5.3.1.3	Laboratory: Urinalysis by Treatment and Visit (> 16 years old subject) -Safety Population
Table 14.3.5.3.1.4	Laboratory: Urinalysis by Treatment and Visit (All subject) -Safety Population
Table 14.3.5.3.2.1	Laboratory: Urinalysis (Categorical result) by Treatment and Visit (6-11 years old subject) -Safety Population
Table 14.3.5.3.2.2	Laboratory: Urinalysis (Categorical result) by Treatment and Visit (12 -16 years old subject) -Safety Population
Table 14.3.5.3.2.3	Laboratory: Urinalysis (Categorical result) by Treatment and Visit (> 16 years old subject) -Safety Population
Table 14.3.5.3.2.4	Laboratory: Urinalysis (Categorical result) by Treatment and Visit (All subject) -Safety Population
Table 14.3.6.1.1	ECG Parameters by Treatment and Visit (6-11 years old subject) -Safety Population
Table 14.3.6.1.2	ECG Parameters by Treatment and Visit (12 -16 years old subject) -Safety Population
Table 14.3.6.1.3	ECG Parameters by Treatment and Visit (> 16 years old subject) -Safety Population
Table 14.3.6.1.4	ECG Parameters by Treatment and Visit (All subject) -Safety Population
Table 14.3.6.2.1	ECG Interpretation by Treatment and Visit (6-11 years old subject) -Safety Population
Table 14.3.6.2.2	ECG Interpretation by Treatment and Visit (12 -16 years old subject) -Safety Population
Table 14.3.6.2.3	ECG Interpretation by Treatment and Visit (> 16 years old subject) -Safety Population
Table 14.3.6.2.4	ECG Interpretation by Treatment and Visit (All subject) -Safety Population
Table 14.3.7.1	Vital Signs by Treatment and Visit (6-11 years old subject) -Safety Population
Table 14.3.7.2	Vital Signs by Treatment and Visit (12 -16 years old subject) -Safety Population
Table 14.3.7.3	Vital Signs by Treatment and Visit (> 16 years old subject) -Safety Population
Table 14.3.7.4	Vital Signs by Treatment and Visit (All subject) -Safety Population
Table 14.3.8.1.1	Physical Examination by Treatment and Visit (6-11 years old subject) -Safety Population

Table 14.3.8.1.2	Physical Examination by Treatment and Visit (12 -16 years old subject) -Safety Population
Table 14.3.8.1.3	Physical Examination by Treatment and Visit (> 16 years old subject) -Safety Population
Table 14.3.8.1.4	Physical Examination by Treatment and Visit (All subject) -Safety Population
Table 14.3.8.2.1	Physical Examination - Shift Tables by Treatment and Visit (6-11 years old subject) -Safety Population
Table 14.3.8.2.2	Physical Examination - Shift Tables by Treatment and Visit (12 -16 years old subject) -Safety Population
Table 14.3.8.2.3	Physical Examination - Shift Tables by Treatment and Visit (> 16 years old subject) -Safety Population
Table 14.3.8.2.4	Physical Examination - Shift Tables by Treatment and Visit (All subject) -Safety Population

12.1.2. Listings

Listings No	**Title**
Listing 16.2.1.1	Final Termination - All Population
Listing 16.2.2.1	Protocol deviations - Safety Population
Listing 16.2.3.1	Patients excluded from the PK Population
Listing 16.2.4.1	Demographic Data - Safety Population
Listing 16.2.4.2	Past Medical History - Safety Population
Listing 16.2.4.3	Seizure Medical History - Safety Population
Listing 16.2.6.1	Individual PK Summary Data of - PK Population
Listing 16.2.6.2	Individual - PK Population
Listing 16.2.6.3.1	Concentration Data of - Plasma - PK Population
Listing 16.2.6.3.2	Concentration Data of - Urine - PK Population
Listing 16.2.7.1	Adverse Events - Safety Population
Listing 16.2.8.1	Laboratories Results - Chemistry/ Hematology Test Assessments - Safety Population
Listing 16.2.8.2	Urine Test Assessments : Continuous Results - Safety Population
Listing 16.2.8.3	Urine Test Assessments : Categorical Results - Safety Population
Listing 16.2.8.4	Laboratories Results - Urine Drug Screening - Safety Population
Listing 16.2.8.5	Laboratories Results - Serology Assessments at Screening - Safety Population
Listing 16.2.8.6	Laboratories Results - Pregnancy - Safety Population
Listing 16.2.9.1	Vital Signs Results and Change from Baseline - Safety Population
Listing 16.2.9.2	Physical Examination - Safety Population
Listing 16.2.9.3.1	ECG Interpretation - Safety Population
Listing 16.2.9.3.2	ECG Results - Safety Population

Listing 16.2.9.3.3	ECG Rhythms and Arrhythmias - Safety Population
Listing 16.2.9.4	Concomitant Medication - Safety Population
Listing 16.2.9.5	Study Drug Administration - Safety Population
Listing 16.2.9.6	Visual Analogue Scale - Safety Population
Listing 16.2.9.7	Nasal Irritation Assessments - Safety Population
Listing 16.2.9.8.1	Columbia-suicidality severity-Baseline /Screening Version - Safety Population
Listing 16.2.9.8.2	Columbia-suicidality severity-Since Last Visit - Safety Population
Listing 16.2.9.8.3	Columbia-suicidality severity-Children's Baseline/Screening - Safety Population
Listing 16.2.9.8.4	Columbia-suicidality severity-Children's Since Last Visit - Safety Population
Listing 16.2.9.9	NIH Toolbox Odor Identification Test - Safety Population
Listing 16.2.9.10	Sedation Score Assessment - Safety Population
Listing 16.2.9.11	Mucosal Erythema - Safety Population
Listing 16.2.9.12	Mucosal Edema - Safety Population
Listing 16.2.9.13	Nasal Discharge - Safety Population
Listing 16.2.9.14	Mucosal Crusting - Safety Population
Listing 16.2.9.15	Mucosal Epistaxis - Safety Population
Listing 16.2.9.16	Seizure - Safety Population
Listing 16.2.9.17	Eligibility - Safety Population
Listing 16.2.9.18	Admission to Clinical Site - Safety Population
Listing 16.2.10.1	Comments - Safety Population

12.1.3. Figures

Figures	**Title**
Figure 14.2.1.1	Nasal Irritation Assessments Mean and Standard Deviation by Treatment and Visit (6-11 years old subject) - Safety Population
Figure 14.2.1.2	Nasal Irritation Assessments Mean and Standard Deviation by Treatment and Visit (12 -16 years old subject) - Safety Population
Figure 14.2.1.3	Nasal Irritation Assessments Mean and Standard Deviation by Treatment and Visit (> 16 years old subject) - Safety Population
Figure 14.2.1.4	Nasal Irritation Assessments Mean and Standard Deviation by Treatment and Visit - Safety Population
Figure 14.2.2.1	Visual Analogue Scale Mean and Standard Deviation by Treatment and Visit (6-11 years old subject) - Safety Population
Figure 14.2.2.2	Visual Analogue Scale Mean and Standard Deviation by Treatment and Visit (12 -16 years old subject) - Safety Population

Figure 14.2.2.3	Visual Analogue Scale Mean and Standard Deviation by Treatment and Visit (> 16 years old subject) - Safety Population
Figure 14.2.2.4	Visual Analogue Scale Mean and Standard Deviation by Treatment and Visit - Safety Population
Figure 14.2.3.1	Mucosal Erythema Mean and Standard Deviation by Treatment and Visit (6-11 years old subject) - Safety Population
Figure 14.2.3.2	Mucosal Erythema Mean and Standard Deviation by Treatment and Visit (12 -16 years old subject) - Safety Population
Figure 14.2.3.3	Mucosal Erythema Mean and Standard Deviation by Treatment and Visit (> 16 years old subject) - Safety Population
Figure 14.2.3.4	Mucosal Erythema Mean and Standard Deviation by Treatment and Visit - Safety Population
Figure 14.2.4.1	Mucosal Edema Mean and Standard Deviation by Treatment and Visit (6-11 years old subject) - Safety Population
Figure 14.2.4.2	Mucosal Edema Mean and Standard Deviation by Treatment and Visit (12 -16 years old subject) - Safety Population
Figure 14.2.4.3	Mucosal Edema Mean and Standard Deviation by Treatment and Visit (> 16 years old subject) - Safety Population
Figure 14.2.4.4	Mucosal Edema Mean and Standard Deviation by Treatment and Visit - Safety Population
Figure 14.2.5.1	Nasal Discharge Mean and Standard Deviation by Treatment and Visit (6-11 years old subject) - Safety Population
Figure 14.2.5.2	Nasal Discharge Mean and Standard Deviation by Treatment and Visit (12 -16 years old subject) - Safety Population
Figure 14.2.5.3	Nasal Discharge Mean and Standard Deviation by Treatment and Visit (> 16 years old subject) - Safety Population
Figure 14.2.5.4	Nasal Discharge Mean and Standard Deviation by Treatment and Visit - Safety Population
Figure 14.2.6.1	Mucosal Crusting Mean and Standard Deviation by Treatment and Visit (6-11 years old subject) - Safety Population
Figure 14.2.6.2	Mucosal Crusting Mean and Standard Deviation by Treatment and Visit (12 -16 years old subject) - Safety Population
Figure 14.2.6.3	Mucosal Crusting Mean and Standard Deviation by Treatment and Visit (> 16 years old subject) - Safety Population
Figure 14.2.6.4	Mucosal Crusting Mean and Standard Deviation by Treatment and Visit - Safety Population
Figure 14.2.7.1	Mucosal Epistaxis Mean and Standard Deviation by Treatment and Visit (6-11 years old subject) - Safety Population

Figure 14.2.7.2	Mucosal Epistaxis Mean and Standard Deviation by Treatment and Visit (12 -16 years old subject) - Safety Population
Figure 14.2.7.3	Mucosal Epistaxis Mean and Standard Deviation by Treatment and Visit (> 16 years old subject) - Safety Population
Figure 14.2.7.4	Mucosal Epistaxis Mean and Standard Deviation by Treatment and Visit - Safety Population
Figure 14.2.8.1	NIH TOOLBOX ODOR IDENTIFICATION TEST Mean and Standard Deviation by Treatment and Visit (6-11 years old subject) - Safety Population
Figure 14.2.8.2	NIH TOOLBOX ODOR IDENTIFICATION TEST Mean and Standard Deviation by Treatment and Visit (12 -16 years old subject) - Safety Population
Figure 14.2.8.3	NIH TOOLBOX ODOR IDENTIFICATION TEST Mean and Standard Deviation by Treatment and Visit (> 16 years old subject) - Safety Population
Figure 14.2.8.4	NIH TOOLBOX ODOR IDENTIFICATION TEST Mean and Standard Deviation by Treatment and Visit - Safety Population
Figure 14.2.9.1	Sedation Score Assessment Mean and Standard Deviation by Treatment and Visit (6-11 years old subject) - Safety Population
Figure 14.2.9.2	Sedation Score Assessment Mean and Standard Deviation by Treatment and Visit (12 -16 years old subject) - Safety Population
Figure 14.2.9.3	Sedation Score Assessment Mean and Standard Deviation by Treatment and Visit (> 16 years old subject) - Safety Population
Figure 14.2.9.4	Sedation Score Assessment Mean and Standard Deviation by Treatment and Visit - Safety Population

13. REFERENCES

1. U.S. Department of Health and Human Services, FDA, Center for Drug Evaluation and Research (CDER). Center for Biologics Evaluation and Research (CBER). Guidance for Industry. E6 Good Clinical Practice: Consolidated Guidance. ICH, 1996, Rockville, Maryland.

2. U.S. Department of Health and Human Services, FDA, Center for Drug Evaluation and Research (CDER). Center for Biologics Evaluation and Research (CBER). Guidance for Industry. E6 Good Clinical Practice: Consolidated Guidance. ICH, 1996, Rockville, Maryland.