STATISTICAL ANALYSIS PLAN

08SEP2017 V1.0

A Phase 2, Randomized, Open Label, Multiple-Dose, Comparator, Parallel-Group, Safety and Tolerance Study of Buprenorphine Sublingual Spray (0.5 mg TID) versus Standard of Care Post-Operative Narcotic Therapy for the Treatment of Post-Operative Pain

Protocol Number: INS005-17-111 / NCT03254459

Protocol Version 1.0 (02AUG2017)

INS005-17-111_Admin Protocol Clarification_Final 1.0 (10AUG2017)

INS005-17-111_Admin Protocol Clarification_Final 2.0 (22AUG2017)

INS005-17-111_Admin Protocol Clarification_Final 3.0 (30AUG2017)

INS005-17-111_Admin Protocol Clarification_Final 4.0 (07SEP2017)

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DOCUMENT VERSION CONTROL

Version Number	Date	Comments/Changes
V0.1	17AUG2017	First Draft for Internal review
V0.2(S)	22AUG2017	First Draft for Sponsor review
V0.3(s)	05SEP2017	Incorporate sponsor comments, include Mock Shells for review
V1.0	08Sep2017	Final v1.0

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LIST OF ABBREVIATIONS

ADaM	Analysis Data Model
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BP	Blood Pressure
CRF	Case Report Form
CSR	Clinical Study Report
ECG	Electrocardiogram
ET	Early Termination
HEENT	Head, Ears, Eyes, Nose and Throat
HIV	Human Immunovirus
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IP	Investigational Product
IV	Intra-Venous
IWRS	Interactive Web Response System
MedDRA	Medical Dictionary for Regulatory Activities
ODT	Oral Dissolvable Tablet
PONV	Post-Operative Nausea and Vomiting
PT	Preferred Term
RTF	Rich Text Format
SAE	Serious Adverse Event/Experience
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDTM	Standard Data Table Model
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
TID	Three Times Per Day

WHO	World Health Organization

1. PURPOSE OF THE ANALYSES

This statistical analysis plan (SAP) is being developed after review of the Insys Development Company. Inc., protocol number INS005-17-111 Final Version 1.0, dated 02Aug2017 but before any analyses of the data. The SAP contains detailed information to aid in the performance of the statistical analysis and reporting of the study data for use in the final clinical study report (CSR). This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonization (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials and the most recent ICH E3 Guideline, entitled Guidance for Industry: Structure and Content of Clinical Study Reports and the most recent FDA draft Guidance for Industry - Analgesic Indications: Developing Drug and Biological Products, dated February 2014.

This SAP describes the data sets that will be analyzed and the subject characteristics, and safety assessments that will be evaluated. There will be no efficacy analysis in this study. This SAP provides details of the specific statistical methods that will be used. If additional analyses are required to supplement the planned analyses described in this SAP, they may be completed and will be identified in the CSR.

2. PROTOCOL SUMMARY

2.1 Study Objectives

2.1.1 Safety

To evaluate the safety and tolerability based on the incidence of adverse experiences of Buprenorphine Sublingual Spray (0.5 mg three times daily [TID]) compared with standard post-operative narcotic therapy in subjects with postoperative pain. Standard post-operative narcotic therapy is defined as Morphine Intravenous Injection (IV) (4 mg TID) followed by Oxycodone Hydrochloride Tablet (10 mg TID).

2.1.2 Efficacy

This is a safety and tolerability only study and so has no efficacy objectives.

2.2 Overall Study Design and Plan

This is a Phase 2, randomized (stratified according to surgery and postoperative nausea and vomiting risk factors), open label, multiple-dose, comparator controlled, parallel-group, study to evaluate the safety and tolerability of Buprenorphine Sublingual Spray (0.5 mg TID) versus standard postoperative narcotic therapy in subjects with postoperative pain. Standard postoperative narcotic therapy is defined as Morphine IV (4 mg TID) for 24 hours followed by Oxycodone Hydrochloride Tablet (10 mg TID).

Subjects will be admitted to the study site on the morning of the scheduled surgery (Day 1), will remain at the study site until Postoperative Day 4 (a total of 3 nights at the study site) then be evaluated to participate in the outpatient setting and meet criteria in order to proceed to the outpatient treatment period Days 4 to 7. Subjects will subsequently return to the clinic for the Follow-up Visit on Day 8 (+2 day window). Subjects will be allowed rescue medication for pain and /or nausea at the investigator's discretion.

Screening Period: Subjects who meet all inclusion and no exclusion criteria will be eligible for enrollment. After providing written Informed Consent, subjects will undergo study specific screening procedures (please refer to the Protocol for complete list of procedures), including a review of inclusion and exclusion, demographics, medical history, concomitant medication use, assessment of postoperative nausea and vomiting (PONV) risk factors, physical and oral cavity examination, baseline laboratory testing, alcohol breath test, urine drug screening, HIV and hepatitis screening, 12-lead electrocardiogram (ECG), and pregnancy testing. Eligible subjects will complete all screening procedures within 28 days before the surgery (Days -28 to -1).

Surgical Period: On Day 1, anesthesia will be established using standardized techniques, as appropriate, for each surgical procedure. The surgical procedures will be either bunionectomy, breast augmentation, or abdominoplasty. For nausea prophylaxis, all subjects will receive a uniform standard of care regimen including 10 mg of dexamethasone at induction and 8 mg of ondansetron near the end of surgery. Vitals, pulse oximetry, and ECG measurements will be taken. Concomitant medications and Adverse Events will be recorded. Please refer to the Protocol for complete list of procedures.

Post-surgery and prior to randomization, subjects may be treated with intravenous morphine and or fentanyl for post-surgical analgesia (dose and frequency per the discretion of the investigator).

Treatment Period - Inpatient: After meeting post-surgical eligibility requirements and subsequently being randomized to treatment, subjects may receive their first dose of investigational drug any time between 0-4 hours after surgery. The first dose does not need to be immediately administered after meeting post-surgical eligibility requirements. Study medication administration after the first dose are to be administered every 8 hours (Treatment Period Days 1 – 7).

During the Treatment Period, approximately 100 subjects will be randomly assigned to 1 of 2 treatment groups: Buprenorphine Sublingual Spray 0.5 mg TID, or standard of care postoperative narcotic therapy. Randomization will be assigned by IWRS and stratified according to surgical procedure and baseline PONV risk factors. Vitals, pulse oximetry, and ECG measurements will be taken. Concomitant medications and Adverse Events will be recorded.

Pulse oximetry will be monitored continuously after surgery as a safety measure. An electrocardiogram (ECG) will be conducted after surgery but before the first dose of the study drug and serve as a baseline for comparison to subsequent tracings. The time of administration of the first dose of study drug will be defined as Time 0. The inpatient Treatment Period will continue through 72 hours after Time 0. Additional ECGs will be performed at 90 minutes, 12 hours, 24 hours, 48 hours and 72 hours after Time 0. Please refer to the Protocol for complete list of procedures.

Treatment Period – Outpatient: Investigators will determine if patients are able to proceed with the outpatient treatment period. After discharge to the outpatient portion of the trial, study drug will be administered by subjects at home according to the directions provided by study staff. Study personnel will dispense outpatient diary, study drug, and rescue medication for pain and nausea. Please refer to the Protocol for complete list of procedures.

Follow-up Visit on Day 8 (+2 day window): Subjects will be instructed to return any unused outpatient study drug to study personnel. Vitals, pulse oximetry, and ECG will be measured.

Concomitant medications and Adverse Events will be recorded. Subject outpatient diary will be collected and reviewed by study staff. Please refer to the Protocol for complete list of procedures.

Rescue medication: Rescue for inadequate analgesic response during confinement to the study center during the first 72 hours for pain will be acetaminophen 1000 mg every six hours and/or ketorolac 30 mg every six hours, as needed. On outpatient days 4-7 subjects will be provided with acetaminophen, and will be advised to take acetaminophen 1000 mg every six hours as needed for rescue analgesia.

Rescue for postoperative nausea during confinement to the study center during the first 72 hours will be Zofran 4 mg IV per the discretion of the clinician. On outpatient days 4-7, subjects will be provided with Zofran ODT (oral dissolvable tablet) to be taken as needed.

Subjects whose pain or nausea cannot be adequately managed (in the investigator's opinion) by a combination of study drug and rescue medication or who develop unacceptable side effects during the study will be discontinued from further study participation. Their pain or nausea will be managed according to usual standard of care at the investigator's discretion.

The protocol-defined visits are presented in the following table:

Table 2-1 Protocol-Specified Visits and Visit Windows

Study Phase	*Visit Time*
Screening	From days -28 to -1
Surgical Period	Day 1
Treatment Period - Inpatient	Days 1 to 4
Treatment Period - Outpatient	Days 4 to 7
Follow-up Visit	Day 8 (±2 days)

2.3 Study Population

The study population will be males or females ≥18 and ≤65 years of age, with body weight ≥45 kg and a body mass index (BMI) ≤40 kg/m2, and scheduled for elective bunionectomy, breast augmentation (in women only), or abdominoplasty.

2.4 Treatment Regimens

2.4.1 Study Material

Buprenorphine Sublingual Spray, 0.5 mg TID manufactured for and supplied by Insys Development Company, Inc.

2.4.2 Comparator Group

Morphine IV, 4 mg TID for 24 hrs, followed by Oxycodone Hydrochloride Tablet, 10 mg TID.

2.5 Treatment Group Assignments or Randomization

Randomized treatment will be assigned utilizing a computer generated randomization scheme. Subjects who meet the inclusion criteria, do not fulfill any of the exclusion criteria and meet post-surgical eligibility requirements will be eligible for randomization into the study.

All study doses administered will be according to the IWRS specified treatment to ensure that study personnel will not be aware of the next subject's treatment assignment before the decision to randomize that subject has been made. The IWRS randomization algorithm will be such that the subjects will be stratified by surgical procedure and baseline PONV risk factors and randomly assigned to treatment administered in a 1:1 assignment ratio within the stratification categories. PONV risk will be assessed at screening to assess the likelihood of nausea and vomiting after surgery using the Apfel scale

(PONV) Risk Factor Assessment Risk Factors	**Points**
Post-operative Opioids (if planned)	1
Non Smoker	1
Female Gender	1
History of postoperative nausea and vomiting / Motion Sickness	1
Risk score = sum	0…4

Patients with PONV risk factors of 0-2 will be stratified as low risk and 3-4 as high risk.

2.6 Sample Size Determination

No formal sample size estimate has been completed. A sample size of 50 subjects per treatment group is expected to be sufficient to achieve the study objectives.

3. GENERAL ANALYSIS AND REPORTING CONVENTIONS

This section discusses general policies to be employed in the analysis and reporting of the data from the study. Departures from these general policies are provided in the specific detailed sections of this SAP. When this situation occurs, the rules set forth in the specific section take precedence over the general policies.

All continuous study assessments will be summarized by treatment and time point (as applicable) using descriptive statistics (n, mean, SD, median, minimum, and maximum). All of the categorical study assessments will be summarized by treatment and time point (as applicable) using frequency counts and percentages. Changes from baseline for continuous outcomes will be presented as their corresponding continuous measures for post-baseline visits. All relevant study data will be listed by treatment group, subject, and time point (as applicable).

No preliminary rounding will be performed; rounding will only occur after the analysis. To round, consider the digit to the right of the last significant digit: if <5, then round down; if ≥5, then round up. Means and medians will be presented with one more decimal place than the precision of the data. Standard deviations will be presented with two more decimal places than the precision of the data. Percentages will be presented with one decimal place. Minimums and maximums will be presented with the same precision as the original data.

All analyses will be performed using the SAS System® version 9.3 or higher. The domain (Study data tabulation Model [SDTM]) and analysis (Analysis Data Model [ADaM]) data sets will be taken as input to the SAS programs that generate the report-ready tables, figures and listings. The submission ready SDTM and ADaM data sets will be provided to the sponsor along with display deliveries. The specifications for the domain data sets and analysis data sets will be provided in a separate document.

For all analyses, subjects will be analyzed by treatment group according to the actual product received during treatment, i.e., “as treated.”

The following conventions will be used throughout the study analysis:

- Assessment visit times are defined by time of treatment administration.
- Baseline value is defined as the last valid measurement prior to the first treatment administration.

- Change from baseline is defined as post-baseline value minus baseline value.

- Duration of an AE will be computed in days as the stop date of the event minus the start date plus 1. If reported as ongoing at the time of database lock, the stop date is defined as the date of the last visit or the last date of any AE for the subject in the database, whichever is later. Missing dates will be imputed as described in Section 7.2.

- The number of days in the study is computed as:
  Date of study completion /withdrawal - the date of first treatment administration (Day 1) + 1.

- If duplicate values are obtained at a given visit (e.g., repeated vital sign measurements), the last value will be used unless it is noted that the measurement was in error for that value. Values that compromise interpretation will not be used in summaries (e.g., values that were obtained post-dose will not be summarized as pre-dose values).

4. ANALYSIS POPULATIONS

4.1 Efficacy Population

This study has no efficacy analysis and so no efficacy population.

4.2 Safety Population

The *safety population* will include all subjects who received at least 1 dose of study drug.

4.3 Disposition of Subjects

Subjects will be considered enrolled into the study only when they have received study drug. If a subject is randomized but does not receive study drug, they will not be counted in any summaries.

All enrolled subjects will be listed. Subjects who are screened and who fail screening or withdraw consent prior to randomization will not be entered into the database or presented in summaries or data listings. Subjects who are randomized, treated, subjects included in the safety population, subjects who complete follow-up as well as subjects who withdraw early from the study and the reason for withdrawal will be summarized by treatment group and overall in the subject disposition summary table.

4.4 Major Protocol Deviations

Patient specific protocol deviation information will be collected on the CRF. Site specific deviations will be collected by the CRA and logged in the trip reports. [redacted] will prepare a final Excel export of all CRF deviations and append to this Excel all Site specific deviations to create a final Excel Database of Deviations. All protocol deviations in this database will be designated as major or minor prior to CRF database lock by the sponsor's medical monitor. A major deviation is typically one that may affect the outcome, analysis or interpretation of the study. All protocol deviations will be presented in a by-subject listing.

5. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

5.1 Demographics and Baseline Characteristics

Demographic variables include age, gender, race, ethnicity, surgical procedure, and PONV risk factor. Baseline characteristics include height (cm), weight (kg), and BMI (kg/m2). Demographics and baseline characteristics will be presented in by-subject listings and summarized overall and by treatment group.

5.2 Medical History

Medical history, as collected at screening, will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 19.0 and presented in a by-subject listing using the coded and verbatim history terms.

5.3 Prior and Concomitant Medications/Surgeries Details

Prior medications/surgeries are those that stop prior to the start of the first study drug treatment administration. Any medication/therapy that stops at or after this time or with missing stop dates is considered concomitant medication/therapy.

Prior and concomitant medications are collected at screening and updated throughout the study as needed. Prior and concomitant medications will be coded using WHO/ATC classification index version March 2016 and summarized separately by drug class and preferred name, overall and by treatment group, for the safety population.

Prior and concomitant therapies will be presented in a by-subject listing of verbatim and coded terms. Non-medical therapies will appear in a separate data listing.

6. MEASUREMENTS OF TREATMENT COMPLIANCE

6.1 Study Medication Compliance

The exposure to study medication during the treatment periods will be listed by-subject and summarized by descriptive statistics for both the inpatient and outpatient portions of the study, and overall. As the dose administration during the inpatient period is under the control of the study sites, compliance during that time will not be summarized.

Compliance of the subject during the outpatient portion of the study will be assessed by summarizing the number of doses taken during the outpatient portion of the trial, and by the average number of doses taken per day during the outpatient portion of the trial, calculated as the number of doses taken divided by the number of days the subject remains in the outpatient portion of the study.

Subjects assigned to standard of care during the outpatient portion of the trial were instructed to take study medication only when they experienced pain. Subjects assigned Buprenorphine were instructed to maintain the TID dosing for the entire outpatient period.

7. SAFETY EVALUATION

7.1 Overview of Safety Analysis Methods

The primary safety endpoints are the incidence of TEAEs.
The secondary safety endpoints are as follows:

- Proportion of subjects using rescue medication for nausea
- Time to first use of rescue medication for nausea following each dose of the investigational product (IP)
- Total use of rescue medication for nausea over 0-8 hours, 0 to 24 hours, over 0 to 48 hours, over 0-72 hours and 0-7 days
- Pulse oximetry
- ECGs at 90 minutes, 12, 24, 48 and 72 hours
- Oral examinations

7.2 Adverse Events

Treatment-emergent AEs are defined as AEs that start or worsen in severity after the first exposure to study medication. Verbatim terms used by investigators to identify AEs in the CRFs will be mapped to the appropriate preferred term (PT) and system organ class (SOC) using a standardized coding dictionary (MedDRA Version 19.0). All coding will be reviewed prior to database lock. All recorded AEs will be listed, but only TEAEs will be summarized.

A serious adverse event (SAE) is any AE that meets any of the following causes:

- Results in death;
- Is life-threatening;
- Requires in-subject hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant disability or incapacity;
- Is a congenital anomaly or birth defect;
- Is medically significant or requires intervention to prevent one of the outcomes listed above.

Serious AEs will be captured from the time of consent through the end of the study.

An overall summary will be prepared giving, for each treatment group and overall, both the number of events, and the number of subjects with events for the following events:

- all TEAEs,
- serious TEAEs
- treatment related TEAEs,
- SAEs and TEAEs leading to premature discontinuation of study.

In addition, the overall summary will be produced by the study stratification variables: PONV risk group and surgical procedure.

Incidence of TEAEs will be summarized for each treatment group by SOC and PT sorted in descending frequency by system organ class (SOC), and then by preferred term (PT) within SOC. Separate tables will be created for each of the following event sets:

- All TEAEs
- Treatment related TEAEs (defined as Possibly, Probably or Definitely related)
- TEAEs leading to premature discontinuation from study
- Serious AEs
- TEAEs by maximum severity

The following AE listings will be created: all AEs, treatment related AEs, serious AEs, deaths, and AEs leading to premature discontinuation.

If a given subject experiences a TEAE that maps to the same PT more than once, the subject will be counted once for the PT at its greatest severity (i.e., mild, moderate, or severe) and causality (i.e., attribution to treatment).

Duration of a TEAE will be computed in days as the stop date of the event minus the start date plus 1 and included in by subject listings. If reported as ongoing at the time of database lock, the stop date is defined as the date of the last visit or the last date of any event for the subject in the database, whichever is later. If a TEAE is considered resolved, but the stop date is missing, the last day of the month will be imputed if the month and year are available. If only the year is available, and the year is the same as the year of the last visit, the stop date will be the latest of the last visit date or latest event for the subject in the database. If the year of the event is prior to the year of the last treatment, the end day and month will be set to 31 December.

For missing or partial start dates, it is most conservative to impute them as temporally related to the first dose of study medication. The following chart will be used to impute start date:

Table 7-1 Table of AE Start Date Imputation Rules

Missing Start Date Portion	*Prior to Treatment*	*Same as Treatment Start Date*	*After Treatment Start Date*
Day	*Month and Year < Month and Year of first treatment:* Day = 1	*Month and Year = Month and Year of first treatment:* Day = Day of first treatment	*Month and Year > Month and Year of First Treatment:* Day = 1
Day and Month	*Year < Year of first treatment:* Day = 1, Month = July	*Year = Year of first treatment:* Day = Day of first treatment, Month = Month of first treatment	*Year > Year of first treatment:* Day = 1, Month = January
Day, Month, and Year	To be conservative, completely missing start dates will be set to the date of first treatment		

After following these imputation rules, if the start date is imputed as a date after the end date, the start date will be set to the end date to provide a positive duration for the event incidence.

Missing assessments for AE study medication relationship or severity will be summarized as definitely related or severe respectively. No other imputation is planned for safety data.

7.3 Rescue Medication

The total use of rescue and the proportion of patients given rescue medication for nausea relief will be summarized by treatment group and by cumulative time point (0-8 hours, 0-24 hours, 0-48 hours, 0-72 hours and 0-7 days) and overall. A by-subject listing presenting the use of nausea rescue medication over time will be given.

Time to first rescue medication for nausea is the time (in minutes) elapsed from the time of first dose of IP to time the first dose of rescue medication for nausea is given. A

summary table will present the median time to first rescue use and 95% confidence intervals of the medians by treatment group as determined by log-rank analysis performed using SAS PROC LIFETEST. A summary figure will present the time to first rescue use as a Kaplan-Meier survival plot. If a subject does not take rescue medication for nausea but prematurely discontinues from the study, then for analysis purposes the subject will be censored at the time of discontinuation. If a subject never takes rescue medication for nausea and completes the treatment phase of the study, then the subject will be considered censored for analysis purposes at 7 days.

7.4 Clinical Laboratory Evaluation

The following clinical laboratory tests will be performed for individual subjects.

Serum Chemistry: Albumin, total bilirubin, total protein, calcium, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, cholesterol, glucose, sodium, potassium, chloride, bicarbonate, lactate dehydrogenase, uric acid, creatinine with calculated creatinine clearance (Cockcroft-Gault method).

Hematology: Hemoglobin, hematocrit, red blood cell count, red blood cell indices, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count (or estimate), and white blood cell count including differential.

Urinalysis: pH, specific gravity, blood, glucose, protein, and ketones.

Baseline for clinical laboratory parameters will be defined as the last evaluation before dosing with study treatment. For each continuous parameter, summary statistics of values and change from baseline will be presented by treatment group and overall; categorical urinalysis test parameters will be summarized using number and proportion of normal and abnormal results at each visit. All clinical laboratory values will be listed.

7.5 Vital Signs

Vital signs results including pulse oximetry, BP [systolic and diastolic], pulse rate, respiration rate, and body temperature will be listed for individual subjects. Baseline for vital signs measurements will be defined as the last evaluation before dosing with study medication. Summary statistics of values and changes from baseline to each study time point will be presented by treatment group and overall

7.6 Physical, Oral and ECG Exams

All findings of physical, oral and ECG examinations will be listed for individual subjects and abnormal findings will be summarized by time point.

A physical exam will be conducted at screening, before surgery on Day 1, 72 hours (±4 hours) after first dose of study drug (Time 0), and at the Follow-up Visit/ET. Physical examination systems include HEENT, cardiovascular, respiratory, gastrointestinal, neurological, dermatologic, and musculoskeletal systems.

An oral cavity exam will consist of a sublingual assessment, noting the colour of mucosa and whether inflammation is present, a check for mucositis and local irritation. The oral cavity examinations should be conducted at screening, pre-surgery, before the first dose of study drug, and then at 90 minutes (±10 minutes), and at 12, 24, 48 hours, 72 hours (±10 minutes) after Time 0, and at Follow-up Visit/ET. Assessments will be repeated based on the Investigator's discretion.

The ECG will be evaluated for any clinically relevant cardiovascular conditions, defined as any clinically significant abnormalities identified by the reader related to coronary artery disease, coronary spasm, abnormal heart rhythm, hypertrophic cardiomyopathy, heart failure, rheumatic heart disease, or myocarditis. An ECG will be performed at screening, before the first dose of study drug, and then at 90 minutes (±10 minutes), and at 12, 24, 48 hours, 72 hours (±10 minutes) after Time 0 and at Follow-up Visit/ET

7.7 Serology Screens, Drug of Abuse and Alcohol Screens, Pregnancy Test

Results of, HIV and hepatitis B and C screens, drug of abuse and alcohol screens, and pregnancy tests will be listed for individual subjects. Each test result will be defined to be "negative" or "positive" according to the normal reference range from the clinical laboratory.

8. EFFICACY EVALUATION

There is to be no efficacy analysis in this study.

9. OTHER ANALYSES

Any additional analyses conducted will be considered exploratory and enumerated in the CSR.

10. INTERIM ANALYSES AND DATA MONITORING

There are no planned interim analyses for this study.

11. CHANGES TO THE ANALYSES PLANNED IN THE PROTOCOL

Any deviations from the statistical plan will be described and a justification given in the CSR.

12. REFERENCES

US Federal Register. (1998) *International Conference on Harmonization; Guidance for Industry: Statistical Principles for Clinical Trials*. Department of Health and Human Services: Food and Drug Administration. Federal Register, Vol. 63, No. 179, September 16, 1998, page 49583.

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Guidance for Industry (2014) *Analgesic Indications: Developing Drug and Biological Products - Draft Guidance*. Department of Health and Human Services: Food and Drug Administration. Center for Drug Evaluation and Research (CDER) February 2014 Clinical/Medical.

13. APPENDICES

13.1 List of Tables for Final Study Report

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14. GENERAL PROGRAMMING NOTES

All continuous study assessments will be summarized by treatment and time point (as applicable) using descriptive statistics (n, mean, standard deviation, median, and range (minimum, maximum)). All categorical study assessments will be summarized by treatment and time point (as applicable) using frequency counts and percentages. All study data will be listed by treatment group, subject and time point (as applicable).

No preliminary rounding should be performed; rounding should only occur after analysis. To round, consider digit to right of last significant digit: if < 5 then round down, if ≥ 5 then round up. Means and medians will be presented with one more decimal place than the precision of the data. Standard deviations will be presented with two more decimal places than the precision of the data. Percentages will be presented with one decimal place. Minimums and maximums will be presented with the same precision as the original data.

Study Conventions:

- Day 1 is the day of baseline and first exposure study treatment.
- Assessment time point times are defined by time after administration of study drug.
- Baseline value is defined as the last valid measurement prior to treatment.
- Change from baseline is defined as post-baseline value minus baseline value.
- Duration of an adverse event will be computed in days as the [stop date of the event minus the start date] plus 1. See SAP for imputation rules for missing dates.
- The number of days in the study is computed as: [Date of study completion (or withdrawal) - the date of first dose (Day 1)] + 1.
- If duplicate values are obtained at a given time point (e.g., repeated vital sign measurements), the last value will be used unless it is noted that the measurement was in error for that value. Values that compromise interpretation will not be used in summaries (e.g., values that were obtained post-dose will not be summarized as pre-dose values).

Table 14.1.1
Summary of Subject Disposition
All Subjects

	Standard Narcotic Therapy[1] N=xxx	Buprenorphine SL Spray (0.5 mg TID) N=xxx	Overall N=xxx
Subjects Randomized	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Subjects in Safety Population (received treatment), n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Subjects completing study, n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Completed Inpatient Treatment/Completed Outpatient Treatment/ Completed Follow-up	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Completed Inpatient Treatment/ Not Completed Outpatient Treatment/ Not Completed Follow-up	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Completed Inpatient Treatment/Completed Outpatient Treatment/ Not Completed Follow-up	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Treatment/Not completed Outpatient Treatment/ Not completed Follow-up	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Subjects with early termination, n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Adverse event, n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Death, n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Withdrawal of consent by subject, n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Subject Non-compliance, n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Protocol Violation, n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Lost to follow-up, n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Other, n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)

Footnote:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Table 14.1.2
Summary of Demographic and Baseline Characteristics
Safety Population

	Standard Narcotic Therapy[1] **N = xx**	**Buprenorphine SL Spray (0.5 mg TID)** **N = xx**	**Overall** **N = xx**
Age			
N	XXX	XXX	XXX
Mean (SD)	XXX.X (XX.X)	XXX.X (XX.X)	XXX.X (XX.X)
Median	XXX	XXX	XXX
Range (Min, Max)	XXX, XXX	XXX, XXX	XXX, XXX
Sex, n (%)			
Male	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Female	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Race, n (%)			
White	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Black or African American	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Asian	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
American Indian or Alaskan Native	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Native Hawaiian or Pacific Islander	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Multiple	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Other			
Ethnicity, n (%)			
Hispanic or Latino	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Non-Hispanic or Latino	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Unknown	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Baseline Height (cm)			
N	XXX	XXX	XXX
Mean (SD)	XXX.X (XX.X)	XXX.X (XX.X)	XXX.X (XX.X)
Median	XXX	XXX	XXX
Range (Min, Max)	XXX, XXX	XXX, XXX	XXX, XXX

	Standard Narcotic Therapy[1] **N = xx**	**Buprenorphine SL Spray (0.5 mg TID)** **N = xx**	**Overall** **N = xx**
Baseline Weight (kg)			
N	XXX	XXX	XXX
Mean (SD)	XXX.X (XX.X)	XXX.X (XX.X)	XXX.X (XX.X)
Median	XXX	XXX	XXX
Range (Min, Max)	XXX, XXX	XXX, XXX	XXX, XXX
Baseline BMI (kg/m^2) [2]			
N	XXX	XXX	XXX
Mean (SD)	XXX.X (XX.X)	XXX.X (XX.X)	XXX.X (XX.X)
Median	XXX	XXX	XXX
Range (Min, Max)	XXX, XXX	XXX, XXX	XXX, XXX
Baseline PONV Risk Factor			
0	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
1	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
2	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
3	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
4	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Baseline PONV Risk Factor			
Low Risk	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
High Risk	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Surgical Procedure			
Bunionectomy	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Breast Implant	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Abdominoplasty	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)

Footnotes:
Percentages are based on the number of subjects (N) in a given treatment group for the population analyzed.
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
[2] BMI is calculated as BMI = Weight(kg) / [Height(m)^2].

Programmer Notes:
For categorical variables, missing categories (e.g. no Hispanics) should appear with an n and % of zero.

Table 14.1.3
Summary of Prior Medications [1]
Safety Population

System Organ Class **Preferred Term**	**Standard Narcotic Therapy[2]** **N=xx**	**Buprenorphine SL Spray (0.5 mg TID)** **N=xx**	**Overall** **N=xx**
Number of Subjects with Any Prior Medication, n (%) [3]	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
ATC Class 1[4]	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Preferred Term 1	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Preferred Term 2	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
ATC Class 2	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Preferred Term 1	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Preferred Term 2	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Etc.			

Footnotes:
[1] Prior medications include all medications that were started and stopped prior to study drug initiation.
[2] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
[3] n = Number of subjects reporting at least one medication within an ATC Class and Preferred Term;(%) = Percentage of subjects among Treatment Group (N). A subject reporting more than one medication for a particular ATC Class or Preferred Term is counted only once for each ATC Class or Preferred Term.
[4] ATC Class and Preferred Term are based on the WHO/ATC classification index version March 2016 drug coding dictionary.

Programmer Notes:
Table entries should be sorted in decreasing order by overall n of ATC Class and by PT overall n within ATC Class based on the pooled EB-001 column.

Table 14.1.4
Summary of Concomitant Medications
Safety Population

System Organ Class **Preferred Term**	**Standard Narcotic Therapy[1]** **N=xx**	**Buprenorphine SL Spray (0.5 mg TID)** **N=xx**
Number of Subjects with Any Concomitant Medication, n (%)	XXX (XX.X%)	XXX (XX.X%)
ATC Class 1	XXX (XX.X%)	XXX (XX.X%)
Preferred Term 1	XXX (XX.X%)	XXX (XX.X%)
Preferred Term 2	XXX (XX.X%)	XXX (XX.X%)
ATC Class 2	XXX (XX.X%)	XXX (XX.X%)
Preferred Term 1	XXX (XX.X%)	XXX (XX.X%)
Preferred Term 2	XXX (XX.X%)	XXX (XX.X%)
Etc.		

Footnotes:
[1]Concomitant medications include all medications that were started or stopped after study drug initiation or those with missing stop dates.
[2] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
[3] n = Number of subjects reporting at least one medication within an ATC Class and Preferred Term;(%) = Percentage of subjects among Treatment Group (N). A subject reporting more than one medication for a particular ATC Class or Preferred Term is counted only once for each ATC Class or Preferred Term.
[4] ATC Class and Preferred Term are based on the WHO/ATC classification index version March 2016 drug coding dictionary.

Programmer Notes:
Table entries should be sorted in decreasing order by overall n of ATC Class and by PT n within ATC Class based on the pooled EB-001 column.

Table 14.1.5
Summary of Study Medication Compliance (Outpatient)
Safety Population

	Standard Narcotic Therapy[1] N = xx	**Buprenorphine SL Spray (0.5 mg TID)** N = xx	**Overall** N = xx
Total Number of Doses taken during Outpatient period [2]			
n	X	X	X
Mean	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX
Median	X.X	X.X	X.X
Range (Min, Max)	(X.X – X.X)	(X.X – X.X)	(X.X – X.X)
Average Number of Doses per Day During Outpatient period [3]			
n	X	X	X
Mean	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX
Median	X.X	X.X	X.X
Range (Min, Max)	(X.X – X.X)	(X.X – X.X)	(X.X – X.X)

Footnote:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
[2] The number of doses taken is the number dispensed – number returned. Subjects assigned Standard Narcotic Therapy during the outpatient portion of the trial were instructed to take study medication only when they experienced pain. Subjects assigned Buprenorphine SL Spray (0.5 mg TID) were instructed to maintain the TID dosing for the entire outpatient period.
[3] Average number of doses is calculated as the number of doses taken divided by the number of days the subject remained in the outpatient portion of the study.

Table 14.1.6
Summary of Study Medication Exposure
Safety Population

	Standard Narcotic Therapy [1]		**Buprenorphine SL Spray (0.5 mg TID) [2]**
	Morphine N = xx	Oxycodone N = xx	N = xx
Total Exposure during Inpatient period (mg)			
n	X	X	X
Mean	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX
Median	X.X	X.X	X.X
Range (Min, Max)	(X.X - X.X)	(X.X - X.X)	(X.X - X.X)
Total Exposure during Outpatient period (mg) [3]			
n		X	X
Mean		X.X	X.X
SD		X.XX	X.XX
Median		X.X	X.X
Range (Min, Max)		(X.X - X.X)	(X.X - X.X)
Total Exposure Overall (mg)			
n	X	X	X
Mean	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX
Median	X.X	X.X	X.X
Range (Min, Max)	(X.X - X.X)	(X.X - X.X)	(X.X - X.X)

Footnotes:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
[2] Subjects assigned to Buprenorphine SL Spray (0.5 mg TID) received Buprenorphine sublingual spray 0.5 mg TID for the entire treatment period.
[3] During the outpatient portion of the trial, subjects assigned to Standard Narcotic Therapy were instructed to take study medication only when they experienced pain, while subjects assigned to Buprenorphine SL Spray (0.5 mg TID) were instructed to maintain the TID dosing for the entire outpatient period.

Table 14.3.1.1.1
Overall Summary of Treatment-Emergent Adverse Events (TEAEs)
Safety Population

	Standard Narcotic Therapy[4] N=xx	Buprenorphine SL Spray (0.5 mg TID) N=xx	Overall N=xx
Number of TEAEs Reported	XX	XX	XX
Number of Subjects with Any TEAEs Reported [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Treatment related TEAEs Reported	XX	XX	XX
Number of Subjects with Treatment related TEAE Reported [1][2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Serious TEAEs Reported			
Number of Subjects with Any Serious TEAE Reported [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Subjects with TEAEs by Severity [3]			
Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Subjects with TEAEs Resulting in Study Drug Discontinuation			

Footnotes:
[1] Subjects are only counted once at each level of summarization.
[2] AEs are considered treatment related if they are identified as definitely, probably or possibly treatment (study drug) related. They are considered unrelated if they are identified as unlikely related or not related.
[3] Subjects are counted once under the maximum severity if a subject experiences multiple adverse events.
AEs with 'Severity Unknown or Not Reported' are summarized as serious AEs in summary tables by system organ class and preferred term.
[4] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Programming Note: The row 'Number of AEs Reported' displays the number of unique AE counts. For example, if a subject has the same AE (same preferred term) more than once, the subject is counted only once for the same AE. If a subject has different AEs (like headache

and skin rash), then the subject is counted more than once. (In other words, a subject is counted more than once for different AEs, but only once for the same AE occurring multiple times).

Table 14.3.1.1.2
Overall Summary of Treatment-Emergent Adverse Events (TEAEs) By PONV Classification
Safety Population

PONV	Low Risk			High Risk		
	Standard Narcotic Therapy[4]	Buprenorphine SL Spray (0.5 mg TID)	Overall	Standard Narcotic Therapy[4]	Buprenorphine SL Spray (0.5 mg TID)	Overall
	N=xx	N=xx	N=xx	N=xx	N=xx	N=xx
Number of TEAEs Reported	XX	XX	XX	XX	XX	XX
Number of Subjects with Any TEAEs Reported [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Treatment related TEAEs Reported	XX	XX	XX	XX	XX	XX
Number of Subjects with Treatment related TEAE Reported [1][2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Serious TEAEs Reported						
Number of Subjects with Any Serious TEAE Reported [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Subjects with TEAEs by Severity [3]						
Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Subjects with TEAEs Resulting in Study Drug Discontinuation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Footnotes:
[1] Subjects are only counted once at each level of summarization.
[2] AEs are considered treatment related if they are identified as definitely, probably or possibly treatment related. They are considered unrelated if they are identified as unlikely related or not related.
[3] Subjects are counted once under the maximum severity if a subject experiences multiple adverse events.
AEs with 'Severity Unknown or Not Reported' are summarized as serious AEs in summary tables by system organ class and preferred term.
[4] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Programming Note: The row 'Number of AEs Reported' displays the number of unique AE counts. For example, if a subject has the same AE (same preferred term) more than once, the subject is counted only once for the same AE. If a subject has different AEs (like headache and skin rash), then the subject is counted more than once. (In other words, a subject is counted more than once for different AEs, but only once for the same AE occurring multiple times).

Table 14.3.1.1.3
Overall Summary of Treatment-Emergent Adverse Events (TEAEs) By Type Of Surgery
Safety Population

Surgery Type	Bunionectomy			Breast Augmentation			Abdominoplasty		
	Standard Narcotic Therapy[4]	Buprenor-phine SL Spray (0.5 mg TID)	Overall	Standard Narcotic Therapy[4]	Buprenor-phine SL Spray (0.5 mg TID)	Overall	Standard Narcotic Therapy[4]	Buprenor-phine SL Spray (0.5 mg TID)	Overall
	N=xx	N=xx	N=xx	N=xx	N=xx	N=xx	N=xx	N=xx	N=xx
Number of TEAEs Reported	XX	XX	XX	XX	XX	XX	XX	XX	XX
Number of Subjects with Any TEAEs Reported [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Treatment related TEAEs Reported [2]	XX	XX	XX	XX	XX	XX	XX	XX	XX
Number of Subjects with Treatment related TEAE Reported [1][2]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Serious TEAEs Reported									
Number of Subjects with Any Serious TEAE Reported [1]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Subjects with TEAEs by Severity [3]									
Mild	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Moderate	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Severe	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Surgery Type	Bunionectomy			Breast Augmentation			Abdominoplasty		
	Standard Narcotic Therapy[4]	Buprenor-phine SL Spray (0.5 mg TID)	Overall	Standard Narcotic Therapy[4]	Buprenor-phine SL Spray (0.5 mg TID)	Overall	Standard Narcotic Therapy[4]	Buprenor-phine SL Spray (0.5 mg TID)	Overall
	N=xx	N=xx	N=xx	N=xx	N=xx	N=xx	N=xx	N=xx	N=xx
Number of Subjects with TEAEs Resulting in Study Drug Discontinuation	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Footnotes:
[1] Subjects are only counted once at each level of summarization.
[2] AEs are considered treatment related if they are identified as definitely, probably or possibly treatment related. They are considered unrelated if they are identified as unlikely related or not related.
[3] Subjects are counted once under the maximum severity if a subject experiences multiple adverse events.
AEs with 'Severity Unknown or Not Reported' are summarized as serious AEs in summary tables by system organ class and preferred term.
[4] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Programming Note: The row 'Number of AEs Reported' displays the number of unique AE counts. For example, if a subject has the same AE (same preferred term) more than once, the subject is counted only once for the same AE. If a subject has different AEs (like headache and skin rash), then the subject is counted more than once. (In other words, a subject is counted more than once for different AEs, but only once for the same AE occurring multiple times).

Table 14.3.1.2
Summary of TEAEs by System Organ Class (SOC) and Preferred Term (PT)
Safety Population

System Organ Class **Preferred Term**	**Standard Narcotic Therapy[1]** **N=xx**			**Buprenorphine SL Spray (0.5 mg TID)** **N=xx**			**Overall** **N=xx**		
	n	(%)	#AEs	n	(%)	#AEs	n	(%)	#AEs
Subjects with any TEAE [Overall Number of AEs]	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]
System Organ Class 1	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]
Preferred Term 1	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]
Preferred Term 2	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]
System Organ Class 2	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]
Preferred Term 1	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]
Preferred Term 2	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]	XX	(XX.X%)	[XX]

Footnotes:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
Subjects are counted only once at each level of summarization (SOC or PT).
Summaries are sorted by SOC and PT within SOC by descending order of frequency of subjects.
System Organ Class and Preferred Term are based on the Version 19.0 of the MedDRA coding dictionary.
Programmer Notes:
Table entries should be sorted in decreasing order by overall n of SOC and then by PT n within SOC based on the pooled EB-001 column.

Non-unique tables:

Table 14.3.1.3
Summary of Treatment Related TEAEs by SOC and PT
Safety Population

Programmer Notes:
1) *Change row label 'Subjects With Any TEAE' to 'Subjects With Any Treatment Related TEAE'*
2) *Table entries should be sorted in decreasing order by overall n of SOC and then by PT n within SOC based on the pooled EB-001 column.*

Table 14.3.1.4
Summary of SAEs by SOC and PT
Safety Population

Programmer Notes:
1) *Change row label 'Subjects With Any TEAE' to 'Subjects With Any SAE'*
2) *Table entries should be sorted in decreasing order by overall n of SOC and then by PT n within SOC based on the pooled EB-001 column.*

Table 14.3.1.5
Summary of TEAEs Leading To Study Drug Discontinuation by SOC and PT
Safety Population

Programmer Notes:
1) *Change row label 'Subjects With Any TEAE' to 'Subjects With Any TEAE Leading to Discontinuation'*
2) *Table entries should be sorted in decreasing order by overall n of SOC and then by PT n within SOC based on the pooled EB-001 column.*

Table 14.3.1.6
Summary of TEAEs by System Organ Class, Preferred Term and Maximum Severity
Safety Population

	Standard Narcotic Therapy[1] N = xx			Buprenorphine SL Spray (0.5 mg TID) N = xx			Overall N = xx		
	Mild n (%)	Moderate n (%)	Severe n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Patients with any TEAE	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
System Organ Class 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Preferred Term 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
… Etc.									

Footnotes:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
Subjects are counted only once at each level of summarization (SOC or PT). A patient will be counted once in each row of the table at the maximum severity reported for that system organ class or preferred term.
Patients missing severity for an AE are categorized as severe for that AE.
Programmer Notes:
Table entries should be sorted in decreasing order by overall n of SOC and then by PT n within SOC based on the pooled EB-001 column.

Table 14.3.1.7
Summary of Total Rescue Use and Proportion Of Subjects Using Rescue Medication For Nausea By Time Interval
Safety Population

	Standard Narcotic Therapy[1] **N=xx**	**Buprenorphine SL Spray (0.5 mg TID)** **N=xx**	**Overall** **N=xx**
Total Use of Rescue for Nausea (number of doses)			
Within 0-8 Hours	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**
Within 0-24 Hours	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**
Within 0-48 Hours	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**
Within 0-72 Hours	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**
Within 0-7 Days	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**
At any time during the treatment period	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**
Proportion of Subjects given Rescue for Nausea			
Within 0-8 Hours	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Within 0-24 Hours	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Within 0-48 Hours	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Within 0-72 Hours	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Within 0-7 Days	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At any time during the treatment period	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Footnote:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Table 14.3.1.8
Summary Of Time To First Rescue For Nausea
Safety Population

	Standard Narcotic Therapy[4] (N = XX)	Buprenorphine SL Spray (0.5 mg TID) (N = XX)	Overall (N = XX)
Time to First Rescue use for Nausea (min)			
Median Time [1]	XXX	XXX	XXX
Range (Min,max) [2]			
95% CI [3]	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)
Censored Observations n (%)[4]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Subjects receiving nausea rescue medication n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Footnotes:
[1] Median Time = Median time to first use of nausea rescue medication.
[2] Min and Max of uncensored observations.
[3] CI = Confidence Interval.
[4] If a subject does not take rescue medication for nausea but prematurely discontinues from the study, then the subject will be censored at the time of discontinuation. If a subject never takes rescue medication for nausea and completes the treatment phase of the study, then the subject will be considered censored at 7 days.
[5] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Table 14.3.2.1.1
Summary of Chemistry Results by Study Visit
Safety Population

Albumen (for example)						
	Standard Narcotic Therapy[1] N=XX		**Buprenorphine SL Spray (0.5 mg TID) N=xx**		**Overall N=xx**	
Time point Statistic	Value	Change From Baseline	Value	Change From Baseline	Value	Change From Baseline
Screening (Baseline)						
N	XXX		XXX		XXX	
Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)		XX.X (XX.XX)	
Median	XXX		XXX		XXX	
Range (Min, Max)	(XXX, XXX)		(XXX, XXX)		(XXX, XXX)	
Follow-up						
N	XXX	XXX	XXX	XXX	XXX	XXX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XXX	XXX	XXX	XXX	XXX	XXX
Range (Min, Max)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)

Footnote:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Programmer note:
Chemistry parameters are listed alphabetically.
Include scheduled time points only.
Include the following for Serum Chemistry: albumin, total bilirubin, total protein, calcium, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, cholesterol, glucose, sodium, potassium, chloride, bicarbonate, lactate dehydrogenase, uric acid, creatinine with calculated creatinine clearance (Cockcroft-Gault method).

Non-unique tables:

Table 14.3.2.1.2
Summary of Hematology Results by Study Visit
Safety Population

Footnotes:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
Programmer note:
Hematology parameters are listed alphabetically.
Include scheduled time points only.
Include the following for hematology values: Hemoglobin, hematocrit, red blood cell count, red blood cell indices, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count (or estimate), and white blood cell count including differential.

Table 14.3.2.1.3
Summary of Urinalysis Results by Study Visit
Continuous Assays
Safety Population

Footnotes:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
Programmer note:
Laboratory parameters are listed alphabetically
Include scheduled time points only.
Include continuous urinalysis assays only.

Table 14.3.2.1.4
Summary of Urinalysis Results by Study Visit
Categorical Assays
Safety Population

pH (for example)			
System Organ Class Preferred Term	**Standard Narcotic Therapy[1] N=xx**	**Buprenorphine SL Spray (0.5 mg TID) N=xx**	**Overall N=xx**
Lab Parameter			
Screening (Baseline)			
Category 1	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Category 2	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Category 3	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Category 4	XXX (XX.X%)		
	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Follow-up			
Category 1	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Category 2	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Category 3	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Category 4	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)

Footnote:
Footnotes:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
Programmer note:
Laboratory parameters are listed alphabetically
Include scheduled time points only.
Include categorical urinalysis assays only.

Table 14.3.3
Summary of Vital Signs and Changes From Baseline by Study Visit
Safety Population

Systolic blood pressure (mmHg) (for example)						
	Standard Narcotic Therapy[2] N=XX		**Buprenorphine SL Spray (0.5 mg TID) N=XX**		**Overall N=XX**	
Study Visit/ Time point [1] Statistic	Actual	Change From Baseline	Actual	Change From Baseline	Actual	Change From Baseline
Screening (Baseline)						
n	XXX		XXX		XXX	
Mean (S.D.)	XX.X (XX.XX)		XX.X (XX.XX)		XX.X (XX.XX)	
Median	XXX		XXX		XXX	
Range (Min, Max)	(XXX, XXX)		(XXX, XXX)		(XXX, XXX)	
Pre-surgery						
n	XXX	XXX	XXX	XXX	XXX	XXX
Mean (S.D.))	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XXX	XXX	XXX	XXX	XXX	XXX
Range (Min, Max)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)
Pre-dose						
n	XXX	XXX	XXX	XXX	XXX	XXX
Mean (S.D.))	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XXX	XXX	XXX	XXX	XXX	XXX
Range (Min, Max)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)
Etc.						

Footnotes:

[1] During treatment period:
Blood Pressure will be measured every 4 hours after first dose.
Pulse rate and respiratory rate will be measured at T0, 1h and every 2 hours after first dose.
Pulse Oximetry will be measured at 90 min, 12h, 24h, 48h, and 72h after first dose.
[2] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Programmer note: Vital signs are: Systolic and diastolic blood pressure, heart rate, respiratory rate, oral temperature and pulse oximetry. Include scheduled time points only.

Table 14.3.4
Summary of Physical Exam Findings
Safety Population

Study Visit	Exam Finding	Standard Narcotic Therapy[1] N=xx n (%) [1]	Buprenorphine SL Spray (0.5 mg TID) N=xx n (%) [1]	Overall N=xx n (%) [1]
Screening	n	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Not Done	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Pre-surgery	n	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Not Done	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Treatment Period/ 72 h	n	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Not Done	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Etc.				

Footnote:
[1] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Programmer note:
Include scheduled time points only.

Table 14.3.5
Summary of Oral Cavity Exam Findings
Safety Population

Study Visit/ Time point [1]	Exam Finding	Standard Narcotic Therapy[2] N=xx [1] n (%)	Buprenorphine SL Spray (0.5 mg TID) N=xx [1] n (%)	Overall N=xx [1] n (%)
Screening	n	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Active Infection	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Mucositis	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Cold Sores	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	…			
	Recent Hx Dental Disease	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Other			
Pre-surgery	n	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Active Infection	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Mucositis	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Cold Sores	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	…			
Pre-dose	n	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Active Infection	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Mucositis	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	Cold Sores	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
	…			
Etc.				

Footnote:
[1] During treatment period, oral cavity exam will be performed at 90 min, 12h, 24h, 48h, and 72h after dosing.
[2] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

Programmer note:
Include scheduled time points only.

Table 14.3.6
Summary of ECG Exam Findings
Safety Population

		Standard Narcotic Therapy[2]	Buprenorphine SL Spray (0.5 mg TID)	Overall
	ECG Findings	N = xx	N = xx	N = xx
Study Visit / Time Points [1]				
Screening	**n**	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Normal	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Abnormal	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Not Done	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
Pre-dose	**n**	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Normal	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Abnormal	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Not Done	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
Treatment Period / 90 min	**n**	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Normal	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Abnormal	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Not Done	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
Etc.				

Footnotes:
[1] During treatment period, ECG exam will be performed at 90 min, 12h, 24h, 48h, and 72h after dosing.
[2] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.
Programmer note:
Include scheduled time points only.

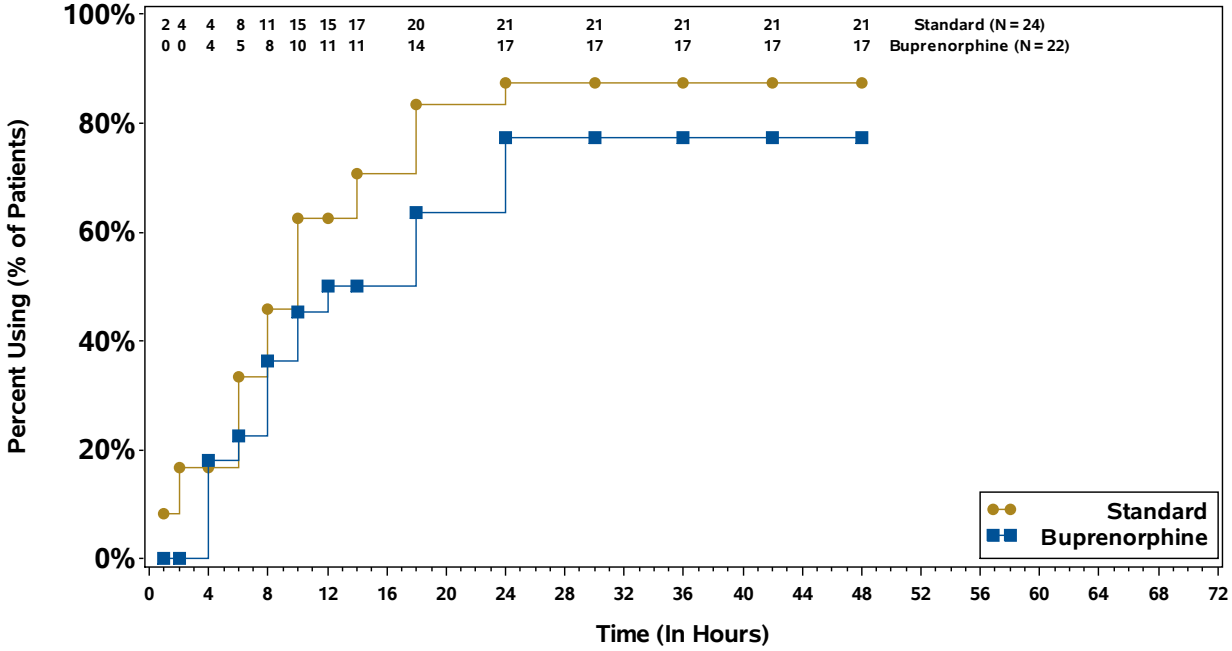
Table 14.3.7
Summary of ECG Results and Changes from Baseline by Study Visit
Safety Population

HR (beats/min) (for example)						
	Standard Narcotic Therapy[2] N=XX		**Buprenorphine SL Spray (0.5 mg TID) N=XX**		**Overall N=XX**	
Study Visit/ Time point [1] Statistic	Actual	Change From Baseline	Actual	Change From Baseline	Actual	Change From Baseline
Screening (Baseline)						
n	XXX		XXX		XXX	
Mean (S.D.)	XX.X (XX.XX)		XX.X (XX.XX)		XX.X (XX.XX)	
Median	XXX		XXX		XXX	
Range (Min, Max)	(XXX, XXX)		(XXX, XXX)		(XXX, XXX)	
90 min						
n	XXX	XXX	XXX	XXX	XXX	XXX
Mean (S.D.))	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XXX	XXX	XXX	XXX	XXX	XXX
Range (Min, Max)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)
Etc..						
n	XXX	XXX	XXX	XXX	XXX	XXX
Mean (S.D.))	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XXX	XXX	XXX	XXX	XXX	XXX
Range (Min, Max)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)	(XXX, XXX)
Etc.						

[1] During treatment period, ECG exam will be performed at 90 min, 12h, 24h, 48h, and 72h after dosing
Footnotes:
[2] Subjects assigned Standard Narcotic Therapy were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period.

14.1 FIGURE SPECIFICATIONS

Figure 14.1
Time To First Use Of Rescue Medication
Safety Population



Footnote:
If a subject does not take rescue medication for nausea but prematurely discontinues from the study, then the subject will be censored at the time of discontinuation. If a subject never takes rescue medication for nausea and completes the treatment phase of the study, then the subject will be considered censored at 7 days.
Points on graph represent censored events.

14.2 LISTING SPECIFICATIONS

Listing 16.2.1.1
Subject Enrollment and Randomization
All Subjects

Site-Subject	Subject Initials	Date of Informed Consent	Protocol Version Date	ICF Version Date	Randomized?	Date (Time) of Randomization	Rand Number	Randomized Treatment	Safety Population
XXX-XXX	XXX	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	Yes	ddMMMyyyy (hh:mm)	XXXX	Buphrenorphine SL Spray (0.5 mg TID)	Yes/No
XXX-XXX	XXX	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	No				
XXX-XXX	XXX	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	Yes	ddMMMyyyy (hh:mm)	XXXX	Standard Narcotic Therapy	Yes/No
Etc.									

Listing 16.2.1.3
Subject Disposition
All Subjects

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	End of Study status [1]	Date of Last Study Visit (Study Day[2])	Date of Last Subject Contact	Primary Reason for Early Termination [3]	If AE Specify AE #	If Protocol Deviation, Specify #	If Death, Specify Date	If Other - Specify
XXX-XXX	XXXXXX	ddMMMyyyy (xx)	ddMMMyyyy	XXXXXXX	XX	XX	ddMMMyyyy	XXXXXXX
XXX-XXX	XXXXXX	ddMMMyyyy	ddMMMyyyy	XXXXXXX	XX	XX	ddMMMyyyy	XXXXXXX
XXX-XXX	XXXXXX	ddMMMyyyy	ddMMMyyyy	XXXXXXX	XX	XX	ddMMMyyyy	XXXXXXX
Etc.								

Footnotes:
[1] End of study status can be: Study completer, Early termination.
[2]Study Day = Date of Last Visit - Date of First Treatment + 1.
[3] Primary Reason for Early Termination can be: Adverse event (specify AE #), Death (specify date), Lost to follow-up, Protocol Violation (specify deviation #), Withdrawal of Consent by Subject, Subject Noncompliance, Study Enrollment Stopped, Other (Specify).

Listing 16.2.2.1
Protocol Deviations
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Any Deviation?	Deviation Number	Date of Deviation	Deviation Category [1]	Deviation Description	Major Deviation?
XXX-XXX	Yes/No/NA	XX	ddMMMyyyy	XXX	XXXXXXXXXXXXXXXXXXXXX	Yes/No
XXX-XXX	Yes/No/NA	XX	ddMMMyyyy	XXX	XXXXXXXXXXXXXXXXXXXXX	Yes/No
XXX-XXX	Yes/No/NA	XX	ddMMMyyyy	XXX	XXXXXXXXXXXXXXXXXXXXX	Yes/No
Etc.		**XX**				

Footnote:
[1] Deviation category can be: Informed consent procedure, inclusion/exclusion criteria, study medication, prohibited medications, study procedures, visit or assessment time window, missed visit or assessment, other.

Listing 16.2.4.1
Demographics and Baseline Characteristics
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Date of Birth	Age (yrs) [1]	Sex	Race [2]	Ethnicity [3]	Baseline PONV Score [4] /Category	Baseline Height (cm)	Baseline Weight (kg)	Baseline BMI (kg/m2)
XXX-XXX	ddMMMyyyy	XX	M/F	XXXXX	XXXXX	X /Low Risk	XXX	XX.X	XX.X
XXX-XXX	ddMMMyyyy	XX	M/F	XXXXX	XXXXX	X /High Risk	XXX	XX.X	XX.X
XXX-XXX	ddMMMyyyy	XX	M/F	XXXXX	XXXXX	X	XXX	XX.X	XX.X
Etc.									

Footnotes:
[1] Age is calculated at date of Informed Consent.
[2] Race can be: White, Black or African American, Asian, American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander, or Other.
[3] Ethnicity can be: Hispanic or Latino or Not Hispanic or Latino.
[4] PONV score can be from 0 to 4, Scores of 0-2 are categorized as Low Risk, Scores of 3-4 are categorized as High Risk.

Listing 16.2.4.2
Medical/Surgical History
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Any Medical Hx?	HX Number	Diagnosis / Condition / Event	System Organ Class[1]	Preferred Term[1]	Start Date (Time)	Stop Date (Time)	Ongoing?
XXX-XXX	Yes/No	XX	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No
XXX-XXX	Yes/No	XX	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No
XXX-XXX	Yes/No	XX	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No
Etc.	Yes/No	XX	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No

Footnotes:
[1] System Organ Class and Preferred Term are based on the Version 19.0 of the MedDRA coding dictionary.

Listing 16.2.4.3
Prior and Concomitant Medications
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Any meds?	Med #	ATC Class / Pref. Term/ Verbatim Term	Dose / Units / Frequency / Route [1]	Start Date (Time)	Stop Date (Time)	On-going?	Prior/ Con-comitant[3]	Category [2]/ Indication	Was treatment given for AE or MH?	AE #	MH #
XXX-XXX	Yes /No	XX	Antithrombotic Agent/ Acetylsalicylic acid / Aspirin	81 mg / QID / PO	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No	P/C	Concomitant Med / Cerebrovascular Accident Prophylaxis	Yes/No	XX	XX
XXX-XXX	Yes /No	XX	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XX XX / XXX / XXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No			Yes/No	XX	XX
XXX-XXX	Yes /No	XX	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XX XX / XXX / XXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No			Yes/No	XX	XX
Etc.	Yes /No	XX			ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No			Yes/No	XX	XX

Footnote:
[1] Unit can be: Mg, mcg, ml, Capsule, Tablet, or Other.
Route can be: Oral, Inhalation, Topical, IV, IM, Other.
Frequency can be: QD, BID, TID, QID, Once, PRN, or Other.
[2] Category can be: Prior Medication, Concomitant Medication, or Prophylaxis.
[3] Prior medications are those that stop prior to the start of the first study drug administration. Any medication that stops at or after the start of the first study drug administration or with missing stop dates is considered a concomitant medication.

Listing 16.2.4.4
Non-Medication Therapy
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Any Therapy?	Therapy Number	ATC Class / Pref. Term/ Rescue Medication Name	Dose / Units / Frequency / Route	Indication	Start Date (Time)	Stop Date (Time)	On-going?	Prior/ Concomitant[1]	Was treatment given for AE or MH?	AE #	MH #
XXX-XXX	Yes/No	X	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	81 mg / QID / PO	XXXXXXXXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No	P/C	Yes/No	X X	X X
XXX-XXX	Yes/No	X	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XX XX / XXX / XXX	XXXXXXXXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No		Yes/No	X X	X X
XXX-XXX	Yes/No	X	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XX XX / XXX / XXX	XXXXXXXXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No		Yes/No	X X	X X
Etc.	Yes/No	X	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XX XX / XXX / XXX	XXXXXXXXX	ddMMMyyyy (hh:mm)	ddMMMyyyy (hh:mm)	Yes/No		Yes/No	X X	X X

Footnote:
[1] Prior therapies are those that stop prior to the start of the first study drug administration. Any therapy that stops at or after the start of the first study drug administration or with missing stop dates is considered a concomitant therapy.

Listing 16.2.4.5
Serology Laboratory And Pregnancy Test Results
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Age	Sex	If Female, Is Subject of Child Bearing Potential?	Test Performed	Study Visit	Date (Time)	Result
XXX-XXX	XX	M/F	**Yes/No**	**HIV Test Results**	Screening	ddMMMyyyy (HH:MM)	Negative/Positive
XXX-XXX	XX	M/F	**Yes/No**	**Hep B Antigen Results**	Screening	ddMMMyyyy (HH:MM)	Negative/Positive
XXX-XXX	XX	M/F	**Yes/No**	**Hep C Antigen Results**	Screening	ddMMMyyyy (HH:MM)	Negative/Positive
XXX-XXX	XX	M/F	**Yes/No**	Serum Pregnancy	Screening	ddMMMyyyy (HH:MM)	Negative/Positive
XXX-XXX	XX	M/F	**Yes/No**	Urine Pregnancy	Pre-Surgery	ddMMMyyyy (HH:MM)	
XXX-XXX	XX	M/F	**Yes/No**	**HIV Test Results**	Screening	ddMMMyyyy (HH:MM)	
Etc.							

Listing 16.2.4.6
Alcohol Breath Test and Urine Drug Screen[1]
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Test performed?	Study Visit	Was Test Performed?	Date (Time)	Result
XXX-XXX	Alcohol Test	Screening	Y	ddMMMyyyy (HH:MM)	Negative/Positive
XXX-XXX		Day 1	Y	ddMMMyyyy (HH:MM)	Negative/Positive
XXX-XXX	Urine Drug Screen	Screening	Y	ddMMMyyyy (HH:MM)	Negative/Positive
Etc.		Day 1	N		

Footnote:
[1]Screened Drugs Found can be: Amphetamines, Barbiturates, Benzodiazepines, Cocaine, Marijuana, Methadone, Methamphetamines, Opiates, Oxycodone, Phencyclidine (PCP) Tricyclic antidepressant, or Methylenedioxymethamphetamine, Other.

Listing 16.2.4.7
Surgery
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Surgical Procedure [1]	Target foot for Bunionectomy	Breast Implant Size: Left/Right	Date	Start Time	Stop Time
XXX-XXX	XXXXXXXX		xxx / yyy	ddMMMyyyy	hh:mm	hh:mm
XXX-XXX	XXXXXXXX	Left		ddMMMyyyy	hh:mm	hh:mm
XXX-XXX	XXXXXXXX			ddMMMyyyy	hh:mm	hh:mm
Etc.	XXXXXXXX			ddMMMyyyy	hh:mm	hh:mm

Foootnote:
[1] The surgical procedures will be bunionectomy, breast augmentation, or abdominoplasty.

Listing 16.2.5.1
Study Drug Administration
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Study Treatment Period [1]	Study Medication Dose [2]	Was Dose Administered?	Date (Time)	If No, Specify?	Did the subject hold spray under tongue for 30 sec before swallowing?[3]
XXX-XXX	Inpatient	Dose 1	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXX	Yes/No
XXX-XXX	Inpatient	Dose 2	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXX	Yes/No
XXX-XXX	Inpatient	Etc.	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXX	Yes/No
XXX-XXX	Outpatient	Dose 1	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXX	Yes/No
XXX-XXX	Outpatient	Etc.	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXX	Yes/No
XXX-XXX	Inpatient	Dose 1	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXX	Yes/No
Etc.						

Footnote:
[1] Study Treatment Period can be Inpatient (Days 1-4), or Outpatient (Days 4-7).
[2] There are a possible 12 doses each for each Treatment Period.
[3] For Buprenorphine SL Spray (0.5 mg TID) subjects only.

Listing 16.2.5.2
Discharge to Outpatient Treatment
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Did subject continue to Outpatient Treatment	Did subject sign the Opioid Agreement?	Discharge Date (Time)	Did subject receive all Outpatient instructions per protocol?	Did staff dispense outpatient diaries?	Did staff dispense study drug?
XXX-XXX	Yes/No	Yes/No	ddMMMyyyy (HH;MM)	Yes/No	Yes/No	Yes/No
XXX-XXX	Yes/No	Yes/No	ddMMMyyyy (HH;MM)	Yes/No	Yes/No	Yes/No
XXX-XXX	Yes/No	Yes/No	ddMMMyyyy (HH;MM)	Yes/No	Yes/No	Yes/No
XXX-XXX	Yes/No	Yes/No	ddMMMyyyy (HH;MM)	Yes/No	Yes/No	Yes/No
XXX-XXX	Yes/No	Yes/No	ddMMMyyyy (HH;MM)	Yes/No	Yes/No	Yes/No
XXX-XXX	Yes/No	Yes/No	ddMMMyyyy (HH;MM)	Yes/No	Yes/No	Yes/No
XXX-XXX	Yes/No	Yes/No	ddMMMyyyy (HH;MM)	Yes/No	Yes/No	Yes/No
	Yes/No	Yes/No	ddMMMyyyy (HH;MM)	Yes/No	Yes/No	Yes/No

Note:
Subjects assigned Standard Narcotic Therapy of care were given morphine IV 4 mg TID for 24 hours, followed by Oxycodone Hydrochloride tablet, 10 mg TID for the remainder of the treatment period. Subjects assigned to Buprenorphine SL Spray (0.5 mg TID) received Buprenorphine sublingual spray 0.5 mg TID for the entire treatment period. During the outpatient portion of the trial, subjects assigned to Standard Narcotic Therapy of care were instructed to take study medication only when they experienced pain, while subjects assigned to Buprenorphine SL Spray (0.5 mg TID) were instructed to maintain the TID dosing for the entire outpatient period.

Listing 16.2.5.3
Study Drug Accountability
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Dispensed Date (Time)[1]	Number of study devices or pills dispensed	Did subject return Outpatient Diaries? If No, specify reason	Date	Did the subject return study drug?	Date	Number of unused study devices or pills returned	Number of used study devices returned	Did the subject return fewer than expected devices or pills? If Yes, was an IP irregularities form completed?
XXX-XXX	ddMMMyyyy (HH;MM)	XX	Yes	ddMMMyyyy	Yes/No	ddMMMyyyy	XX	XX	Yes, Yes
XXX-XXX	ddMMMyyyy (HH;MM)	XX	No, XXXXXXX		Yes/No	ddMMMyyyy	XX	XX	No
XXX-XXX	ddMMMyyyy (HH;MM)	XX	Yes/No	ddMMMyyyy	Yes/No	ddMMMyyyy	XX	XX	Yes/No
XXX-XXX	ddMMMyyyy (HH;MM)	XX	Yes/No	ddMMMyyyy	Yes/No	ddMMMyyyy	XX	XX	Yes/No
XXX-XXX	ddMMMyyyy (HH;MM)	XX	Yes/No	ddMMMyyyy	Yes/No	ddMMMyyyy	XX	XX	Yes/No
XXX-XXX	ddMMMyyyy (HH;MM)	XX	Yes/No	ddMMMyyyy	Yes/No	ddMMMyyyy	XX	XX	Yes/No

Footnote:
[1] Subjects were dispensed diaries and study drug for outpatient treatment period at the Site Discharge.

Listing 16.2.5.4
Rescue Medication Administration
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Was Rescue Medication Administered?	Rescue Medication #	ATC Class / Pref. Term/ Rescue Medication Name	Dose / Unit / Route [1]	Date (Time)	Medication Category
XXX-XXX	Yes/No	1	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XXX / XXX/ XXXX	ddMMMyyyy (HH:MM)	Pain/Nausea
XXX-XXX	Yes/No	2	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XXX / XXX/ XXXX	ddMMMyyyy (HH:MM)	Pain/Nausea
XXX-XXX	Yes/No	Etc.	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XXX / XXX/ XXXX	ddMMMyyyy (HH:MM)	Pain/Nausea
XXX-XXX	Yes/No	XX	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XXX / XXX/ XXXX	ddMMMyyyy (HH:MM)	Pain/Nausea
XXX-XXX	Yes/No	XX	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XXX / XXX/ XXXX	ddMMMyyyy (HH:MM)	Pain/Nausea
XXX-XXX	Yes/No	XX	XXXXXXXXXX / XXXXXXXXXX / XXXXXXXXXX	XXX / XXX/ XXXX	ddMMMyyyy (HH:MM)	Pain/Nausea
Etc.						

Footnote:
[1] Route can be Oral or Intravenous.

Listing 16.2.7.1
All Treatment Emergent Adverse Events (TEAEs)
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	AE Number	System Organ Class / Preferred Term[1] / Verbatim Term	Start Date (Time) / Stop Date (Time) / Duration	Ongoing? / Outcome [2]	Causality[3]/ Severity[4]/ Action Taken[5]	Serious? / Specify Cause[6]/ SAE Outcome[7]
XXX-XXX	1	Injury, poisoning and procedural complications / Concussion / Concussion secondary to xxxx	01Jan2013 (8:45) / 10Jan 2013 (9:00) / 10 days	No / Resolved	Not related /Severe /None	Yes / Is Life Threatening / Drug Withdrawn
XXX-XXX						
XXX-XXX						
XXX-XXX						
Etc.						

Footnotes:
[1] SOC and PT are determined by coding the verbatim term using the MedDRA Version 19.0 dictionary.
[2] Outcome can be: Event Resolved, Resolved with sequelae, Ongoing, or Death. If SAE, outcome can be: Not Recovered/Not Resolved, Death or Other.
[3] Causality can be: Definitely Related, Probably Related, Possibly Related, Unlikely Related, or Not Related.
[4] Severity can be: Mild, Moderate, or Severe.
[5] Action Taken can be: None, Study Drug Discontinued, Dose Modified, Required Concomitant Medication, Required Procedure, or Other.
[6] Specify cause can be: Death, Life-threatening, In-patient hospitalization or prolongation of existing hospitalization, Persistent or significant disability or incapacity, Congenital anomaly or birth defect, is medically significant or requires intervention to prevent one of the outcomes listed above.
[7] If SAE, action taken can be: None, Treatment, Unknown or Drug Withdrawn.

Non-Unique Tables

Listing 16.2.7.2
Treatment Related TEAEs
Safety Population

Listing 16.2.7.3
Serious TEAEs
Safety Population

Listing 16.2.7.4
Deaths
Safety Population

Listing 16.2.7.5
TEAEs Leading To Premature Study Discontinuation
Safety Population

Listing 16.2.8.1.1
Chemistry Laboratory Results
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Study Visit	Date (Time)	Test[1,2]	Value	Units	Lower Limit of Normal	Upper Limit of Normal
XXX-XXX	Screening	ddMMMyyyy (hh:mm)	Albumin	XX.X	XX	XX.X	XX.X
		ddMMMyyyy (hh:mm)	Alk Phos	XX.X	XX	XX.X	XX.X
	Follow-up	ddMMMyyyy (hh:mm)	Albumin	XX.X	XX	XX.X	XX.X
			Alk Phos	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X
XXX-XXX	Screening	ddMMMyyyy (hh:mm)	Albumin	XX.X	XX	XX.X	XX.X
			Alk Phos	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X
	Follow-up	ddMMMyyyy (hh:mm)	Albumin	XX.X	XX	XX.X	XX.X
			Alk Phos	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X

Footnotes:
[1] Laboratory parameters are listed alphabetically.
[2] Include the following tests for Serum Chemistry: albumin, total bilirubin, total protein, calcium, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, cholesterol, glucose, sodium, potassium, chloride, bicarbonate, lactate dehydrogenase, uric acid, creatinine with calculated creatinine clearance (Cockcroft-Gault method).

Listing 16.2.8.1.2
Hematology Laboratory Results
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Study Visit	Date	Test [1,2]	Value	Units	Lower Limit of Normal	Upper Limit of Normal
XXX-XXX	Screening	ddMMMyyyy	WBC Count	XX.X	XX	XX.X	XX.X
		ddMMMyyyy	RBC Count	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X
XXX-XXX	Follow-up	ddMMMyyyy	WBC Count	XX.X	XX	XX.X	XX.X
			RBC Count	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X
XXX-XXX	Screening	ddMMMyyyy	WBC Count	XX.X	XX	XX.X	XX.X
		ddMMMyyyy	RBC Count	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X
XXX-XXX	Follow-up	ddMMMyyyy	WBC Count	XX.X	XX	XX.X	XX.X
			RBC Count	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X

Footnotes:
[1] Laboratory tests are listed alphabetically.
[2] Include the following tests for hematology values: hemoglobin, hematocrit, red blood cell count, red blood cell indices, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count (or estimate), and white blood cell count including differential.

Listing 16.2.8.1.3
Urinalysis Laboratory Results
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Study Visit	Date	Test [1,2]	Value	Units	Lower Limit of Normal	Upper Limit of Normal
XXX-XXX	Screening	ddMMMyyyy	Specific Gravity	XX.X	XX	XX.X	XX.X
		ddMMMyyyy	pH	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X
XXX-XXX	Follow-up	ddMMMyyyy	Specific Gravity	XX.X	XX	XX.X	XX.X
			pH	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X
XXX-XXX	Screening	ddMMMyyyy	Specific Gravity	XX.X	XX	XX.X	XX.X
		ddMMMyyyy	pH	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X
XXX-XXX	Follow-up	ddMMMyyyy	Specific Gravity	XX.X	XX	XX.X	XX.X
			pH	XX.X	XX	XX.X	XX.X
			Etc.	XX.X	XX	XX.X	XX.X

Footnotes:
[1]Urinalysis tests are listed alphabetically.
[2] Include the following for urinalysis: pH, specific gravity, blood, glucose, protein, and ketones.

Listing 16.2.8.2
Vital Signs
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Study Visit / Time Point	Date (Time)	Height (cm)	Weight (kg)	OralTemp (°C)	Systolic BP (mmHg) [1]	Diastolic BP (mmHg) [1]	Pulse Rate (bpm) [2]	Respiratory Rate (bpm) [2]	Pulse Oximetry (Spo2) [3]
XXX-XXX	XXXXXXXXX / XXXXXX	ddMMMyyyy (HH;MM)	XXX	XXX	XX.X	XXX	XXX	XXX	XX	XXX
XXX-XXX	XXXXXXXXX / XXXXXX	ddMMMyyyy (HH;MM)	XXX	XXX	XX.X	XXX	XXX	XXX	XX	XXX
XXX-XXX	XXXXXXXXX / XXXXXX	ddMMMyyyy (HH;MM)	XXX	XXX	XX.X	XXX	XXX	XXX	XX	XXX
XXX-XXX	XXXXXXXXX / XXXXXX	ddMMMyyyy (HH;MM)	XXX	XXX	XX.X	XXX	XXX	XXX	XX	XXX
XXX-XXX	XXXXXXXXX / XXXXXX	ddMMMyyyy (HH;MM)	XXX	XXX	XX.X	XXX	XXX	XXX	XX	XXX
XXX-XXX	XXXXXXXXX / XXXXXX	ddMMMyyyy (HH;MM)	XXX	XXX	XX.X	XXX	XXX	XXX	XX	XXX
XXX-XXX	XXXXXXXXX / XXXXXX	ddMMMyyyy (HH;MM)	XXX	XXX	XX.X	XXX	XXX	XXX	XX	XXX
		ddMMMyyyy (HH;MM)	XXX	XXX	XX.X	XXX	XXX	XXX	XX	XXX

Footnotes:
During treatment period,
[1] Blood Pressure is measured every 4 hours after first dose.
[2] Pulse rate and respiratory rate are measured at T0, 1h and every 2 hours after first dose.
[3] Pulse Oximetry is measured at 90 min, 12h, 24h, 48h, and 72h after first dose.

Listing 16.2.8.3.1
Physical Examinations
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Study Visit	Was the Physical Examination performed?	Date (Time)	Body System [1]	Status [2]	Clinical Significance [3]
XXX-XXX		Yes/No	ddMMMyyyy (HH:MM)	Dermatologic	XXXXX	XXX
XXX-XXX		Yes/No	ddMMMyyyy (HH:MM)	HEENT	XXXXX	XXX
XXX-XXX		Yes/No	ddMMMyyyy (HH:MM)	Etc.		XXX
XXX-XXX		Yes/No	ddMMMyyyy (HH:MM)	Dermatologic	XXXXX	XXX
XXX-XXX		Yes/No	ddMMMyyyy (HH:MM)	HEENT	XXXXX	XXX
XXX-XXX		Yes/No	ddMMMyyyy (HH:MM)	Etc.		XXX

Footnotes:
[1] Body System can be: HEENT, Cardiovascular, Respiratory, Gastrointestinal, Neurologic, Dermatologic, Musculoskeletal, or Other (Specify).
[2] Status can be: Normal, Abnormal, or Not Done.
[3] Clinical Significance can be: CS=Clinically Significant or NCS=Not Clinically Significant.

Listing 16.2.8.3.2
Oral Cavity Examinations
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Study Visit / Time Point [1]	Was the Oral Cavity Examination performed?	Date (Time)	Observation [2]
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)	Active Infection, Tongue piercing
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXXXXXXXXXX
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXXXXXXXXXX
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXXXXXXXXXX
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXXXXXXXXXX
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)	XXXXXXXXXXXXXXXXXX

Footnotes:
[1] During treatment period, oral cavity exam will be performed at 90 min, 12h, 24h, 48h, and 72h after dosing.
[2] Observation can be: None, Active Infection, Mucositis, Cold Sores, Viral Lesions, Local Irritation, Periodontal Disease, Current piercings of the tongue or anywhere in the oral cavity, Evidence of prior piercings of the tongue or anywhere in the oral cavity, recent history of significant dental disease. Subjects may have multiple findings at each exam.

Listing 16.2.8.4
ECG Exam Assessment
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Study Visit / Time Point [1]	Was the ECG performed?	Date (Time)	Parameter	Findings [2]	If Abnormal, Please Describe Findings
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)	HR	XX	
				P-R Interval	XX	
				…		
				Interpretation	Normal	
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)	HR	XX	
				P-R Interval	XX	
				…		
				Interpretation	Abnormal-CS	XXXXXXXXX
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)		XX	
XXX-XXX	XXXXXXXXX / XXXXXX	Yes/No	ddMMMyyyy (HH:MM)		XX	

Footnotes:
[1] During treatment period, ECG exam will be performed at 90 min, 12h, 24h, 48h, and 72h after dosing.
[2] Findings can be: Normal, Abnormal Clinically Significant (CS) or Abnormal Not Clinically Significant (NCS).

Listing 16.2.8.5
Comments
Safety Population

Treatment: Buprenorphine SL Spray (0.5 mg TID)

Site-Subject	Study Visit	Date	CRF Page	Comment
XXX-XXX	XXXXXXXX	ddMMMyyyy	XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
XXX-XXX	XXXXXXXX	ddMMMyyyy	XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
XXX-XXX	XXXXXXXX	ddMMMyyyy	XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Etc.	XXXXXXXX	ddMMMyyyy	XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX