STATISTICAL ANALYSIS PLAN

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy, Safety, and Pharmacokinetics of Brachial Plexus Block with EXPAREL for Postsurgical Analgesia in Subjects Undergoing Total Shoulder Arthroplasty or Rotator Cuff Repair

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Prepared by:	Richard Willey, M.S.
Sponsor:	Pacira Pharmaceuticals, Inc. 5 Sylvan Way Parsippany, NJ 07054 Tel: 973-254-3560

1. SIGNATURE PAGE

Hassan Danesi, MD Senior Medical Director, Clinical Research	6/26/17 Date
James Jones, MD Chief Medical Officer	6/26/17 Date
Michael Rozycki, PhD Vice President, Regulatory Affairs	6/26/2017 Date
Richard Willey, MS Senior Manager, Biostatistics	26JUN2017 Date
Vincent Yu, PhD Senior Director, Biometrics	26JUN2017 Date

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3. LIST OF ABBREVIATIONS

Abbreviation	Description
AE	Adverse event
ANOVA	Analysis of variance
ATC	Anatomical therapeutic class
AUC	Area under the curve
BLOQ	Below the limit of quantification
BMI	Body mass index
bpm	Beats per minute
CI	Confidence interval
CMH	Cochran-Mantel-Haenszel
CRF	Case report form
CSR	Clinical study report
d	Day
ECG	Electrocardiogram
EMA	European Medicines Agency
FDA	Food and Drug Administration
FNB	Femoral nerve block
hr, h	hour
ICF	Informed consent form
ICH	International Conference on Harmonization
IV	Intravenous
LOCF	Last observation carried forward
LS	Least square
MedDRA	Medical dictionary for regulatory affairs
MPADSS	Modified Postanesthesia Discharge Scoring System
min	minutes
MED mg	Morphine equivalent dose in mg
n	Number of subjects
OBAS	Overall benefit of analgesia
OR	Operating room
PACU	Postanesthesia care unit
PCA	Patient-controlled analgesia
PK	Pharmacokinetics
PO	Oral
ROW	Rest of world
RCR	Rotator cuff repair
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SE	Standard error
SPI	Sum of pain intensity scores
TEAE	Treatment-emergent adverse event
TLF	Table, listings and figures
TSA	Total shoulder arthroplasty
VAS	Visual analog scale
WHO	World Health Organization
WHO-DD	World Health Organization – Drug Dictionary
wWOCF	Windowed worst observation carried forward

4. INTRODUCTION

This Statistical Analysis Plan (SAP) describes the planned statistical analysis and reporting of the clinical study 402-C-327 titled "A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy, Safety, and Pharmacokinetics of Brachial Plexus Block with EXPAREL for Postsurgical Analgesia in Subjects Undergoing Total Shoulder Arthroplasty or Rotator Cuff Repair". This study is intended to evaluate the magnitude and duration of the analgesic effect of a single-dose injection brachial plexus block with EXPAREL in subjects undergoing primary unilateral total shoulder arthroplasty (TSA) or rotator cuff repair (RCR).

The structure and content of this SAP provide sufficient detail to meet the requirements identified by the US Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials[1]. All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association[2] and the Royal Statistical Society[3], for statistical practice.

The purposes of this SAP are to:

- Outline the types of analyses and presentations of data that will form the basis for drawing conclusions to the study objectives and hypotheses outlined in the protocol.
- Explain in detail how the data will be handled and analyzed, adhering to commonly accepted standards and practices for Good Statistical Practice.

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or manuscripts. Post-hoc exploratory analyses not necessarily identified in this SAP may be performed to further examine study data. Any post-hoc, unplanned, or exploratory analyses performed will be clearly identified as such in the final CSR.

The following documents were reviewed in preparation of this SAP:

- Amendment 1 of Protocol 402-C-327 issued on 15Feb2016.
- Amendment 2 of Protocol 402-C-327 issued on 17Nov2016.
- Original Protocol 402-C-327 issued on24Nov2015.
- CRF version 1.0 issued on 04Dec2015.
- ICH Guidance on Statistical Principles for Clinical Trials (E9).

The reader of this SAP is encouraged to also read the clinical protocol and other identified documents for details on the planned conduct of this study. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analyses.

5. STUDY OBJECTIVES

5.1. Primary Objective

The primary objective of this study is to evaluate the magnitude and duration of the analgesic effect achieved following single-dose injection brachial plexus block with EXPAREL in subjects undergoing primary unilateral total shoulder arthroplasty or rotator cuff repair.

5.2. Secondary Objectives

The secondary objectives of this study are to assess the efficacy, safety, and pharmacokinetic (PK) profiles of EXPAREL, as well as the onset and duration of sensory and motor function blockade, following administration for analgesia in subjects undergoing primary unilateral total shoulder arthroplasty or rotator cuff repair.

6. STUDY OVERVIEW

This is a Phase 3, double-blind, placebo-controlled, randomized study. Subjects will be monitored for 5 days after surgery and followed for 30 days after surgery. Subjects will be randomized (1:1) to receive a 20mL injection of EXPAREL 133mg (10mL of EXPAREL 266mg/20mL expanded with 10mL of normal saline) via an ultrasound guided single-injection brachial plexus, interscalene or supraclavicular, nerve block at least 1 hour before surgery.

Major changes impacting the statistical analysis plan between Protocol Amendment 1 and Protocol Amendment 2 are as follows (for a complete record of the changes, see Protocol Amendment 2):

- Under Protocol Amendment 1, subjects were randomized to (1:1:1) to receive EXPAREL 133mg, EXPAREL 266mg or placebo. Under Protocol Amendment 2 the EXPAREL 266mg dose was removed from the randomization scheme and efficacy endpoints for the study.
- Under Protocol Amendment 1, 300 subjects were planned to be randomized into the study. Under Protocol Amendment 2, approximately 120 subjects were planned to be randomized into the study in order to achieve 50 subjects on EXPAREL 133mg and 50 subjects on placebo.
- Under Protocol Amendment 1, the VAS was not scheduled to be measured every 15 minutes while in the PACU and prior to PACU discharge as it is in Protocol Amendment 2.
- Under Protocol Amendment 1, subjects had their PK assessments scheduled under the same sampling schedule, where under Protocol Amendment 2, a population PK sampling scheme was implemented.
- Under Amendment 2, assessments at 84, 96, 108, and 120 hours were removed.
- The Study Stopping Rules were modified.
- Under Amendment 2, postsurgically, all subjects will receive acetaminophen/paracetamol up to 1000 mg PO or IV every 8 hours (q8h) unless contraindicated. The total daily dose of acetaminophen/paracetamol should not exceed 3000 mg.

Subjects will be allowed rescue medication upon request to control their pain. Rescue medication will be oral (PO) immediate release oxycodone. If subject cannot tolerate PO medication, intravenous (IV) morphine or hydromorphone may be used as rescue medication.

Pain will be assessed using a 10 cm visual analog scale (VAS). Pain will be assessed at multiple timepoints during the study.

Plasma bupivacaine concentrations will be determined at multiple timepoints during the study.

Other postsurgical assessments include:

- Postsurgical opioid consumption;

- Overall benefit of analgesia score (OBAS);
- Subject satisfaction with overall analgesia using a 5-point Likert scale;
- Subject's discharge readiness as assessed by Modified Postanesthesia Discharge Scoring System (MPADSS);
- Unscheduled phone calls or office visits related to pain;
- Clinical laboratories;
- Vital sign measurements;
- ECGs;
- Neurological assessment;
- Sensory function assessment at 2 locations as measured by:
    - Cold,
    - Pinprick,
    - Light touch;
- Degree of motor nerve block (Lovett scale) assessments :
    - Thumb,
        - Abduction (radial nerve),
        - Adduction (ulnar nerve),
        - Opposition (median nerve),
    - Elbow flexion (musculocutaneous nerve);
- Adverse events;
- Concomitant medications.

7. DEFINITIONS

Study Day

Study Day is calculated as the date of event minus the date of surgery plus one (1), if the date of event is on or after the date of surgery. Study Day is based on the calendar dates, thus days before the date of surgery have negative values while those on or after the date of surgery are positive.

This Study Day definition differs from the protocol defined Study Day. By this definition Day 1 is the day of the operation while the protocol defines this as Day 0. The definition assigning the operation to Day 1 aligns with the CDISC implementation guidance and FDA expectations.

Treatment-emergent Adverse Events

Treatment-emergent adverse events (TEAEs) are those with onset between the start date and time of study drug administration and end of study (Study Day 30±3 days).

Time 0 (zero)

Time 0 is defined as the date and time of the start of study drug administration.

Time Periods

All schedule times have a window associated with them (see Time and Events Schedule for individual timepoint windows). Various time frames are used in the data analyses which are dependent on these windows. The table below defines the actual elapsed times with allowance for the windows that can be included in the window.

Defined time frame (hrs)	Acceptable elapsed times (hrs)
0-12	[0 to 13]
0-24	[0 to 25]
0-48	[0 to 50]
0-72	[0 to 76]
0-96	[0 to 100]
0-Day 5	[0 to 144]
0-Day 10	[0 to 264]
24-48	[23 to 50]
48-72	[46 to 76]
72-96	[68 to 100]
48-96	[46 to 100]

If there are two or more data points that fit the time window the data point that occurs the latest and with highest value in the window should be used. For example when selecting the data point for the 48 hour timepoint, if a subject has data points collected at 47 and 49 hours then the 49 hour timepoint should be used. In this example the 49 hour timepoint record will be used as the end and start of all time intervals, thus the 0-48 hour interval will end using the 49 hour record and the 48-72 hour interval will start using the same 49 hour record. In addition, if there are two measurements for a given assessment at the exact same time, the measurement with the highest value should be used.

Baseline

Baseline is defined as the last available measurement or assessment prior to start of study treatment.

Sensation Loss

Sensation loss is when the subject reports absence of sensation for the sensory test (cold, pinprick or light touch) at each location (dermatome) [shoulder (axillary), forearm (musculocutaneous), middle finger (median), fifth finger (ulnar) and thumb (radial)]. Subjects may experience loss of sensation multiple times and at different times in different locations. A subject must have a return of sensation in the same sensory test in the same location before another loss of sensation can occur.

Time to Sensation Loss

Time to first loss of sensation is the first timepoint after baseline at which one of the three sensations (cold, pinprick and light touch) is absent at any of the test locations (dermatomes). If sensation is not lost, time to sensation loss will be censored at the last available sensory assessment available for that subject. Subjects who experience multiple losses of sensation will have multiple times to sensation loss but the time to first sensation loss will be used for analysis of time to first sensation loss.

Return of Sensation

Return of sensation is when a subject reports the presence of sensation after reporting a loss of sensation for the same sensory test (cold, pinprick and light touch) and location (dermatome). Subjects may experience returns of sensation multiple times. A subject must experience multiple losses of sensation before multiple returns can be experienced. Subjects who experience multiple returns of sensation will have multiple times to sensation return.

Time to Return of Sensation

Time to return of sensation is when all three sensations (cold, pinprick and light touch) are present after a subject experienced a loss of sensation in at least one of the sensory tests. If sensation doesn't return, it will be censored at the time of the last sensory assessment available for that subject. Only subjects who experience a loss of sensation can experience a return of sensation.

Duration of Sensory Loss

Duration of sensory loss is defined as the time from sensation loss to the time of sensation return. Subjects who never lost sensation will not be included in any analysis of Duration of Sensory Loss. If sensation doesn't return, then duration will be censored and is defined as the time between sensation loss and last sensory assessment.

Duration will be calculated for each loss-return cycle for those subjects with multiple cycles. If after the last sensation loss there is no return of sensation, the duration of the last cycle will be censored and defined as the time between sensation loss for that cycle and last sensory assessment.

Total duration is the sum of all durations for a subject.

Onset of Motor Function Loss

Onset of loss motor function is the first timepoint after baseline where the Lovett score drops below a three for at least one of the motor function assessments.

Return of Motor Function

Return of motor function is defined as when the Lovett score returns to three or above for any motor function assessment.

Time to Return of Motor Function

Time to return of motor function is the time from first loss of motor function to return of motor function for the motor assessment. If a subjects doesn't have return of motor function, the time to return of motor function will be censored on the date and time of last motor function assessment. For those subjects who never lose motor function, time to return will be missing; these subjects will not be included in any analysis of time to return.

Loss-Return Cycle

A loss-return cycle is the event where a subject has loss and return of sensory or motor function. Subjects may experience multiple cycles. Cycles are defined separately for each sensory and motor function tests.

Ready for Discharge

Ready for discharge is defined as a total score of 9 or more on the MPADSS. The total score is the sum of all scores. If there are missing data then the total score will not be calculated.

Sum of Pain Intensity Score (SPIS)

Sum of pain intensity scores (SPIS) are calculated by summing the imputed VAS scores for the timeframes of interest. Only scheduled VAS assessments under Protocol Amendment 1 will be used to derive SPIS.

Region

Region is defined as US and ROW where ROW is any site outside of the US.

8. ANALYSIS SETS

The safety analysis set will include all subjects who receive study drug. All analyses based on the safety set will be by actual treatment received.

The efficacy analysis set will include all subjects in the safety analysis set who undergo the planned surgery. All analyses based on the efficacy analysis set will be by randomized treatment regardless of treatment actually received.

The per-protocol efficacy analysis set will include all subjects in the efficacy analysis set and do not have any important protocol deviations. Important protocol deviations may include, but are not limited to, the following:

1) Planned concurrent surgical procedure;
2) 50% or more of the rescue medications are missing a VAS assessment (baseline through 48 hours +/- 2 hours) within 30 minutes prior to rescue medication use **and** at least 4 rescue medication doses are missing the associated VAS assessments within 30minutes prior to rescue medication use.;
3) Missing two or more scheduled VAS assessments between start study drug administration as the baseline VAS assessment and the 48 hour VAS assessment;
4) Subject did not receive the study treatment to which he/she was randomized (determined after database lock and unblinding).

All analyses for the per-protocol analysis set will be by randomized treatment.

9. STATISTICAL METHODS OF ANALYSIS

9.1. General Principles

The statistical analyses will be reported using summary tables, listings, and figures (TLFs). All analyses and tabulations will be performed using SAS® Version 9.1 or later. Continuous variables will be summarized using descriptive statistics [sample size (n), mean, standard deviation (SD), minimum, median, and maximum]. Categorical variables will be tabulated with number and percentage of subjects. Unless otherwise noted, percentages will be based on the number of subjects in the treatment group within the population.

Individual subject data will be provided in listings. All listings will be sorted by treatment, site, subject and, if applicable, collection date and time.

Unless otherwise stated summaries will present data across all sites (overall).

Unless otherwise noted, tabulations of categorical data will present only those categories appearing in the data.

On all figures, the comparator treatment will be represented in black with solid lines and filled squares; EXPAREL will be represented in red with solid lines and dots.

For tables presenting summaries of VAS scores, if more than one VAS score is presented for a specific timeframe/timepoint of interest, the highest score within that specific timeframe/timepoint should be used.

Plots of the VAS scores will show both observed and imputed scores. A change in color and line type will differentiate the imputed VAS scores. Imputed values will be represented by blue and green symbols and dashed lines for the comparator and EXPAREL respectively. VAS scores obtained immediately prior to rescue will be indicated by a change in symbol. For the comparator the symbol should be a triangle, for EXPAREL the symbol is a star. The following table shows the SAS symbol statements:

Treatment	VAS Score	SAS Statement
Comparator	Observed	symbol font=marker interpol=j line=1 value=U color=black
	Imputed	symbol font=marker interpol=j line=3 value=C color=blue
EXPAREL	Observed	symbol font=marker interpol=j line=1 value=W color=red
	Imputed	symbol font=marker interpol=j line=3 value=V color=green

Note the symbol statement number will be dependent on the sort order of the treatment and VAS score group indicator variables.

Sites with fewer than 5 subjects per treatment arm will be pooled with other sites for analysis. US sites will be pooled with other small US sites based on the US Census Bureau geographic regions (see Table 1) and European sites will be pooled with other small European sites based on country. Sites meeting the criteria for pooling will be pooled with other similar sites within their census division. If the resulting pooled site within a division still doesn't have enough subjects per treatment group, it will be pooled with the site within the division with the smallest enrollment that doesn't meet the pooling criteria. If all sites within a division are pooled and the resulting pooled site still meets the pooling criteria, the site will be pooled with other small sites within the region. If the pooled site with the region still meets the pooling criteria it will be pooled with the site with the smallest enrollment from the neighboring regions.

Table 1: US Census Regions and Divisions

Region	Division	State
Midwest	East North Central	Illinois, Indiana, Michigan, Ohio, Wisconsin
	West North Central	Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, South Dakota
Northeast	Middle Atlantic	New Jersey, New York, Pennsylvania
	New England	Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont
South	East South Central	Alabama, Kentucky, Mississippi, Tennessee
	South Atlantic	Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia
	West South Central	Arkansas, Louisiana, Oklahoma, Texas
West	Mountain	Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, Wyoming
	Pacific	Alaska, California, Hawaii, Oregon, Washington

Subjects who use opioid rescue medication will have the pain scores obtained after rescue replaced using pain scores obtained prior to rescue medication use. Pain scores obtained during the opioid medication window will be replaced. For this study the prescribed opioid rescue medication is oxycodone; however morphine or hydromorphone may be used. The durations of effect for various opioids are listed in Table 2.

Table 2: Opioid Windows

Medication	Route	Window Used to Impute VAS
Oxycodone, Oxycocet, Percocet, acetaminophen-oxycodone, Oxycontin	PO, IM, IV, SC	6 hours
Morphine	IV, PO, SC	4 hours
Hydromorphone (Dilaudid), Hydromorphone hydrochloride	IV	2 hours
Hydromorphone (Dilaudid)), Hydromorphone hydrochloride	PO, IM, SC	4 hours
Hydrocodone	PO	6 hours
Fentanyl	IV, PO, IM	6 hours
Vicodin, Norco, Lorcet, Lortab, hydrocodone-acetaminophen	PO	6 hours
Codeine (Tylenol 3, acetaminophen-coedine, Paracetamol Forte, Tylenol 4)	PO	6 hours
Ultram, Tramadol, Tramacol hydrochloride	PO	6 hours

PO = oral; IV = intravenous; VAS = visual analog scale.
If other rescue medications are given then the window will be determined post-hoc. If a combination opioid product is given then the window will be determined by the opioid part of the medication.
Opioids given post surgically with an indication such as 'anesthesia maintenance' will not be included for imputation purposes.

All non-efficacy tables will present EXPAREL 133 mg, EXPAREL 266 mg, All EXPAREL (combined doses), placebo, and all treatments as separate columns.

Efficacy tables will present EXPAREL 133 mg and placebo as separate columns. EXPAREL 266 mg will not be presented in the efficacy tables and figures, but will be presented in the efficacy listings.

If there are multiple VAS records with the same actual date/time for a given subject, then the record with the highest VAS score will be used for that actual date/time for all endpoint derivations, summaries, and analyses.

9.1.1. Handling Missing Values

9.1.1.1. Area under the VAS-Time Curve

9.1.1.1.1. Multiple Imputation Method

Rubin's (1987)[4] multiple imputation procedure will be applied to replace each missing value with a set of plausible values that represent the uncertainty about the right value to impute. This multiple imputation method is being implemented per the advice provided in "The prevention and treatment of missing data in clinical trials."[5] For calculation of area under the curve (AUC) of VAS pain intensity scores, the windowed worst observation carried forward (wWOCF) multiple imputation procedure will be used in the following order:

a) Windowed worst observation carried forward (wWOCF) for rescue medications.

   For subjects who take a rescue medication, their VAS scores recorded within the window of controlled type of rescue medication (see Table 2) will be replaced by the 'worst' observation. The non-rescue VAS score recorded right before taking a rescue medication (start of Rescue window) is considered as the 'worst' observation. This non-rescue worst VAS score shall be after the end of previous rescue window, where a rescue window ends once a subject is no longer considered under the effect of opioids (see Table 2 for individual rescue medication durations). If there is no value available between the end of previous rescue window and the start of the current rescue window, then the first VAS score recorded on or right after the start of the current rescue window will be used for the imputation. VAS scores recorded prior to the end of surgery will not be considered.

b) After the wWOCF imputation, described in Step a, subject data still missing scheduled assessments with a non-monotone missing pattern (i.e., all pain scores between the last non-missing score and last timepoint) will have missing scores imputed using the Markov-Chain Monte-Carlo (MCMC) method (Schafer 1997)[6] within each surgery and treatment, which will be applied in the multiple imputation procedure for arbitrary missing patterns. This MCMC method will simulate 10 datasets with only monotone missing data. In order to achieve the stationary distribution and to avoid dependency within samples generated by MCMC method, the number of iteration for the burn in period will be set to 2000 and the number of iterations between each sample will be set to 1000 (i.e., NBITER=2000 and NITER=1000.)

c) The AUC and SPIS at various time intervals will be derived from the imputed VAS scores resulting from Step b.

d) Rubin's (1987) synthesizing procedure for the multiple imputed data will be applied to synthesize analysis results for each imputation. SAS PROC MIANALYZE will be used for this procedure. The mean parameter estimates, the asymptotic variance for this mean from the imputed data analysis in Step c will be created based on Rubin and Schenker method (1986)[7].

SAS pseudo-code for multiple imputations is provided in Section 13.

9.1.1.2. Exposure, Surgery, and Rescue Medication Date or Time

It is expected that all necessary information on study drug exposure, surgery, and postsurgical rescue medication (dates and times) will be complete. Any such information that is missing and cannot be obtained through query resolution may be imputed, on a case-by-case basis, in a conservative manner that minimizes bias. For example, if pain medication taken on Day 1 has no time of administration recorded, the imputed time will be the end of surgery.

9.1.1.3. Rescue Pain Medication

For calculation of the total rescue pain medication usage (IV Morphine Equivalent) through a time point, if a subject is discontinued early (e.g., dies, withdraws consent, is withdrawn from the study, or is lost to follow-up) before the end of the time interval (e.g., 24 hours after study drug administration), his or her total rescue pain medication usage through the time interval will be a projected amount. For example, if a subject discontinues early at 6 hours after surgery, the projected amounts through 24 hours will be actual amount + average amount (actual amount/6 hours) multiplied by the number of hours remaining in the time interval (18=24-6).

9.1.1.4. Adverse Event or Concomitant Medications Dates or Times

For AEs or concomitant medications with missing or partially missing start/stop date/time, the following imputation rules will be applied:

For partial start date/time:

- If the year is unknown, then the date will be assigned the date and time of first dose of study treatment.
- If the month is unknown, then:
  - i) If the year matches the year of the dose of study drug date, then the month and day of the dose of study drug date will be used to impute the missing month and corresponding day.
  - ii) Otherwise, 'January' will be assigned.
- If the day is unknown, then:
  - i) If the month and year match the month and year of the dose of study drug date, then the day of the dose of study drug date will be imputed.
  - ii) Otherwise, '01' will be assigned.
- If the time is unknown, then:
  - i) If the date (day, month, and year) matches the date of the administration of study drug, then the time of the dose of study drug time will be imputed.

ii) Otherwise, '00:00' will be assigned.

For partial stop date/time:

- If the year is unknown, then the date will be assigned the date subject discontinued from study, time will be set to the last time of the day ('23:59').
- If the month is unknown, then month subject discontinued from study will be assigned.
- If the day is unknown, then the last day of the month will be assigned.
- If the time is unknown, then the last time of the day will be assigned ('23:59').

9.1.1.5. Adverse Event Severity or Relationship to Study Drug

If severity of an AE is not reported, then for tables of AEs by severity, the event will be classified as 'Severe'. If relationship to study drug is not reported for an AE, then for tables of study-drug related AEs, the event will be assigned the relationship of 'definite'. Tables presenting related AEs will include all AEs with relationships of 'possible', 'probable' or 'definite' as assessed by the investigator.

9.1.1.6. Time to Event

For calculating time to an event when only the hour is reported, the minutes will be set to zero.

9.1.2. Multiplicity Adjustments

For the efficacy analyses, EXPAREL 133 mg will be compared to placebo at the 0.05 alpha level for the efficacy analysis set. In order to maintain strong type I error control, a hierarchical gatekeeping structure will be utilized. If a test fails to reject the null hypothesis at the 0.05 alpha level, then no additional hypothesis testing will be conducted. The hierarchical gatekeeping order will be as follows:

1) AUC of the VAS pain intensity scores through 48 hours [AUC(0-48)]
2) Total postsurgical opioid consumption (mg) through 48 hours
3) Percentage of opioid-free subjects through 48 hours
4) Time to first rescue medication (opioid) dose through 48 hours

Any analyses of tertiary efficacy endpoints are for sensitivity or exploratory purposes. No multiplicity adjustments will be made for these endpoints.

9.1.3. By-Center Analyses

By-site summaries will present descriptive statistics only; no statistical analyses will be performed on individual sites. By-site summaries will be presented for disposition, demographics, the primary efficacy endpoint, and the secondary efficacy endpoints. By-site summaries will present both pooled and individual sites. The pooled site should be presented first immediately followed by the sites within that pool.

9.2. Subject Disposition

Subject disposition summaries will include the number of subjects that were:

- Screened,
  - Screen failure

    - Enrolled
- Randomized
    - Randomized not treated,
    - Randomized treated,
- In the safety analysis set,
- In the efficacy analysis set,
- In the per-protocol analysis set,
- Protocol
    - Enrolled under Amendment 2
    - Enrolled under Amendment 1
    - Enrolled under Original Protocol
- Completed the study as planned,
- Discontinued from the study, and
- Reasons for discontinuation from the study.

Percentages will be reported for the screen failures and enrolled using the number of subjects screened as the denominator; efficacy analysis set and per-protocol analysis set will use the number of subjects randomized, treated, and having surgery as denominator for percentages; all other percentages will use the number of subjects randomized and treated as denominator.

The safety analysis set data and enrollment data will be presented as treated. All other data will be presented as randomized.

The disposition summary will present the data for each treatment group (EXPAREL 133 mg, EXPAREL 266 mg, placebo), EXPAREL treatments combined (All EXPAREL), and across treatment groups (Total). This summary table will present overall sites and for each site separately.

9.3. Description of Demographics and Baseline Characteristics

9.3.1. Demographics

The summary of demographic data will present:

- Age (years) – descriptive statistics
- Sex – n (%)
- Ethnicity – n (%)
- Race – n (%)
- Country – n (%)
- Dominant hand – n (%)

Age is calculated from the date the subject signed the informed consent form (ICF) and birth. It is presented as the number of years between, rounding down to the nearest integer year. For partial birthdates, impute the first of the month for missing day and January for missing month to calculate age. It is presumed that birth year is known.

The demographic summary will present the data for each treatment group (EXPAREL 133 mg, EXPAREL 266 mg, placebo), EXPAREL treatments combined (All EXPAREL), and across treatment groups (Total). Summaries will be provided for all (safety, efficacy, and per-protocol) analysis sets. This summary will present overall sites and for each site separately.

9.3.2. Baseline Characteristics

The summary of baseline characteristic data will present:

- American Society of Anesthesiologists (ASA) Classification – n (%)
- Baseline VAS scores
- Baseline neurological assessments
- Baseline ECG interpretation
- Baseline degree of motor nerve block assessments
    - Thumb abduction
    - Thumb adduction
    - Thumb opposition
    - Elbow flexion
- Height (cm)
- Weight (kg)
- Body Mass Index (BMI) (kg/m^2)
- Baseline vital signs
    - Heart rate (bpm)
    - Systolic blood pressure (mmHg)
    - Diastolic blood pressure (mmHg)

The formula for BMI is $w/(h^2)$, where w is weight in kilograms and h is height in meters. Weight in pounds will be converted to kilograms using the conversion factor of 2.2046 pounds to 1 kilogram. Height in inches will be converted to centimeters using the conversion factor of 2.54 centimeters to 1 inch. Height in centimeters will be converted to meters using the conversion factor of 100 centimeters to 1 meter.

Baseline characteristics summaries will present the data for each treatment group (EXPAREL 133 mg, EXPAREL 266 mg, All EXPAREL doses, placebo) and across treatment groups (Total). Summaries will be provided for all (safety, efficacy, and per-protocol) analysis sets. This summary table will show summaries across all sites and for each site separately.

Descriptive statistics (n, mean, SD, median, minimum and maximum) will be provided for VAS scores, degree of motor blockade, height, weight, BMI and vital signs. The number and percent of subjects will be tabulated for the various categories of sensory assessments, neurological assessments and ECG interpretation.

9.4. Surgery Characteristics

Surgery characteristics include surgery type (TSA or RCR), and if TSA then the type of TSA (conventional or reverse), nerve block type (interscalene or supraclavicular), duration of surgery, and total incision length. Duration of surgery is calculated as the difference between the end of surgery and start of surgery times and reported in hours. Descriptive statistics will be provided for the duration of surgery and total incision length by treatment group and across all treatment groups. Surgery, TSA type, and nerve block type will be tabulated by treatment group and across all treatment groups.

9.5. Intraoperative, Prior, and Concomitant Medications

Intraoperative, Prior, and concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO-DD) and will be classified according to the default anatomical therapeutic chemical (ATC 4) classification term and standard medication name.

Intraoperative medications are defined as medications given as part of the surgical procedure. These may include anesthesia, opioids or other medications with start and stop dates on the day of surgery and start and stop times overlapping with the surgery start and stop times.

Prior medications are defined as medications with a stop date and time prior to the start of study drug administration.

Concomitant medications are defined as medications taken after the start of study drug administration (i.e., started prior to the start of study drug administration and continued after or started after the start of study drug administration).

Intraoperative, prior and concomitant medications will be summarized separately using n (%) of subjects for each treatment group and across treatment groups by ATC class term and standard medication name for the safety analysis set. Subjects may have more than one medication per ATC category and standard medication name. At each level of subject summarization, a subject will be counted once if one or more medications are reported by the subject at that level.

A listing mapping the ATC term and standard medication name to verbatim term will be presented.

9.6. Measurements of Treatment Compliance

Study treatment is administered by a party other than the subject, therefore compliance is assured.

9.7. Efficacy Analysis

For Primary and Secondary Efficacy Analyses, descriptive statistics that are appropriate for the efficacy variable will also be shown by site but no statistical analyses will be performed within a site. The primary and secondary efficacy analyses will be performed on the efficacy and per-protocol analysis sets. Tertiary efficacy analyses will be performed on the efficacy analysis set only.

9.7.1. Efficacy Endpoints

9.7.1.1. Primary Efficacy

The primary endpoint is AUC of the VAS pain intensity scores through 48 hours [AUC(0-48)].

9.7.1.2. Secondary Efficacy

The following secondary endpoints will be analyzed as described in Section 9.1.2:

- Total postsurgical opioid consumption (in IV morphine equivalents per mg) through 48 hours.
- Percentage of opioid-free subjects through 48 hours.
- Time to first rescue medication (opioid) dose through 48 hours.

9.7.1.3. Tertiary Efficacy

- The AUC of the VAS pain intensity scores through 12, 24, and 72 hours.
- The AUC of VAS pain intensity scores from 24-48 and 48-72 hours.
- VAS pain intensity scores at each assessed timepoint.
- Proportion of subjects who are pain free (VAS score of ≤ 1.5) at each assessed timepoint.
- SPIS through 24, 48, and 72hours.
- SPIS from 24-48 and 48-72 hours.
- Total opioid consumption in IV morphine equivalents through 24 and 72 hours.
- Total opioid consumption in IV morphine equivalents from 24-48 and 48-72 hours.
- Percentage of subjects who are opioid-free through 24 and 72 hours.
- Overall benefit of analgesia scale (OBAS) total score at 24 and 72 hours and Day 10.
- Subject satisfaction with overall analgesia (using a 5-point Likert scale) at 24 and 72 hours, and Day 10.
- Proportion of subjects ready for discharge at 12, 24, 36, 48, 60, and 72 hours
- Number of unscheduled phone calls or office visits related to pain after discharge through Day 10.

9.7.1.4. Area under the Curve

Area under the pain-time curve is derived using the trapezoidal rule (see formula below) on the pain scores adjusted for rescue medication use using the imputed values (see Section 9.1.1.1). AUC will start with the first pain assessment obtained after surgery and use all following pain assessments including those collected prior to rescue medication and unscheduled. Actual assessment times will be used in deriving AUC.

$$AUC = [\sum_{i=3}^{n}(p_i + p_{(i-1)})(t_i - t_{(i-1)})]/2$$

Where p_i is the VAS pain score at time i and t_i is the time, in hours, from end of surgery. Note that i starts at 3 since t_1 is not used in AUC calculation (prior to surgery) and t_2 is arrival at PACU.

9.7.1.5. Opioid Consumption

Opioids will be converted to IV morphine equivalent dose (MED mg) using the appropriate conversion factor from Table 3 for all summaries. Total opioid dose is the IV morphine equivalent sum of all opioids taken after surgery up to the timepoint of interest. Subjects with no opioid use during the period in question will be assigned a dose of 0 for summaries and changed to the lesser of 0.1 or half of the smallest total amount observed in the study, whichever is smaller, prior to being transformed with the natural logarithm for analysis.

Table 3: IV Morphine Equivalents

Medication	Unit	Route	Conversion (Multiplication) Factor

Oxycodone, Oxycocet, Percocet, acetaminophen-oxycodone, Oxycontin	mg	PO, IV,IM,SC	2
Morphine	mg	IV,IM,SC	1
Morphine	mg	PO	0.33
Hydromorphone (Dilaudid), Hydromorphone hydrochloride	mg	IV,IM	7.7
Hydromorphone (Dilaudid), Hydromorphone hydrochloride	mg	PO	1.3
Hydromorphone (Dilaudid), Hydromorphone hydrochloride	mg	SC	4
Fentanyl	mg	IV,PO,IM	100
Vicodin, Norco, Lorcet, Lortab, hydrocodone-acetaminophen	mg	PO	2
Codeine (Tylenol 3, acetaminophen-coedine, Paracetamol Forte, Tylenol 4)	mg	PO	0.05
Ultram, Tramadol, Tramacol hydrochloride	mg	PO, IM	0.08
PO = oral; IV = intravenous; VAS = visual analog scale. If other rescue medications are given then the conversion to IV Morphine Equivalent will be determined post-hoc. If a combination opioid product is given then the IV Morphine Equivalent will be determined by the opioid part of the medication. Opioids given post surgically with an indication such as 'anesthesia maintenance' will not be included.			

9.7.1.6. Time to First Opioid Rescue Medication Use

Time to first opioid rescue medication use will be calculated as the time from end of surgery to time of event in hours.

9.7.1.7. Pain-free

Pain-free is defined as an observed VAS score less than or equal to 1.5 with no prior rescue medication and all prior VAS scores less than or equal to 1.5.

9.7.1.8. Overall Benefit of Analgesia Score (OBAS)

The OBAS is derived as follows:

1. Add all of the scores of questions 1 to 6.
2. To this number, add four.
3. Subtract the score of question 7 from this number.

If a response is missing to any question in the OBAS, the total score will not be calculated.

9.7.2. Methods of Analysis

For Primary and Secondary Efficacy Analyses, descriptive statistics that are appropriate for the efficacy variable will also be shown by site but no statistical analyses will be performed within a site.

9.7.2.1. Primary Efficacy Analysis

The primary efficacy variable is the AUC of VAS scores through 48 hours [AUC(0-48)] using the multiple imputation method described in Section 9.1.1.1.

Tests for the treatment effect of EXPAREL 133 mg versus placebo will be based on the following null hypothesis (H_o) and two-sided alternative hypothesis (H_a):

$$H_o: \mu_s = \mu_p \text{ versus } H_a: \mu_s \neq \mu_p$$

where μ_s and μ_p are the mean of AUC(0-48) for EXPAREL 133 mg and the mean of AUC(0-48) for placebo, respectively. A two-sided test will be performed at 5% level of significance comparing EXPAREL 133 mg to placebo. The treatment effect of EXPAREL 133 mg will be considered significantly better than that of placebo if the null hypothesis of no difference is rejected and a difference in mean of AUC(0-48) in favor of EXPAREL 133 mg (mean for EXPAREL 133 mg less than the mean for placebo) is observed.

For the primary efficacy variable of AUC(0-48), EXPAREL 133 mg will be compared to placebo using analysis of variance (ANOVA) with age, weight, and height as covariates. Based on the model, the least squares (LS) mean and the standard error (SE) of the LS mean, will be reported for each treatment group. The LS treatment difference for the active minus placebo, 95% CI for the active minus placebo treatment difference, and p-value will be reported as well as for each active treatment.

Descriptive statistics of the primary efficacy variable will also be shown by site but no statistical analyses will be performed within a site.

9.7.2.2. Secondary Efficacy Analyses

9.7.2.2.1. Postsurgical Opioid Consumption

Postsurgical narcotic consumption (MED mg) will be summarized (n, Geometric Mean, coefficient of variation, minimum, and maximum) by treatment group for the total dose consumed over the 48 hours after the end of surgery. The number and percentages of the types of opioids used will be presented by treatment group, subjects will be counted only once for each opioid used. This summary table will show summaries across all sites and for each site separately.

Prior to analysis, the natural logarithm transformation will be applied to the total amount. When total amount of opioids (IV Morphine Equivalent) used is 0, the result will be changed to 0.1 or half of the smallest total amount observed in the study, whichever is smaller, prior to being transformed with the natural logarithm. To test for significant differences between EXPAREL 133 mg and placebo, the same ANOVA model used in the primary efficacy analysis will be used. The LS means, LS mean difference between the two treatment groups, 95% CI for the LS mean difference between EXPAREL and placebo, and p-value will be reported. The LS means, LS mean differences and 95% CI will be back transformed for presentation (note the LS mean difference becomes the ratio when back-transformed) along with the descriptive statistics (untransformed) by treatment.

9.7.2.2.2. Opioid-free

Percentage of opioid-free subjects through 48 hours will be analyzed using a Cochran-Mantel-Haenszel (CMH) test. The p-value from the CMH analysis and mean treatment difference and 95% CI about the mean difference using the Newcombe[8] method (SAS pseudo-code below) will be presented. The tabulation of opioid-free subjects will be presented across all sites and surgeries separately. No inferential statistics will be calculated for individual sites.

The number and percentage of subjects opioid-free will also be tabulated by timepoint.

Pseudo-code for Newcombe method:

```
PROC FREQ;
        TABLE TREATMENT*RESPONSE / RISKDIFF(CL=NEWCOMBE COMMON);
RUN;
```

9.7.2.2.3. Time to First Opioid Rescue Medication

Time to first opioid rescue medication will be computed in hours as the date and time of the first opioid rescue medication minus the date and time of the end of surgery. If a subject is not administered an opioid rescue medication, the time to first administration will be censored at 48 hours after surgery or at the time of last follow-up, whichever is earliest. Time of last follow-up will be defined as the latter of (1) the last pain assessment, (2) the start time of the last concomitant medication, or (3) the start time of the last AE.

Time to first opioid rescue will be analyzed by the Kaplan-Meier method and the log-rank test. The n (%) of subjects administered an opioid as well as the n (%) of censored observations will be presented for each treatment group. In addition, Kaplan-Meier estimates in terms of the median and its 95% CI, and the 25th and 75th percentiles will be presented for each treatment. Log-rank tests will be used to compare EXPAREL to placebo.

9.7.2.3. Tertiary Efficacy Analyses

P-values computed for the tertiary endpoints are for descriptive purposes only and are not adjusted for multiple comparisons.

9.7.2.3.1. Visual analog scale (VAS) AUC

Summary statistics will be presented by treatment for VAS AUC(0-12), VAS AUC(0-24), VAS AUC(0-72), AUC(24-48), and AUC(48-72). For each of these variables, EXPAREL 133 mg will be compared to placebo using analysis of variance (ANOVA) with age, weight, and height as covariates. Based on the model, the LS mean and SE of the LS mean will be reported for each treatment. The LS treatment difference for the active minus placebo, 95% CI for the active minus placebo treatment difference, and p-value will be reported as well as for the active treatment.

9.7.2.3.2. Visual analog scale (VAS)

Summary statistics will be presented by treatment for VAS at each assessment timepoint. This summary will be based on the observed VAS values.

9.7.2.3.3. Proportion of Pain-Free Subjects

The proportion of pain-free subjects will be tabulated by treatment. The number and proportion of subjects who are pain-free and not pain-free (or VAS score is missing) will be presented at assessment timepoint. For the proportion of pain-free subjects, EXPAREL 133 mg will be

compared to placebo using a Cochran-Mantel-Haenszel (CMH) test. The p-value from the CMH analysis and mean treatment difference and 95% CI about the mean difference derived using the Newcombe[9] method.

9.7.2.3.4. Sum of Pain Intensity Scores (SPIS)

Summary statistics will be presented by treatment for SPIS(0-12), SPIS(0-24), SPIS(0-48), SPIS(0-72), SPIS(24-48), and SPIS(48-72). For each of these variables, EXPAREL 133 mg will be compared to placebo using analysis of variance (ANOVA) with age, weight, and height as covariates. Based on the model, the LS mean and SE of the LS mean will be reported for each treatment. The LS treatment difference for the active minus placebo, 95% CI for the active minus placebo treatment difference, and p-value will be reported as well as for each active treatment.

9.7.2.3.5. Total Opioid Consumption through 24 and 72 hours

Total opioid consumption through 24 and 72 hours will be summarized and analyzed by treatment group. These summaries and analyses will be calculated similar to the postsurgical opioid consumption through the 48 hour secondary endpoint (see Section 9.7.1.2).

9.7.2.3.6. Total Opioid Consumption during Specific Time Intervals

Total opioid consumption from 24-48 and 48-72 hours will be summarized and analyzed by treatment group. These summaries and analyses will be calculated similar to the postsurgical opioid consumption through the 48 hour secondary endpoint (see Section 9.7.1.2).

9.7.2.3.7. Percentage of Opioid-free Subjects through 24 and 72 hours

The percentage of opioid-free subjects will be tabulated and analyzed by treatment. These summaries and analyses of the percentage of opioid-free subjects at 24 and 72 hours will be calculated similar to the percentage of opioid-free subjects at 48 hours secondary endpoint (see Section 9.7.2.2.2).

9.7.2.3.8. Overall Benefit of Analgesia (OBAS)

The OBAS total score will be summarized by treatment and individual question responses tabulated at following timepoints: 24 and 72 hours and postsurgical Day 10. For the OBAS total score, EXPAREL 133 mg will be compared to placebo using a Kruskal-Wallis test at 24 and 72 hours and postsurgical Day 10.

9.7.2.3.9. Subject Satisfaction with Overall Analgesia

Subject satisfaction with overall analgesia (obtained using a 5-point Likert scale) will be summarized and individual responses tabulated by treatment for each of the following assessment timepoints: 24 and 72 hours and postsurgical Day 10. The numeric value of the response will be presented using descriptive statistics. For each value of the scale the number and percentage of subjects selecting that value will also be presented. For the subject satisfaction with overall analgesia, EXPAREL 133 mg will be compared to placebo using a Kruskal-Wallis test for each of the following assessment timepoints: 24 and 72 hours and postsurgical Day 10.

9.7.2.3.10. Discharge Readiness

Time to discharge ready will be computed in hours as the date and time of subjects first meeting the discharge readiness criteria and time of the end of surgery. Discharge ready criteria will be met when the MPADSS criterion is met (total score of 9 or more) for discharge readiness or the

subject is discharged, whichever occurs first. If a subject has not met the discharge ready criteria prior to or at a given timepoint (12, 24, 36, 48, 60, and 72 hours), then the time to discharge ready will be censored at the time of their last MPADSS assessment in the study or the specific assessment timepoint (12, 24, 36, 48, 60, and 72 hours), whichever occurs sooner.

Time to discharge ready will be analyzed by the Kaplan-Meier method for each of the following assessment timepoints: 12, 24, 36, 48, 60, and 72 hours. The n (%) of subjects who are discharge ready as well as the n (%) of censored observations will be presented for each treatment group. In addition, Kaplan-Meier estimates in terms of the median and its 95% CI, and the 25th and 75th percentiles will be presented for each treatment at 12, 24, 36, 48, 60, and 72 hours. Log-rank tests will be used to compare EXPAREL 133 mg to placebo at 12, 24, 36, 48, 60, and 72 hours.

The number and percent of subjects meeting the discharge readiness criteria at 12, 24, 36, 48, 60, and 72 hours will be summarized.

If a subject is discharge ready at an early timepoint, the subject will be considered discharge ready at all subsequent (future) timepoints. If a subject has a discharge readiness total score of less than 9 or if the total score is missing, the subject will be considered not discharge ready, unless they were previously considered discharge ready.

9.7.2.3.11. Number of Pain-Related Visits/Phone Calls after Discharge

The number of pain-related unscheduled phone calls or office visits after discharge through postsurgical Day 10 will be summarized (n, mean, SD, median, minimum and maximum) by treatment group. The number and percentage of subjects reporting for each number of pain-related unscheduled phone calls or visits (0, 1, 2, … maximum number observed) will be presented by treatment group. For the number of pain-related unscheduled phone calls or office visits, EXPAREL 133 mg will be compared to placebo using a Kruskal-Wallis test.

9.7.2.3.12. Region Analysis

Summaries and tabulations looking at region will be performed for the following:

- Disposition
- Demographics
- Baseline Characteristics
- Intraoperative medicines
- VAS AUC(0-48)
- Total opioid consumption through 48 hours
- Percentage opioid-free through 48 hours
- Sensory loss and return
- Motor function loss and return
- Overall summary of adverse events
- Incidence of TEAEs
- Incidence of Serious TEAEs

The populations for each the summary and tabulation as planned for the non-region tables will be repeated for the region tables.

For analyses considering region, the age, weight, and height scovariates will be replaced with region, this will be performed for the following:

- VAS AUC(0-48)

- Total opioid consumption through 48 hours
- Percentage opioid-free through 48 hours
- Sensation Loss and Return
- Motor Function Loss and Return

Region summaries, tabulations, and analyses will be the final block within the 14.1, 14.2 and 14.3 series of tables.

9.8. Safety Analyses

Safety assessments in this study consist of vital signs, 12-lead ECGs, neurological assessments, sensory and motor nerve block assessments, motor function assessments and AEs. Vital signs, ECGs, neurological, nerve block assessments (sensory and motor) and motor function assessments will be serially collected (see Time and Events Schedule of Study Procedures). Adverse events will be collected from the time of informed consent through Day 30.

P-values computed for the safety endpoints are for descriptive purposes only and are not adjusted for multiple comparisons.

9.8.1. Vital Signs

Vitals signs are resting heart rate (bpm), systolic blood pressure (mmHg), and diastolic blood pressure (mmHg). Vital signs will be summarized by treatment group and the All EXPAREL group at each assessment timepoint. The assessment timepoints for the vital signs are: at baseline (prior to the nerve block); every 5 minutes during performance of the block up to 30 minutes; and every 15 minutes until entering the OR; at PACU arrival; at 6, 9, 12, 24, 36, 40, 44, 48, 52, 56, 60, and 72 hours; and on postsurgical Days 5 and 10. Summaries will present both actual and change-from-baseline results. Baseline statistics will be presented at each assessment timepoint for those subjects reporting data at that timepoint.

Vital signs will also be assessed for potentially clinically significant abnormal values (see Table 4). The number and percentage of subjects satisfying the potentially clinically significant abnormal criteria (critical value, critical change separately and then value and change concurrently) at any time during the study and at each assessment timepoint will be tabulated by treatment and overall treatments.

Table 4: Criteria for Potentially Clinically Significant Abnormal Vital Signs

Vital Sign	Unit	Critical Value	Critical Change[1]
Resting Heart Rate	beats/minute (bpm)	High: ≥ 120 Low: ≤ 50	Increase of at least 15 Decrease of at least 15
Systolic Blood Pressure	mmHg	High: ≥ 180 Low: ≤ 90	Increase of at least 20 Decrease of at least 20
Diastolic Blood Pressure	mmHg	High: ≥ 105 Low: ≤ 50	Increase of at least 15 Decrease of at least 15

[1]Change criteria not applicable at baseline or screening.

9.8.2. Electrocardiograms

Investigators will classify ECG tracings as ‘normal, ‘abnormal not clinically significant’ or ‘abnormal clinically significant’. The investigator classifications will be tabulated by treatment and overall treatments at any time during the study and each assessment timepoint. The assessment timepoints for the ECGs are: at baseline (prior to the nerve block); upon arrival at the PACU; at 6, 9, 12, 24, 36, 40, 44, 48, 52, 56, 60, and 72 hours; and on postsurgical Days 5 and 10.

A shift table comparing the investigator classification of the ECG results at baseline to each timepoint will also be provided.

9.8.3. Neurological Assessments

Neurological assessments include orientation (orientated, disoriented, not assessable), numbness (of lips, tongue, or around mouth), metallic taste, hearing problems, vision problems, and muscle twitching. The number and percentage of subjects will be tabulated for each neurological assessment by treatment group at any time after baseline and at each assessment timepoint. The assessment timepoints for the neurological assessments are: at baseline (prior to the nerve block); upon arrival at the PACU; at 6, 9, 12, 24, 36, 40, 44, 48, 52, 56, 60, and 72 hours; and on postsurgical Days 5 and 10.

9.8.4. Sensation Tests

Sensations tests are assessed on the shoulder (axillary nerve), forearm (musculocutaneous nerve), middle finger (median nerve), fifth finger (ulnar nerve) and thumb (radial nerve). The number and percentage of subjects will be tabulated for each response (present/absent) within each nerve and sensory test (cold, pinprick and light touch) by treatment group at each assessment timepoint. The assessment timepoints for the sensation tests are: at baseline (prior to the nerve block); at approximately 15, 30, and 45 minutes after the nerve block; prior to discharge from the PACU; at 6, 9, 12, 18, 24, 36, 48, 60, and 72 hours.

The number and percentage of subjects will be tabulated for loss and return of sensation (see Section 7) across all locations and within each location and each sensory test (cold, pinprick and light touch) and combinations of sensory tests (ANY, CPL, CP, CL, and PL) by treatment group at each assessment timepoint. Where the combinations of ANY, CPL, CP, CL and PL are defined as follows:

- ANY = at least one sensation
- CPL = all sensations (cold, pinprick and light touch)
- CP = cold and pinprick
- CL = cold and light touch
- PL = pinprick and light touch

A subject will be considered as having a loss of sensation if either of the locations has a loss of sensation; a return across locations is when both locations have return of sensation for the subject.

The times to loss of and return of sensation (see Section 7, subsections loss of sensation and return of sensation) will be summarized by treatment using Kaplan-Meier estimates. In addition, Kaplan-Meier estimates in terms of the median and its 95% CI (using log-log method), and the 25th and 75th percentiles will be presented for each treatment. Log-rank tests will be used to compare EXPAREL 133 mg to placebo. .

Duration of sensation loss will be summarized across locations and within each location. Total duration is defined as the sum of durations of each lost-return cycle for a subject. If more than 10% of the subjects in at least one treatment group experience multiple lost-return cycles, then duration will be summarized for total duration and within each cycle.

An additional table summarizing the number of cycles and tabulating the distribution number of cycles by treatment group will be presented within each location by treatment group.

9.8.5. Degree of motor nerve block Assessments

Degree of motor nerve block assessments includes thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve) and elbow flexion (musculocutaneous nerve) as assessed using the Lovett scale. The actual and change from baseline values for each of these parameters will be summarized by treatment at each assessment timepoint. At each assessment timepoint the baseline values will be summarized for those subjects who have data at that timepoint.

The assessment timepoints for the degree of motor nerve block are: at baseline (prior to the nerve block);
at approximately 15, 30, and 45 minutes after the nerve block; prior to discharge from the PACU; at 6, 9, 12, 18, 24, 36, 48, 60, and 72 hours. At each assessment timepoint, the number and percent of subjects with loss and return of motor function (see Section 7) will be summarized by treatment.

For each active assessment the time to return to motor function will be analyzed by treatment in the same manner as time to first rescue medication (see Section 9.7.1.6).

9.8.6. Adverse Events

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).

An AE will be considered TEAE if the onset date and time is between the start date and time of study treatment and Day 30.

If an AE has a partial onset date and time the imputed start and stop dates and times will be used to determine treatment-emergence (e.g., stop date and time is before start date and time of study treatment). All AE summaries will present TEAEs only; AEs that are not treatment-emergent will be included in listings but not summarized.

The incidence of subjects reporting TEAEs will be tabulated by the number and percentage of subjects reporting the TEAE. Incidence is defined as a subject reporting at least one TEAE within the summary level. Summary levels are ‘at least one TEAE’, system organ class and preferred term. Subjects will be counted only once within each reporting level on the table. For example if a subject reports a TEAE of headache on two separate occasions, the subject will be counted only once in the headache row of the table. Similarly if a subject reports two separate TEAEs within the same system organ class the subject will only be counted once in the summary row for that system organ class. A summary of subjects reporting at least one TEAE during the study will also be presented.

The first row on every TEAE table will be the number and percentage of subjects reporting at least one TEAE. Subsequent rows will be presented in descending order of subject counts for the overall treatment group with the most common system organ class first, followed within each system organ class by the preferred terms in descending subject count order. For tables presenting the severity or relation to study treatment of AE, the sort order will be determined by the number and percentage of subjects reporting the preferred term, thus the sort order of rows will remain the same for the relation or severity tables as the tables by preferred term. .

The following summaries will be presented for the AEs reported by the subjects:

An overview of all TEAEs, serious TEAEs and TEAEs of Special Interest will present the number and percentage of subjects in the following categories:

- Any TEAE
  - Maximum severity: Mild
  - Maximum severity: Moderate
  - Maximum severity: Severe
- At least one related TEAE
- At least one serious TEAE
- Subjects discontinued due to a TEAE
- Died on study

Subjects will be counted once in each of the above categories except for maximum severity. Subjects will be counted only once at the highest severity reported. For example, if a subject has a mild and severe headache and a moderate rash, the subject will be counted under maximum severity of severe only.

Adverse event tables will present the data by treatment group and across all treatment groups. Incidence tables will be created for the following groups of TEAEs:

- All TEAEs
- Study treatment related TEAEs
- TEAEs leading to study withdrawal
- Study treatment related TEAEs leading to study withdrawal
- All TEAEs by severity
- All TEAEs by relationship to study treatment
- All serious TEAEs
- Study treatment related serious TEAEs
- Serious TEAEs leading to study withdrawal
- Study treatment related serious TEAEs leading to study withdrawal
- Serious TEAEs resulting in death
- Study treatment related serious TEAEs resulting in death
- All TEAEs of special interest
- Study treatment related TEAEs of special interest
- TEAEs of special interest leading to study withdrawal
- Study treatment related TEAEs of special interest leading to study withdrawal
- TEAEs of special interest resulting in death

Study treatment related TEAEs of special interest resulting in deathIf there are no AEs to report on any of the above tables, the table should be created with the line ‘no adverse events were reported’ in the body of the table.

Adverse events will be considered related if the investigator assessment of relationship to study treatment is either ‘possible’, ‘probable’ or ‘definite’.

All AE summaries based on related AEs will be produced based on the investigator assessment of relatedness. Below are the MedDRA terms for the adverse events of special interest:

Group	Protocol term	MedDRA 18.1 Dictionary Terms	
		Term Level	Term
Cardiac	Angina	Preferred term	Angina Pectoris
	Myocardial infarction	Preferred term	Myocardial Infarction
	Bradycardia	Preferred term	Bradycardia
	Tachycardia	Preferred term	Tachycardia
	Extrasystoles	Preferred term	Extrasystoles
	Shortness of breath requiring intervention	Preferred term	Dyspnoea
Neurologic	Altered mental status	Preferred term	Mental Status Changes
	Altered sensorium	Preferred term	Depressed level of consciousness
	Rigidity	Preferred term	Muscle Rigidity
	Dysarthria	Preferred term	Dysarthria
	Seizure	Preferred term	Seizure
	Tremors	Preferred term	Tremor
	Metallic taste	Preferred term	Dysgeusia
	Tinnitus	Preferred term	Tinnitus
	Perioral numbness	Preferred term	Hypoaesthesia Oral
	Visual disturbance	Preferred term	Visual Impairment
	Dizziness	Preferred term	Dizziness
	Hyperesthesia	Preferred term	Hyperaesthesia
	Muscular twitching*	Preferred term	Muscle Twitching
	Tingling*	Preferred term	Paraesthesia
	Paresthesia*	Preferred term	Paraesthesia
Other	Fall	Preferred term	Fall
* if event persists beyond or occurs after 72 hours after start of study treatment dose.			

A listing of the mapping of the system organ class and preferred terms to verbatim terms will be presented.

9.8.7. Laboratory Parameters

Clinical laboratory assessments (hematology, chemistry, and urinalysis) are collected at screening, baseline and Day 10. Laboratory results will be summarized by treatment group and the All EXPAREL group at each assessment timepoint. Summaries will present both actual and change-from-baseline results. Baseline statistics will be presented at each assessment timepoint for those subjects reporting data at that timepoint.

Tabulations of the number and percentage of subjects with value below normal, normal or above normal will be provided by treatment group, All EXPAREL group and across all treatment groups at each timepoint.

Shifts in laboratory results categorized as low (below the lower limit of the normal range), normal (within the normal range, limits inclusive) and above (above the upper limit of the normal range) will be presented in shift tables with baseline categories across the columns and Day 10 down the rows for EXPAREL 133 mg, EXPAREL 266 mg, All EXPAREL and placebo separately. Each cell will present the number and percentage of subjects in that cell. Due to the width of these tables, only 2 treatments can be presented on a page. For ease of comparing active treatments to placebo, placebo data will be presented on each page. Thus the shift table will present all laboratory data for EXPAREL 133 mg and placebo then for EXPAREL 266 mg and placebo and finally for All EXPAREL and placebo.

9.9. Pharmacokinetic Analysis

The analysis of the PK endpoints will be described in a separate document.

9.10. Interim Analysis

9.10.1. Pharmacokinetic Review

An interim PK analysis was completed by QuantPharm LLC after 13 subjects completed the assessments through postsurgical Day 10. All of the plasma samples from the subjects who received EXPAREL were analyzed and the plasma samples from the subjects randomized to placebo were analyzed through the 24-hour timepoint. Enrollment continued while the interim PK data were analyzed. The goal of this third-party analysis was to determine the appropriateness of the PK timepoints selected and make recommendations to Pacira Pharmaceuticals (while maintaining the blind within Pacira Pharmaceuticals) to keep, remove, or revise the PK sampling scheme in order to fully characterize the PK profile.

QuantPharm LLC indicated that the results of this analysis showed a median T_{max} of 48 hours for the 133 mg EXPAREL group and a median T_{max} of 60 hours for the 266 mg EXPAREL group. Based on this information, QuantPharm LLC recommended changes to the PK collection schedule contained protocol amendment 2.

In addition, the safety assessment timepoints, including the neurological exam, vital signs, and ECG were adjusted based on the initial interim PK data.

A confirmatory interim PK analysis was conducted by QuantPharm LLC once 30 subjects had completed the assessments through postsurgical Day 10. No changes to the conduct of the study were recommended by QuantPharm LLC based on the confirmatory interim PK analysis.

9.10.2. Sample Size Review

The Original Protocol 402-C-327 issued on 24Nov2015 and Amendment 1 of Protocol 402-C-327 issued on 15Feb2016 randomized subjects (1:1:1) to one of three treatment-arms (EXPAREL 266 mg, EXPAREL 133 mg, or Placebo). Subjects randomized under Amendment 2 of Protocol 402-C-327 were randomized (1:1) to one of two treatment-arms (EXPAREL 133 mg or Placebo).

The sample size of 120 subjects from Amendment 2 of Protocol 402-C-327 section 15.3 was calculated based on the assumption that the observed efficacy through 72 hours in 402-C-323 would be the same as the observed efficacy through 48 hours in 402-C-327. In 402-C-323, a common standard deviation (SD) of 170 was observed and with a 100-unit treatment difference for pain intensity scores through 72 hours.

At the two-sided alpha level of 0.05, 47 subjects per treatment group would have at least 80% power to detect a 100 unit difference between treatment groups for the AUC of pain intensity scores through 48 hours, if the assumption of a common standard deviation (SD) of 170 is correct. Approximately 120 subjects were planned for enrollment into this study in order to have at least 94 evaluable subjects between the EXPAREL 133 mg and placebo treatment groups.

Within Amendment 2 of Protocol 402-C-327 section 15.8.1, an interim analysis was planned after 66 subjects had completed the assessments through Day 5. This goal of this blinded interim analysis was to assess the assumption of a common standard deviation (SD) of 170. This was to be based on the "quick and simple" procedure described by the Kieser and Friede paper[10]. The procedure was designed to assess a blinded sample with subjects randomized 1:1 to two

treatment-arms, however the blinded 402-C-327 data contained subjects from three different treatment-arms. Based on this revelation, it was concluded that the procedure described by Kieser and Friede would yield an inaccurate estimate of the common standard deviation (SD).

A blinded interim analysis was conducted after 66 subjects had completed their assessments through Day 5. This analysis did not utilize the blinded 402-C-327 data or the procedure described by Kieser and Friede. Instead, this blinded interim analysis focused on the original assumptions linking the 402-C-323 results to the 402-C-327 sample size calculation. Consideration had not been previously given to the differences in statistical analysis methods between 402-C-323 and 402-C-327. There were three key differences identified in the blinded interim analysis, they were:

- In the ANOVA model, 402-C-323 used the baseline pain intensity score as the covariate while 402-C-327 considered age, weight, and height as covariates.
- The 402-C-323 pain intensity score AUC from 0-72 hours was assumed to be the same as the observed 402-C-327 pain intensity score AUC from 0-48 hours.
- The 402-C-323 study addressed missing pain intensity score data using a single imputation technique while 402-C-327 addresses missing pain intensity score data using a multiple imputation technique.

When the 402-C-323 data was reanalyzed using the 402-C-327 statistical analysis methods, the common standard deviation (SD) was found to be approximately 97 and a 46.6-unit treatment difference in 0-48 hour AUC of Pain Intensity scores was identified. The sample size re-estimation was based on these updated assumptions for a common standard deviation (SD) and treatment difference..

9.11. Significance Testing

See section 9.1.2.

10. SAMPLE SIZE CALCULATIONS

The sample size was calculated based on efficacy as measured by the AUC of Pain Intensity scores through 48 hours from a previously conducted nerve block study using the 402-C-327 primary analysis methods. Assuming a 2-sided 0.05 alpha and a common standard deviation (SD) of 97, a sample size of 69 subjects per treatment group should have approximately 80% power to detect a 46.6-unit treatment difference. Approximately 156 subjects are planned for enrollment into this study in order to have at least 138 evaluable subjects between the EXPAREL 133 mg and placebo treatment groups.

11. REFERENCES

[1] American Statistical Association. Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, 07 August 1999. http://www.amstat.org/profession/ethicalstatistics.html

[2] US Federal Register. International Conference on Harmonisation; Guidance on Statistical Principles for Clinical Trials. Department of Health and Human Services: Food and Drug Administration [Docket No. 97D-0174]. Federal Register Volume 63, Number 179, pages 49583-49598. 16 September 1998.

[3] Royal Statistical Society. The Royal Statistical Society: Code of Conduct, August 1993. http://www.rss.org.uk/about/conduct.html.

[4] Rubin, D. B. (1987). Multiple Imputation for Nonresponse in Surveys. New York: John Wiley & Sons.

[5] The National Academies Press. The Prevention and Treatment of Missing Data in Clinical Trials, prepared by the Panel on Handling Missing Data in Clinical Trials and Committee on National Statistics, 2010.

[6] Schafer, J. L. (1997). Analysis of Incomplete Multivariate Data. New York: Chapman & Hall.

7 Rubin DB, Schenker N. Multiple imputation for interval estimation from simple random samples with ignorable nonresponse. J Am Stat Assoc 1986;81:366-374.

[8] Newcombe RG, Interval Estimation for the Difference between Independent Proportions: Comparison of Eleven Methods. Statist. Med. 17, 873-890 (1998).

[9]M Keiser, T Friede. Simple procedures for blinded sample size adjustment that do not affect the type I error rate. Statistics in Medicine. 2003;22:3571-3581.

12. TIME AND EVENTS SCHEDULE OF STUDY PROCEDURES

Please see the Protocol for the full "Time and Events Schedule of Study Procedures". Note that the study days defined in the table and footnotes start with surgery as Day 0; however, the SAP definitions start with surgery as Day 1. The SAP follows the CDISC convention to define study day. Thus in the SAP preop Day 0 is Day 1, Day 7 is Day 8, Day 10 is Day 11 and Day 29 is Day 30.

13. MULTIPLE IMPUTATION EXAMPLE PROGRAM CODE

```
** Note: INPUT_DATA is the dataset that contains the VAS data with the wWOCF imputation performed
**;

** Step 1 use Markov-Chain Monte-Carlo (MCMC) method **;
** Note the value for the random seed is fixed to be 123 so that the results are reproducible **;
proc mi data= INPUT_DATA seed=123 nimpute=10 out= OUTPUT_STEP1 minimum=0 maximum=10;
      by TRT01P;
      mcmc impute=monotone nbiter=2000 niter=1000;
      var aval atptn;
run; quit;

*** Step 2 derive endpoint using appropriate techniques  from INPUT_DATA to create INPUT_DATA2
          **;

*** Step 3 analyze imputations                                                    **;
DATA &a;
          set INPUT_DATA2;
          if param = &select and efffl = 'Y' and trt01pn ne 2;
run; quit;
proc sort data=&a; by _IMPUTATION_; run; quit;

PROC MIXED DATA= &a METHOD=TYPE3;
          by _IMPUTATION_;
          class TRT01P;
          model AVAL = TRT01P AGE WEIGHT HEIGHT;
          lsmeans TRT01P/ diff= CONTROL('Placebo')  CL ;
          ods output LSMeans  = &b;
          ods output diffs    = &c;
run; quit;

proc sort data= &b; by TRT01P; run;
PROC MIANALYZE DATA=&b ALPHA=0.05 THETA0=0;
          by TRT01P;
          modeleffects ESTIMATE;
          stderr STDERR;
          ods output PARAMETERESTIMATES=&d;
run; quit;

** Step 4 build report                                                          **;
```

LAYOUT OF TABLES, LISTINGS AND FIGURES

The following are planned summary tables. Tables will be numbered according to the nomenclature used to support the CSR. The final table numbering may be different from the SAP. No amendment will be made for changes in table numbering. All headers, titles, footnotes, and footers specified in the table templates will be displayed in the produced output unless otherwise specified. Notes to programmers will not be included in the tables.

Tables and listings will have 10 point font size. Listings font size may be reduced to 9 point if needed. The TLFs will have either Times New Roman, Courier New or SAS Monospace type face. All final TLFs will be provided in both PDF and Word (or RTF) file formats.

Percentages should not appear if the count is zero.

Italicized text in the TLF mock-ups indicate notes to programmers and is not to appear on any TLF.

Note headers and footers on mock-ups are reflective of the SAP document and are not intended to appear on the TLFs.

Titles on the TLFs in the mock-ups are presented left-justified as a single line of text. However, the presentation for final TFLs should be center-justified with the TLF number on one line and the remaining titles on multiple lines of text where the line breaks are delimited by hyphens (-) in the TLF mock-ups titles. For example, for Table 14.2-1.1.1 the title in the mock-up appears as:

```
Table 14.2-1.1.1: Analysis of AUC of VAS Pain Intensity Scores through 48
hours - Efficacy Analysis Set - Multiple Imputation Results
```

but should appear as follows on the final TLF:

```
                        Table 14.2-1.1.1
Analysis of AUC of VAS Pain Intensity Scores through 48 hours
                      Efficacy Analysis Set
                   Multiple Imputation Results
```

The title format in the mock-ups is due to limitations of MSWord. The mock-up format enables MSWord to generate a table of contents for the mock-ups.

On all listings the treatments, in order of appearance, are: EXPAREL 133 mg, EXPAREL 266 mg, PLACEBO and, if applicable, NOT RANDOMIZED. Always insert a page break between treatments.

Sort all listings within treatment by site, subject with further sorts dependent on listing.

Table and listing shells follow.

For categorical variables, i*f subjects are missing data for a certain category (example Race), a missing subcategory should be added under the respective category.*

14. TABLE OF CONTENTS FOR TABLE MOCK-UPS

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Table 14.1-1: Summary of Subject Disposition – All Screened Subjects

Site: Overall	EXPAREL				
	133 mg n (%)	266 mg n (%)	All EXPAREL n (%)	Placebo n (%)	Total n (%)
Screened [1]					xx
Screen Failure [1]					xx (xx.x)
Enrolled [1]					xx (xx.x)
Randomized	xx	xx	xx	xx	xx
Not Treated	xx	xx	xx	xx	xx
Treated	xx	xx	xx	xx	xx
Safety Analysis Set [2]#	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Efficacy Analysis Set [3]@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Per-Protocol Analysis Set [4]@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Protocol					
Enrolled under Amendment 2 [2]#	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Enrolled under Amendment 1 [2]#	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Enrolled under Original Protocol [2]#	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Study@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Discontinued from Study@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reasons for Discontinuation@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Adverse Event@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lack of Efficacy@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to Follow-up@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal by Subject@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other@	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

= as treated; @ = as randomized;
[1] Signed the informed consent form; [2] Received study drug; [3] Received study drug and surgery;
[4] All subjects in the efficacy analysis set who do not have any important protocol deviations;
Percentages for screen failure and enrolled based on number screened; others on number randomized.
Subjects randomized to EXPAREL but treated with placebo: *list subjects;*
Subjects randomized to placebo but treated with EXPAREL: *list subjects;*

Source: *list SAS datasets used to create table* *DDMONYYYYTHH:MM*
SAS X.Y *program_name*
Note to programmer: *First page will present overall sites; subsequent pages will present each site – one site per page. For reasons for discontinuation only those reasons that appear in the data will appear on the table. For individual sites the label should be the site number. For the footnotes "Subjects randomized to … treated with..." if no subjects were mistreated, then omit footnote.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Table 14.1-2.1.1: Summary of Subject Demographics - Safety Analysis Set

Site: Overall	Statistic	EXPAREL 133 mg [N=XX]	EXPAREL 266 mg [N=XX]	EXPAREL All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XX]
Age (yrs)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
Sex						
Female	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Male	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ethnicity						
Hispanic or Latino	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Hispanic or Latino	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race						
American Indian/Alaska Native	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black/African American	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Asian	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
White	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Native Hawaiian/Pacific Islander	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Country						
Belgium	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Denmark	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
USA	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Dominant Hand						
Left	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Right	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name
Note to programmer: *First page will present overall sites; subsequent pages will present each site – one site per page. Only categories available in the data will appear on the table. For individual sites the label should be the site number. If subjects are missing data for a category (example Race), a missing subcategory should be added under the respective category. Use this template also for table:*

Table 14.1-2.1.2: Subject Demographics – Efficacy Analysis Set
Table 14.1-2.1.3: Subject Demographics – Per-protocol Analysis Set

Pacira Pharmaceuticals (Page 1 of 4) Protocol: 402-C-327
Table 14.1-2.2.1: Summary of Subject Baseline Characteristics - Safety Analysis Set

Site: Overall		EXPAREL				
	Statistic	133 mg [N=XX]	266 mg [N=XX]	All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XX]
Neurological Assessments						
Subject oriented						
Yes	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
No	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Numb lips, tongue, mouth						
Yes	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
No	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Metallic taste						
Yes	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
No	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Problems hearing						
Yes	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
No	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Problems with vision						
Yes	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
No	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Muscle twitch						
Yes	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
No	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
ECG						
Normal	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Abnormal, NCS	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Abnormal, CS	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

NCS = Not clinically significant CS = Clinically significant
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *If subjects are missing data for a category (example Race), a missing subcategory should be added under the respective category.*

Pacira Pharmaceuticals (Page 2 of 4) Protocol: 402-C-327
Table 14.1-2.2.1: Summary of Subject Baseline Characteristics - Safety Analysis Set

Site: Overall		EXPAREL				
	Statistic	133 mg [N=XX]	266 mg [N=XX]	All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XX]
Motor Assessments						
Thumb Abduction	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
Thumb Adduction	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
Thumb Opposition	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
Elbow Flexion	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Pacira Pharmaceuticals (Page 3 of 4) Protocol: 402-C-327

Table 14.1-2.2.1: Summary of Subject Baseline Characteristics - Safety Analysis Set

Site: Overall	Statistic	EXPAREL 133 mg [N=XX]	EXPAREL 266 mg [N=XX]	EXPAREL All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XX]
VAS Score (cm)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
ASA Classification						
1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
≥ 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Height(cm)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
Weight (kg)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Pacira Pharmaceuticals (Page 4 of 4) Protocol: 402-C-327
Table 14.1-2.2.1: Summary of Subject Baseline Characteristics - Safety Analysis Set

Site: Overall	Statistic	EXPAREL 133 mg [N=XX]	EXPAREL 266 mg [N=XX]	EXPAREL All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XX]
Body Mass Index (kg/m^2)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
Heart Rate (bpm)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
Systolic Blood Pressure (mmHg)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
Diastolic Blood Pressure (mmHg)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *First page will present overall sites; subsequent pages will present each site – one site per page. For individual sites the label should be the site number. Use this template also for table:*

Table 14.1-2.2.2: Subject Baseline Characteristics – Efficacy Analysis Set
Table 14.1-2.2.3: Subject Baseline Characteristics – Per-protocol Analysis Set

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Table 14.1-3.1: Summary of Surgery Characteristics - Safety Analysis Set

Site: Overall		EXPAREL				
Characteristic	Statistic	133 mg [N=XX]	266 mg [N=XX]	All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XX]
Surgery Type						
Rotator Cuff Repair	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Total Shoulder Arthroplasty	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Conventional	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Reverse	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Nerve Block Type						
Interscalene	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Supraclavicular	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Duration of Surgery (hours)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	xx	xx	xx	xx	xx
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx
Total Incision Length (cm)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	xx	xx	xx	xx	xx
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *First page will present overall sites; subsequent pages will present each site – one site per page. For individual sites the label should be the site number. Use this template also for tables:*

Table 14.1-3.2: Summary of Surgery Characteristics (hours) – Efficacy Analysis Set
Table 14.1-3.3: Summary of Surgery Characteristics (hours) – Per-protocol Analysis Set

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.1-4.1: Tabulation of Incidence of Intraoperative Medications - Safety Analysis Set

Anatomical Therapeutic Class (ATC) Preferred Name	EXPAREL 133 mg [N=XX] n (%)	EXPAREL 266 mg [N=XX] n (%)	EXPAREL All EXPAREL [N=XX] n (%)	Placebo [N=XX] n (%)	Total [N=XX] n (%)
Subjects taking at least one medication	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
ATC1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PN1.1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PN1.2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
ATC2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PN2.1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PN2.2	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)	xx (xx.x)
ETC.					

Medications are coded using World Health Organization Drug Dictionary (WHO-DD) March 2015.
Sorted by descending total incidence by ATC for Total column. Subjects using the same intraoperative medication (PT) more than once or multiple medications within an ATC class are counted only once at each ATC summary level.
Intraoperatives medications are those indicated as such by the investigator.
Subjects using the same prior medication more than once are counted only once at each summary level.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *First page will present overall sites; subsequent pages will present each site – one site per page. For individual sites the label should be the site number. Use this template also for tables:*

Table 14.1-4.2: Tabulation of Incidence of Intraoperative Medications - Efficacy Analysis Set
Table 14.1-4.3: Tabulation of Incidence of Intraoperative Medications – Per-Protocol Analysis Set

Note to programmer: *For the following region summaries, 'Site:' will be replaced with 'Region:'. Regions, in order of appearance, are US and ROW. There will be no overall region summary presented on these tables.*

Use template 14.1-1 for table:

Table 14.1-5.1: Summary of Subject Disposition – By Region – All Screened Subjects

Use template 14.1-2.1.1 for tables:

Table 14.1-5.2.1.1: Summary of Subject Demographics – By Region - Safety Analysis Set
Table 14.1-5.2.1.2: Summary of Subject Demographics – By Region – Efficacy Analysis Set
Table 14.1-5.2.1.3: Summary of Subject Demographics – By Region – Per-protocol Analysis Set

Use template 14.1-2.2.1 for tables:

Table 14.1-5.2.2.1: Summary of Summary of Subject Baseline Characteristics – By Region - Safety Analysis Set
Table 14.1-5.2.2.2: Summary of Subject Baseline Characteristics – By Region – Efficacy Analysis Set
Table 14.1-5.2.2.3: Summary of Subject Baseline Characteristics – By Region – Per-protocol Analysis Set

Use template 14.1-3.1 for tables:

Table 14.1-5.3.1: Summary of Surgery Characteristics – By Region - Safety Analysis Set
Table 14.1-5.3.2: Summary of Surgery Characteristics – By Region – Efficacy Analysis Set
Table 14.1-5.3.3: Summary of Surgery Characteristics – By Region – Per-protocol Analysis Set

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.2-1.1.1: Analysis of AUC of VAS Pain Intensity Scores through 48 hours – Efficacy Analysis Set – Multiple Imputation Results

Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
N	xx	xx
Mean	xxx.x	xxx.x
SD	xxx.xx	xxx.xx
Median	xxx.x	xxx.x
Minimum	xx	xx
Maximum	xxx	xxx
LS Mean [1]	xxx.x	xxx.x
Standard Error of LS Mean [1]	xxx.xx	xxx.xx
LS Treatment Difference [1][2]	xx.x	
Treatment Difference 95% Confidence Interval [1][2]	(xx.x, xx.x)	
Treatment Difference p-value [1][2]	0.xxx	

AUC = area under the curve calculated using the trapezoidal method; LS = least squares;
VAS = 10 cm visual analog scale for pain, where 0 = no pain and 10 = worst possible pain;
[1] From an ANOVA with age, weight, and height as covariates.
[2] Treatment difference is EXPAREL – placebo.

Source: *list SAS datasets used to create table* *DDMONYYYYTHH:MM*
SAS *X.Y* *program_name*

Note to programmer: *The raw SAS outputs from the procedures used to produce ALL 14.2-1.1.* & 14.2-1.2 series tables should be saved as a possible appendix to the clinical study report (CSR)..*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.2-1.1.2: Summary of AUC of VAS Pain Intensity Scores through 48 hours by Site and Surgery – Efficacy Analysis Set - Multiple Imputation Results

Site	Surgery	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
XXX	All	n	xx	xx
		Mean	xx.x	xx.x
		SD	x.xx	x.xx
		Minimum	xx	xx
		Median	xx.x	xx.x
		Maximum	xx	xx
	RCR	n	xx	xx
		Mean	xx.x	xx.x
		SD	x.xx	x.xx
		Minimum	xx	xx
		Median	xx.x	xx.x
		Maximum	xx	xx
	TSA-All	n	xx	xx
		Mean	xx.x	xx.x
		SD	x.xx	x.xx
		Minimum	xx	xx
		Median	xx.x	xx.x
		Maximum	xx	xx
	TSA-Conventional	n	xx	xx
		Mean	xx.x	xx.x
		SD	x.xx	x.xx
		Minimum	xx	xx
		Median	xx.x	xx.x
		Maximum	xx	xx
	TSA-Reverse	n	xx	xx
		Mean	xx.x	xx.x
		SD	x.xx	x.xx
		Minimum	xx	xx

Site	Surgery	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
		Median	xx.x	xx.x
		Maximum	xx	xx

RCR = Rotator Cuff Repair; TSA = Total Shoulder Arthoplasty;
AUC = area under the curve calculated using the trapezoidal method;
VAS = 10 cm visual analog scale for pain, where 0 = no pain and 10 = worst possible pain;

Source: *list SAS datasets used to create table* *DDMONYYYYTHH:MM*
SAS *X.Y* *program_name*

Note to programmer: *Present for each site by surgery (All, RCR, TSA-ALL, TSA-Conventional, TSA-Reverse). For pooled sites, present the pooled site first and then each site contributing to the pool immediately after. Do not split a site's/surgery statistics across pages.*

Note to programmer: *The raw SAS outputs from the procedures used to produce ALL 14.2-1.1.* series tables should be saved as a possible appendix to the clinical study report (CSR).*

Note to programmer: *Use the mock-ups indicated to for following tables:*

Mock-up 14.2-1.1.1:

Table 14.2-1.2.1: Analysis of AUC of VAS Pain Intensity Scores through 48 hours – Per-protocol Analysis Set - Multiple Imputation Results

Mock-up 14.2-1.1.2:

Table 14.2-1.2.2: Summary of AUC of VAS Pain Intensity Scores through 48 hours by Site and Surgery – Per-protocol Analysis Set - Multiple Imputation Results

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.2-2.1.1: Analysis of Postsurgical Total Opioid Consumption (MED mg) through 48 hours – Efficacy Analysis Set

Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
N	xx	xx
Geometric Mean	xxx.x	xxx.x
%CV	xxx.xx	xxx.xx
Minimum	xx	xx
Maximum	xxx	xxx
LS Mean [1]	xxx.x	xxx.x
Standard Error of LS Mean [1]	xxx.xx	xxx.xx
LS Treatment Ratio [1][2]	xx.x	
Treatment Ratio 95% Confidence Interval [1][2]	(xx.x, xx.x)	
Treatment Ratio p-value [1][2]	0.xxx	

[1] From an ANOVA with age, weight, and height as covariates on log-transformed total opioid consumption. Subjects without any opioid use are set to 0.1 or half of the smallest total amount observed in the study, whichever is smaller, prior to being transformed with the natural logarithm. Results are back-transformed.
[2] Treatment ratio is EXPAREL / placebo.

Source: *list SAS datasets used to create table* *DDMONYYYYTHH:MM*
SAS X.Y *program_name*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.2-2.1.2: Summary of Total Opioid Consumption (MED mg) through 48 hours by Site and Surgery - Efficacy Analysis Set

Site	Surgery	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
XXX	All	n	xx	xx
		Geometric Mean	xx.x	xx.x
		%CV	x.xx	x.xx
		Minimum	xx	xx
		Maximum	xx	xx
	RCR	n	xx	xx
		Geometric Mean	xx.x	xx.x
		%CV	x.xx	x.xx
		Minimum	xx	xx
		Maximum	xx	xx
	TSA-All	n	xx	xx
		Geometric Mean	xx.x	xx.x
		%CV	x.xx	x.xx
		Minimum	xx	xx
		Maximum	xx	xx
	TSA-Conventional	n	xx	xx
		Geometric Mean	xx.x	xx.x
		%CV	x.xx	x.xx
		Minimum	xx	xx
		Maximum	xx	xx
	TSA-Reverse	n	xx	xx
		Geometric Mean	xx.x	xx.x
		%CV	x.xx	x.xx
		Minimum	xx	xx
		Maximum	xx	xx

RCR = Rotator Cuff Repair; TSA = Total Shoulder Arthoplasty;

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM

SAS X.Y program_name

Note to programmer: *Present for each site by surgery (All, RCR, TSA-ALL, TSA-Conventional, TSA-Reverse). For pooled sites, present the pooled site first and then each site contributing to the pool immediately after. Do not split a site's/surgery statistics across pages.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.2-2.1.3: Analysis of Total Opioid Consumption (MED mg) by Time Period - Efficacy Analysis Set

Time Period	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
0-24 hrs	N	xx	xx
	Geometric Mean	xxx.x	xxx.x
	%CV	xxx.xx	xxx.xx
	Minimum	xx	xx
	Maximum	xxx	xxx
	LS Mean [1]	xxx.x	xxx.x
	Standard Error of LS Mean [1]	xxx.xx	xxx.xx
	LS Treatment Ratio [1][2]	xx.x	xx.x
	Treatment Ratio 95% Confidence Interval [1][2]	(xx.x, xx.x)	
	Treatment Ratio p-value [1][2]	0.xxx	
0-72 hrs	N	xx	xx
	Geometric Mean	xxx.x	xxx.x
	%CV	xxx.xx	xxx.xx
	Minimum	xx	xx
	Maximum	xxx	xxx
	LS Mean [1]	xxx.x	xxx.x
	Standard Error of LS Mean [1]	xxx.xx	xxx.xx
	LS Treatment Ratio [1][2]	xx.x	xx.x
	Treatment Ratio 95% Confidence Interval [1][2]	(xx.x, xx.x)	
	Treatment Ratio p-value [1][2]	xxx.x	

[1] From an ANOVA with age, weight, and height as covariates on log-transformed total opioid consumption.
Subjects without any opioid use are set to 0.1 or half of the smallest total amount observed in the study, whichever is smaller, prior to being transformed with the natural logarithm. Results are back-transformed.
[2] Treatment ratio is EXPAREL / placebo.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Present overall sites and for each site. Time periods to appear on this table, in order, are 0-24, 0-72, 24-48 and 48-72. Do not split a time period statistics across pages.*

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Table 14.2-2.1.4: Summary of the Number of Times Opioid (Rescue) Medication was used by Subject - Efficacy Analysis Set

	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
Count Summary	n	xx	xx
	Mean	xx.x	xx.x
	SD	x.xx	x.xx
	Minimum	xx.x	xx.x
	Median	xx	xx
	Maximum	xx	xx
Count Distribution			
0	n (%)	xx (xx.x)	xx (xx.x)
1	n (%)	xx (xx.x)	xx (xx.x)
2	n (%)	xx (xx.x)	xx (xx.x)
3	n (%)	xx (xx.x)	xx (xx.x)
4	n (%)	xx (xx.x)	xx (xx.x)
5	n (%)	xx (xx.x)	xx (xx.x)
…	n (%)	xx (xx.x)	xx (xx.x)
U	n (%)	xx (xx.x)	xx (xx.x)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Present overall sites and for each site. Distribution should present all counts up to the highest number of times for opioid rescue in the data (U) on each page.*

Note to programmer: *Use the mock-ups indicated to for following tables:*

Mock-up 14.2.1.1:

Table 14.2-2.2.1: Analysis of Postsurgical Total Opioid Consumption (MED mg) through 48 hours – Per-protocol Analysis Set

Mock-up 14.2.1.2:

Table 14.2-2.2.2: Summary of Total Opioid Consumption (MED mg) through 48 hours by Site and Surgery - Per-protocol Analysis

Mock-up 14.2.1.3:

Table 14.2-2.2.3: Analysis of Total Opioid Consumption (MED mg) by Time Period - Per-protocol Analysis Set

Mock-up 14.2.1.4:

Table 14.2-2.2.4: Summary of the Number of Times Opioid (Rescue) Medication was used by Subject - Per-protocol Analysis Set

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Table 14.2-3.1.1: Analysis of Opioid-Free Subjects through 48 hours - Efficacy Analysis Set

	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
No Opioid Use	n (%)	xx (xx.x)	xx (xx.x)
Opioid Used	n (%)	xx (xx.x)	xx (xx.x)
	Treatment Difference [1]	xx.x	
	95% CI for Difference [1]	(xx.x, xx.x)	
	p-value [2]	0.xxxx	

[1] Treatment difference (EXPAREL – placebo) and confidence intervals (CI) are based on the normal approximation to the binomial distribution using SAS PROC FREQ with RISKDIFFC option.
[2] From Cochran-Mantel-Haenszel (CMH) test.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

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Table 14.2-3.1.2: Summary of Opioid-Free Subjects through 48 hours by Site and Surgery - Efficacy Analysis Set

Site	Surgery	Opioid Use	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
XXX	All	No Opioid Use	n (%)	xx (xx.x)	xx (xx.x)
		Opioid Used	n (%)	xx (xx.x)	xx (xx.x)
	RCR	No Opioid Use	n (%)	xx (xx.x)	xx (xx.x)
		Opioid Used	n (%)	xx (xx.x)	xx (xx.x)
	TSA-All	No Opioid Use	n (%)	xx (xx.x)	xx (xx.x)
		Opioid Used	n (%)	xx (xx.x)	xx (xx.x)
	TSA-Conventional	No Opioid Use	n (%)	xx (xx.x)	xx (xx.x)
		Opioid Used	n (%)	xx (xx.x)	xx (xx.x)
	TSA-Reverse	No Opioid Use	n (%)	xx (xx.x)	xx (xx.x)
		Opioid Used	n (%)	xx (xx.x)	xx (xx.x)

RCR = Rotator Cuff Repair; TSA = Total Shoulder Arthoplasty;
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Present for each site on a separate page. For pooled sites, present the pooled site first and then each site contributing to the pool immediately after.*

Note to programmer: *Use the mock-ups indicated to for following tables:*

Mock-up 14.2-3.1.1:

Table 14.2-3.2.1: Analysis of Opioid-Free Subjects through 48 hours - Per-protocol Analysis Set

Mock-up 14.2-3.1.2:

Table 14.2-3.2.2: Summary of Opioid-Free Subjects through 48 hours by Site and Surgery - Per-protocol Analysis Set

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Table 14.2-4.1: Analysis of Time to First Rescue Medication Use (hours) - Efficacy Analysis Set

	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
Number of Subjects on			
Rescue Medication (Opioid)	n (%)	xx (xx.x)	xx (xx.x)
No Rescue Medication (censored)	n (%)	xx (xx.x)	xx (xx.x)
Time to First Rescue			
Quartiles [1]			
First (25% rescued)	Estimate	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Median (50% rescued)	Estimate	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Third (75% rescued)	Estimate	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Minimum	Observed	xx.xx	xx.xx
Maximum	Observed	xx.xx*	xx.xx
p-value [2]		0.xxxx	

* indicates censored observation CI = confidence interval
[1] Estimates from Kaplan-Meier analysis.
[2] p-value from Log-Rank test comparing EXPAREL to placebo.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Use this mock-ups indicated to for following table:*

Table 14.2-4.2: Analysis of Time to First Rescue Medication Use (hours) – Per-protocol Analysis Set

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Table 14.2-5.1: Analysis of VAS AUC at Various Time Intervals - Efficacy Analysis Set

Parameter	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
AUC(0-24)	n	xx	xx
	Mean	xx.x	xx.x
	SD	x.xx	x.xx
	Minimum	xx	xx
	Median	xx.x	xx.x
	Maximum	xx	xx
	LS Mean [1]	xxx.x	xxx.x
	Standard Error of LS Mean [1]	xxx.xx	xxx.xx
	LS Treatment Difference [1][2]	xx.x	
	Treatment Difference 95% Confidence Interval [1][2]	(xx.x, xx.x)	
	Treatment Difference p-value [1][2]	0.xxx	
Etc.	n	xx	xx
	Mean	xx.x	xx.x
	SD	x.xx	x.xx
	Minimum	xx	xx
	Median	xx.x	xx.x
	Maximum	xx	xx
	LS Mean [1]	xxx.x	xxx.x
	Standard Error of LS Mean [1]	xxx.xx	xxx.xx
	LS Treatment Difference [1][2]	xx.x	
	Treatment Difference 95% Confidence Interval [1][2]	(xx.x, xx.x)	
	Treatment Difference p-value [1][2]	0.xxx	

AUC = area under the curve calculated using the trapezoidal method; LS = least squares;
VAS = 10 cm visual analog scale for pain, where 0 = no pain and 10 = worst possible pain;
[1] From an ANOVA with age, weight, and height as covariates.
[2] Treatment difference is EXPAREL – placebo.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *VAS AUCs to be presented on this table are, in order, AUC(0-12), AUC(0-24), AUC(0-72), AUC(24-48), and AUC(48-72). Do not break an AUC's statistics across pages.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Table 14.2-5.2: Summary of VAS at Assessment Timepoints - Efficacy Analysis Set

Timepoint	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
Baseline	n	xx	xx
	Mean	xx.x	xx.x
	SD	x.xx	x.xx
	Minimum	xx	xx
	Median	xx.x	xx.x
	Maximum	xx	xx
PACU	n	xx	xx
	Mean	xx.x	xx.x
	SD	x.xx	x.xx
	Minimum	xx	xx
	Median	xx.x	xx.x
	Maximum	xx	xx
Etc.	n	xx	xx
	Mean	xx.x	xx.x
	SD	x.xx	x.xx
	Minimum	xx	xx
	Median	xx.x	xx.x
	Maximum	xx	xx

PACU is Post Anesthesia Care Unit
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Timepoints to appear on this table are, in order, Baseline, PACU, and 6, 12, 24, 36, 48, 60, and 72 hours.*

Note to programmer: *Use the indicated mock-up for the following tables:*

Use mock-up 14.2-5.1:

Table 14.2-5.3: Analysis of VAS SPIS at Various Time Intervals - Efficacy Analysis Set

VAS SPIS to be presented on Table 14.2-5.3 are, in order, SPIS(0-12), SPIS(0-24), SPIS(0-48), SPIS(24-48), SPIS(48-72), and SPIS(0-72). Do not break an SPIS's statistics across pages.

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Table 14.2-6: Analysis of Pain-free Subjects at Assessment Timepoints - Efficacy Analysis Set

Timepoint	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
Baseline			
Pain-Free	n (%)	xx (xx.x)	xx (xx.x)
Pained	n (%)	xx (xx.x)	xx (xx.x)
	Treatment Difference [1]	xx.x	
	95% CI for Difference [1]	(xx.x, xx.x)	
	p-value [2]	0.xxxx	
Etc.			
Pain-Free	n (%)	xx (xx.x)	xx (xx.x)
Pained	n (%)	xx (xx.x)	xx (xx.x)
	Treatment Difference [1]	xx.x	
	95% CI for Difference [1]	(xx.x, xx.x)	
	p-value [2]	0.xxxx	

[1] Pain-Free Treatment difference (EXPAREL – placebo) and confidence intervals (CI) are based on the normal approximation to the binomial distribution using SAS PROC FREQ with RISKDIFFC option.
[2] From Cochran-Mantel-Haenszel (CMH) test.
Pain-free = VAS score ≤ 1.5 and no prior rescue medication use and all prior VAS scores ≤ 1.5.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Timepoints to appear on this table are, in order, Baseline, PACU and 6, 12, 24, 36, 48, 60, and 72 hours. Do not split a timepoint across pages.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Table 14.2-7: Analysis of Opioid-Free Subjects through 24 and 72 hours - Efficacy Analysis Set

Time Interval Opioid Use	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
0-24			
Yes	n (%)	xx (xx.x)	xx (xx.x)
No	n (%)	xx (xx.x)	xx (xx.x)
	Treatment Difference [1]	xx.x	
	95% CI for Difference [1]	(xx.x, xx.x)	
	p-value [2]	0.xxxx	
0-72			
Yes	n (%)	xx (xx.x)	xx (xx.x)
No	n (%)	xx (xx.x)	xx (xx.x)
	Treatment Difference [1]	xx.x	
	95% CI for Difference [1]	(xx.x, xx.x)	
	p-value [2]	0.xxxx	

[1] Opioid-Free Treatment difference (EXPAREL – placebo) and confidence intervals (CI) are based on the normal approximation to the binomial distribution using SAS PROC FREQ with RISKDIFFC option.
[2] From Cochran-Mantel-Haenszel (CMH) test.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Use the indicated mock-up for the following tables:*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.2-8: Analysis of Overall Benefit of Analgesia Total Score by Timepoint and Question - Efficacy Analysis Set

Timepoint / Question		Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
24 hours				
Total Score	Summary	n	xx	xx
		Mean	xx.x	xx.x
		SD	x.xx	x.xx
		Minimum	xx	xx
		Median	xx.x	xx.x
		Maximum	xx	xx
		p-value[1]	0.xxx	
	Score			
	0	n (%)	xx (xx.x)	xx (xx.x)
	1	n (%)	xx (xx.x)	xx (xx.x)
	2	n (%)	xx (xx.x)	xx (xx.x)
	…	n (%)	xx (xx.x)	xx (xx.x)
	…	n (%)	xx (xx.x)	xx (xx.x)
1. Current Pain	Summary	n	xx	xx
		Mean	xx.x	xx.x
		SD	x.xx	x.xx
		Minimum	xx	xx
		Median	xx.x	xx.x
		Maximum	xx	xx
	Score			
	0	n (%)	xx (xx.x)	xx (xx.x)
	1	n (%)	xx (xx.x)	xx (xx.x)
	2	n (%)	xx (xx.x)	xx (xx.x)
	3	n (%)	xx (xx.x)	xx (xx.x)
	4	n (%)	xx (xx.x)	xx (xx.x)

Total score = sum of scores from questions 1 to 6 plus 4 minus question 7 score.
[1] p-value from Kruskal-Wallis test.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Timepoints to appear on this table, in order, are 24 and 72 hours, and Day 10. Questions to appear on this table, in order, are 'Total Score', '1. Current Pain', '2. Vomiting', '3. Itching', '4. Sweating', '5. Freezing', '6. Dizziness', '7. Satisfaction'. Do not split a question's statistics across pages. P-Values should only be generated for 'Total score'.*
Note to programmer: *Use the indicated mock-up for the following tables:*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.2-9: Analysis of Satisfaction with Postsurgical Pain Control Questionnaire Score by Timepoint - Efficacy Analysis Set

Timepoint	Score	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
24 hours	Summary	n	xx	xx
		Mean	xx.x	xx.x
		SD	x.xx	x.xx
		Minimum	xx	xx
		Median	xx.x	xx.x
		Maximum	xx	xx
		p-value[1]	0.xxx	
	Score			
	1: Extremely dissatisfied	n (%)	xx (xx.x)	xx (xx.x)
	2: Dissatisfied	n (%)	xx (xx.x)	xx (xx.x)
	3: Neither satisfied nor dissatisfied	n (%)	xx (xx.x)	xx (xx.x)
	4: Satisfied	n (%)	xx (xx.x)	xx (xx.x)
	5: Extremely Satisfied	n (%)	xx (xx.x)	xx (xx.x)

[1] p-value from the Kruskal-Wallis test.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Timepoints to appear on this table are 24 and 72 hours and Day 10. Do not split timepoint across pages.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Table 14.2-10.1: Analysis of Time to Discharge Ready - Efficacy Analysis Set

Assessment Time Discharge Ready	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
12 hours			
No	n (%)	xxx (xx.x%)	xxx (xx.x%)
Yes	n (%)	xxx (xx.x%)	xxx (xx.x%)
Time to Discharge Ready			
Quartiles [1]			
First (25% Discharge Ready)	Estimate	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Median (50% Discharge Ready)	Estimate	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Third (75% Discharge Ready)	Estimate	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Minimum	Observed	xx.xx	xx.xx
Maximum	Observed	xx.xx*	xx.xx
p-value [2]		0.xxxx	

* indicates censored observation CI = confidence interval
[1] Estimates from Kaplan-Meier analysis.
[2] p-value from Log-rank test comparing EXPAREL to placebo.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Assessments Time to be presented are 12, 24, 36, 48, 60, and 72 hours.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.2-10.2: Summary of Discharge Ready at Assessment - Efficacy Analysis Set

Assessment Time Discharge Ready	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
12 hours			
No	n (%)	xx (xx.x)	xx (xx.x)
Yes	n (%)	xx (xx.x)	xx (xx.x)
24 hours			
No	n (%)	xx (xx.x)	xx (xx.x)
Yes	n (%)	xx (xx.x)	xx (xx.x)
36 hours			
No	n (%)	xx (xx.x)	xx (xx.x)
Yes	n (%)	xx (xx.x)	xx (xx.x)
48 hours			
No	n (%)	xx (xx.x)	xx (xx.x)
Yes	n (%)	xx (xx.x)	xx (xx.x)
60 hours			
No	n (%)	xx (xx.x)	xx (xx.x)
Yes	n (%)	xx (xx.x)	xx (xx.x)
72 hours			
No	n (%)	xx (xx.x)	xx (xx.x)
Yes	n (%)	xx (xx.x)	xx (xx.x)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Do not split timepoint across pages.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Table 14.2-11: Analysis of Number of Unscheduled Phone Calls or Office Visits Related to Pain - Efficacy Analysis Set

	Statistic	EXPAREL 133 mg [N=XX]	Placebo [N=XX]
Count Summary	n	xx	xx
	Mean	xx.x	xx.x
	SD	x.xx	x.xx
	Minimum	xx.x	xx.x
	Median	xx	xx
	Maximum	xx	xx
	p-value[1]	0.xxx	
Count Distribution			
0	n (%)	xx (xx.x)	xx (xx.x)
1	n (%)	xx (xx.x)	xx (xx.x)
2	n (%)	xx (xx.x)	xx (xx.x)
3	n (%)	xx (xx.x)	xx (xx.x)
4	n (%)	xx (xx.x)	xx (xx.x)
5	n (%)	xx (xx.x)	xx (xx.x)
…	n (%)	xx (xx.x)	xx (xx.x)
U	n (%)	xx (xx.x)	xx (xx.x)

[1] p-value from Kruskal-Wallis test.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Distribution should present all counts up to the highest number of unscheduled visits (phone calls + office visits) related to pain in the data (U).*

Note to programmer: *For the following region summaries, 'Site:' will be replaced with 'Region:' in the statistical models, row labels, footnotes and by lines of summaries as appropriate. When summarizing by region, the regions are, in order of appearance, US and ROW. There will be no overall region summary presented on these tables.*

Use template 14.2-1.1.1 for tables:

Table 14.2-12.1.1.1: Region Analysis of AUC of VAS Pain Intensity Scores through 48 hours – Efficacy Analysis Set - Multiple Imputation Results

Table 14.12-1.2.1: Region Analysis of AUC of VAS Pain Intensity Scores through 48 hours – Per-protocol Analysis Set - Multiple Imputation Results

Use template 14.2-2.1.1 for table:

Table 14.2-12.2.1.1: Region Analysis of Postsurgical Total Opioid Consumption (MED mg) through 48 hours – Efficacy Analysis Set

Use template 14.2-2.1.2 for table:

Table 14.2-12.2.1.2: Region Summary of Total Opioid Consumption (MED mg) through 48 hours by Region - Efficacy Analysis Set

Use template 14.2-2.1.3 for table:

Table 14.2-12.2.1.3: Region Summary of Total Opioid Consumption (MED mg) by Time Period - Efficacy Analysis Set

Use template 14.2-2.1.4 for table:

Table 14.2-12.2.1.4: Region Summary of the Number of Times Opioid (Rescue) Medication was used by Subject - Efficacy Analysis Set

Use template 14.2-2.1.1 for table:

Table 14.2-12.2.2.1: Region Analysis of Postsurgical Total Opioid Consumption (MED mg) through 48 hours – Per-protocol Analysis Set

Use template 14.2-2.1.2 for table:

Table 14.2-12.2.2.2: Region Summary of Total Opioid Consumption (MED mg) through 48 hours by Site - Per-protocol Analysis Set

Use template 14.2-2.1.3 for table:

Table 14.2-12.2.2.3: Region Summary of Total Opioid Consumption (MED mg) by Time Period - Per-protocol Analysis Set

Use template 14.2-2.1.4 for table:

Table 14.2-12.2.2.4: Region Summary of the Number of Times Opioid (Rescue) Medication was used by Subject - Per-protocol Analysis Set

Use template 14.2-3.1.1 for table:

Table 14.2-12.3.1.1: Region Analysis of Opioid-Free Subjects through 48 hours - Efficacy Analysis Set

Use template 14.2-3.1.2 for table:

Table 14.2-12.3.1.2: Region Summary of Opioid-Free Subjects through 48 hours by Site - Efficacy Analysis Set

Use template 14.2-3.1.1 for table:

Table 14.2-12.3.2.1: Region Analysis of Opioid-Free Subjects through 48 hours - Per-protocol Analysis Set

Use template 14.2-3.1.2 for table:

Table 14.2-12.3.2.2: Region Summary of Opioid-Free Subjects through 48 hours by Site - Per-protocol Analysis Set

Table 14.3-1.1.1: Summary of Clinical Laboratory Data by Timepoint – Hematology - Safety Analysis Set

Laboratory parameter (units)

			EXPAREL				
Timepoint	Value	Statistic	133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]	Total [N=XXX]
Baseline	Actual	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx
Day 10	Baseline [1]	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx
	Actual	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx
	Change	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx

[1] Baseline (prior to surgery) for subjects with data at the timepoint.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Only present overall sites. Timepoints to appear on this table are, in order of appearance, Baseline (prior to surgery) and Day 10. Do not split timepoint statistics across pages. See*

protocol for list of lab analytes. Analytes should be sorted in alphabetical order. Use this mock-up for the following tables:

Table 14.3-1.1.2: Summary of Clinical Laboratory Data by Timepoint – Chemistry - Safety Analysis Set
Table 14.3-1.1.3.1: Summary of Clinical Laboratory Data by Timepoint – Urinalysis - Safety Analysis Set

For urinalysis results only numeric results will appear on this table.

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Table 14.3-1.1.3.2: Tabulation of Clinical Laboratory Data by Timepoint – Urinalysis - Safety Analysis Set

				EXPAREL				
Analyte	Timepoint	Category	Statistic	133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]	Total [N=XXX]
Analyte 1	Baseline [1]	*Cat 1*	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Cat 2	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Etc.	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Day 10	*Cat 1*	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Cat 2	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Etc.	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Analyte 2	Baseline [1]	*Cat 1*	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Cat 2	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Etc.	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Day 10	*Cat 1*	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Cat 2	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Etc.	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Etc.								

[1] Baseline (prior to surgery) for subjects with data at the timepoint.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM

SAS X.Y program_name

Note to programmer: Only present overall sites. Timepoints to appear on this table are, in order of appearance, Baseline (prior to surgery) and Day 10. Do not split timepoint statistics across pages, if possible. Present all avaliable lab analytes. Categories are the superset of those reported in the data for both timepoints combined. All categories should appear for both timepoints with zeros (0) as counts where needed.

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Table 14.3-1.2.1: Tabulation of Clinical Laboratory Range by Timepoint – Hematology - Safety Analysis Set

Laboratory parameter (units)			EXPAREL				
Timepoint	Normal Range	Statistic	133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]	Total [N=XXX]
Baseline	Below	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Normal	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Above	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Day 10	Below	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Normal	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Above	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Only present overall sites. Timepoints to appear on this table are, in order of appearance, Baseline (prior to surgery)and Day 10. Do not split timepoint statistics across pages. Present all avaliable analytes. Analytes should be sorted in alphabetical order. Use this mock-up for the following tables:*

Table 14.3-1.2.2: Tabulation of Clinical Laboratory Range by Timepoint – Chemistry - Safety Analysis Set
Table 14.3-1.2.3: Tabulation of Clinical Laboratory Range by Timepoint – Urinalysis - Safety Analysis Set

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Table 14.3-1.3.1: Shift Table for Clinical Laboratory Data by Timepoint – Hematology - Safety Analysis Set

		Baseline					
	Normal Range	EXPAREL All EXPAREL [N=XXX]			Placebo [N=XXX]		
Analyte	Day 10	Below	Normal	Above	Below	Normal	Above
Analyte 1	Below	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Above	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Analyte 2	Below	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Above	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Analyte 3	Below	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Above	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ETC.	Below	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Above	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Only present overall sites. Do not split an analyte across pages. EXPAREL 133 mg and EXPAREL 266 mg will appear on separate pages. All analytes for an EXPAREL group (combined, 133 mg, 266 mg) should appear on consecutive pages before starting the next EXPAREL group. Analytes should be sorted in alphabetical order. Use this mock-up for the following tables:*

Table 14.3-1.3.2: Shift Table for Clinical Laboratory Data by Timepoint – Chemistry - Safety Analysis Set
Table 14.3-1.3.3: Shift Table for Clinical Laboratory Data by Timepoint – Urinalysis - Safety Analysis Set

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Table 14.3-2.1: Summary of Vital Signs by Timepoint – Safety Analysis Set

Heart Rate (bpm)

			EXPAREL				
Timepoint	Value	Statistic	133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]	Total [N=XXX]
Baseline	Actual	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx
PACU	Baseline [1]	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx
	Actual	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx
	Change	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx

[1] Baseline (prior to surgery) for subjects with data at the timepoint.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM

SAS X.Y program_name

Note to programmer: *Only present overall sites. Vital signs are 'Heart Rate (bpm)', 'Systolic Blood Pressure (mmHg)' and 'Diastolic Blood Pressure (mmHg)'. Timepoints to appear on this table are, in order of*

appearance, Baseline (prior to surgery), PACU, and 6, 12, 24, 36, 48, 60, and 72 hours, and Days 7 and 10. Do not split timepoint statistics across pages.

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Table 14.3-2.2: Summary of Potentially Clinically Significant Abnormal Vital Signs – Safety Analysis Set

Heart Rate (bpm)		EXPAREL				
		133 mg [N=XX]	266 mg [N=XX]	All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XXX]
Timepoint	Criteria	n (%)	n (%)	n (%)	n (%)	n (%)
Baseline	<= 50	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease >= 15	NA	NA	NA	NA	NA
	<= 50 & Decrease >= 15	NA	NA	NA	NA	NA
	>= 120	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase >= 15	NA	NA	NA	NA	NA
	>= 120 & Increase >= 15	NA	NA	NA	NA	NA
Any Time After Baseline	<= 50	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	<= 50 & Decrease >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 120	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 120 & Increase >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc.	<= 50	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	<= 50 & Decrease >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 120	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 120 & Increase >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

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Table 14.3-2.2: Summary of Potentially Clinically Significant Abnormal Vital Signs – Safety Analysis Set

Systolic Blood Pressure (mmHg)		EXPAREL				
		133 mg [N=XX]	266 mg [N=XX]	All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XXX]
Timepoint	Criteria	n (%)	n (%)	n (%)	n (%)	n (%)
Baseline	<= 90	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease >= 20	NA	NA	NA	NA	NA
	<= 90 & Decrease >= 20	NA	NA	NA	NA	NA
	>= 180	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase >= 20	NA	NA	NA	NA	NA
	>= 180 & Increase >= 20	NA	NA	NA	NA	NA
Any Time After Baseline	<= 90	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease >= 20	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	<= 90 & Decrease >= 20	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 180	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase >= 20	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 180 & Increase >= 20	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc.	<= 90	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease >= 20	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	<= 90 & Decrease >= 20	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 180	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase >= 20	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 180 & Increase >= 20	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.3-2.2: Summary of Potentially Clinically Significant Abnormal Vital Signs – Safety Analysis Set

Diastolic Blood Pressure (mmHg)		EXPAREL				
Timepoint	Criteria	133 mg [N=XX] n (%)	266 mg [N=XX] n (%)	All EXPAREL [N=XX] n (%)	Placebo [N=XX] n (%)	Total [N=XXX] n (%)
Baseline	<= 50	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease >= 15	NA	NA	NA	NA	NA
	<= 50 & Decrease >= 15	NA	NA	NA	NA	NA
	>= 105	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase >= 15	NA	NA	NA	NA	NA
	>= 105 & Increase >= 15	NA	NA	NA	NA	NA
Any Time After Baseline	<= 50	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	<= 50 & Decrease >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 105	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 105 & Increase >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc.	<= 50	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Decrease >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	<= 50 & Decrease >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 105	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Increase >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	>= 105 & Increase >= 15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Only present overall sites. Timepoints to appear on this table are, in order of appearance, Baseline (prior to surgery), Any Time After Baseline, PACU and, 6, 12, 24, 36, 48, 60, and 72 hours and Days 7 and 10. Do not split timepoint statistics across pages.*

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Table 14.3-3.1: Summary of Electrocardiogram Interpretation – Investigator Read - Safety Analysis Set

		EXPAREL				
Time Point	Interpretation	133 mg [N=XX] n (%)	266 mg [N=XX] n (%)	All EXPAREL [N=XX] n (%)	Placebo [N=XX] n (%)	Total [N=XXX] n (%)
Baseline (Prior to Surgery)	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Any Time After Baseline	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
At Tmax*	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	N/A	N/A
	Abnormal, NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	N/A	N/A
	Abnormal, CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	N/A	N/A
Etc.	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

*QuantPharm LLC indicated that the results of the interim PK analysis showed a median Tmax of 48 hours for the 133 mg EXPAREL group and a median Tmax of 60 hours for the 266 mg EXPAREL group. *The 'at Tmax' timepoint is the time nearest in absolute value to the population PK estimated median Tmax.*

NCS = not clinically significant CS = clinically significant

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM

SAS X.Y program_name

Note to programmer: *Only present overall sites. Timepoints to appear on this table are, in order of appearance, Baseline (prior to surgery), At any time after baseline, At Tmax, PACU, and 6, 12, 24, 36, 48, 60, and 72 hours, and Days 7 and 10. Do not split a timepoint across pages. For the timepoint 'any time after baseline' report the worst interpretation reported at any timepoint but baseline. For the 'at Tmax' timepoint, report the interpretation at the time of Tmax for those subjects with Tmax reported and median Tmax for those subjects without Tmax.*

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Table 14.3-3.2: Shift Table for Electrocardiogram Interpretation – Investigator Read - Safety Analysis Set

		Baseline					
		EXPAREL All EXPAREL [N=XXX]			Placebo [N=XXX]		
			Abnormal			Abnormal	
Time Point	Interpretation	Normal	NCS	CS	Normal	NCS	CS
Any Time After Baseline	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
At Tmax*	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	N/A	N/A	N/A
	NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	N/A	N/A	N/A
	CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	N/A	N/A	N/A
Etc.	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

*QuantPharm LLC indicated that the results of the interim PK analysis showed a median Tmax of 48 hours for the 133 mg EXPAREL group and a median Tmax of 60 hours for the 266 mg EXPAREL group. *The 'at Tmax' timepoint is the time nearest in absolute value to the population PK estimated median Tmax.*

NCS = not clinically significant CS = clinically significant

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM

SAS X.Y program_name

Note to programmer: *Only present overall sites. Timepoints to appear on this table are, in order of appearance, Baseline (prior to surgery), At any time after baseline, At Tmax, PACU, and 6, 12, 24, 36, 48, 60, and 72 hours, and Days 7 and 10. Do not split a timepoint across pages. For the timepoint 'any time after baseline' report the worst interpretation reported at any timepoint but baseline. For the 'at Tmax' timepoint, report the interpretation at the time of Tmax for those subjects with Tmax reported and median Tmax for those subjects without Tmax. EXPAREL 133 mg and EXPAREL 266 mg will appear on separate pages. All timepoints for an EXPAREL group (All EXPAREL, 133 mg, 266 mg) should appear on consecutive pages before starting the next EXPAREL group.*

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Table 14.3-4: Summary of Neurological Assessments by Timepoint- Safety Analysis Set

		EXPAREL				
		133 mg [N=XX]	266 mg [N=XX]	All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XXX]
Timepoint Assessment		n (%)	n (%)	n (%)	n (%)	n (%)
Baseline (Prior to Surgery)						
Subject Oriented	No	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Yes	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Numb lips, tongue or mouth	No	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Yes	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Metallic taste	No	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Yes	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Hearing problems	No	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Yes	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Vision problems	No	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Yes	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Muscle twitching	No	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Yes	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Only present overall sites. Timepoints to appear on this table are, in order of appearance, Baseline (prior to surgery), At any time after baseline, PACU and, 6, 12, 24, 36, 48, 60, and 72 hours and Days 7 and 10. Put one timepoint per page. For the timepoint 'any time after baseline' if there is at least one 'yes' at any timepoint other than baseline, the subject will be a 'yes'.*

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Table 14.3-5.1: Tabulation of Sensation Tests – Safety Analysis Set

Location: *location-name*			EXPAREL				
			133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]	Total [N=XXX]
Timepoint	Sensation		n (%)	n (%)	n (%)	n (%)	n (%)
Baseline	Cold	Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Present	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Pinprick	Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Present	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Light Touch	Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Present	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Etc.	Cold	Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Present	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Pinprick	Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Present	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Light Touch	Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Present	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Locations to appear on this table, in order, are 'Shoulder', 'Forearm', '5th finger', 'Middle finger' and 'Thumb'. Timepoints to appear on this table are, in order, are: Baseline, 15, 30 and 45 minutes and 6, 9, 12, 18, 24, 36, 48, 60, and 72 hours. Do not split a timepoint across pages.*

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Table 14.3-5.2: Summary of Sensation Loss and Return by Timepoint – Safety Analysis Set

Location: *location-name*			EXPAREL				
			133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]	Total [N=XXX]
Timepoint	Sensation		n (%)	n (%)	n (%)	n (%)	n (%)
At Any Time	Any	Loss	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Return	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	CPL	Loss	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Return	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	CP	Loss	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Return	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	CL	Loss	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Return	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	PL	Loss	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Return	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Cold (C)	Loss	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Return	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Pinprick (P)	Loss	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Return	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Light Touch (L)	Loss	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Return	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Loss is the absence of sensation Return is the presence of sensation after a loss of sensation
Sensation: CPL = All; CP = cold & pinprick; CL = cold & light touch; PL = pinprick & light touch
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Locations to appear on this table, in order, are 'Shoulder', 'Forearm', '5th finger', 'Middle finger' and 'Thumb'. Timepoints to appear on this table are, in order, are: At Any Time, 15, 30 and 45 minutes, and 6, 9, 12, 18, 24, 36, 48, 60, and 72 hours. For 'at any time' timepoint subjects'*

experiencing a loss/return at any time during the study will be counted only once. For 'any' sensation, subjects' experiencing a loss/return for at least one of the sensation at that timepoint will be counted only once. Do not split a timepoint across pages.

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Table 14.3-5.3.1: Analysis of Time to First Sensation Loss – Safety Analysis Set

Location: *location-name*		EXPAREL			
		133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]
Sensation	Statistic	n (%)	n (%)	n (%)	n (%)
Loss					
Ever	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Never*	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Time to First Loss (hrs)					
Quartiles [1]					
First (25%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Median (50%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Third (75%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Minimum	Observed	xx.xx	xx.xx	xx.xx	xx.xx
Maximum	Observed	xx.xx*	xx.xx*	xx.xx	xx.xx
p-value [2]		0.xxxx	0.xxxx	0.xxxx	

Loss: absence of at least one of cold, pinprick or light touch sensation. * = censored
Time to sensation loss is the time from end of surgery to first loss of sensation.
[1] Estimates from Kaplan-Meier analysis.
[2] p-value from log-rank test comparing EXPAREL to placebo.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Locations to appear on this table, in order, are 'Shoulder', 'Forearm', '5th finger', 'Middle finger' and 'Thumb'.*

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Table 14.3-5.3.2: Analysis of Time to Last Sensation Loss – Safety Analysis Set

Location: *location-name*		EXPAREL			
		133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]
Sensation	Statistic	n (%)	n (%)	n (%)	n (%)
Time to Last Loss (hrs)					
Quartiles [1]					
First (25%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Median (50%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Third (75%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Minimum	Observed	xx.xx	xx.xx	xx.xx	xx.xx
Maximum	Observed	xx.xx*	xx.xx*	xx.xx	xx.xx
p-value [2]		0.xxxx	0.xxxx	0.xxxx	

Loss: absence of at least one of cold, pinprick or light touch sensation. * = censored
Return: all 3 (cold, pinprick and light touch) sensations are present after loss of sensation
Time to sensation return is the time from first sensation loss to first sensation return.
[1] Estimates from Kaplan-Meier analysis.
[2] p-value from log-rank test comparing EXPAREL to placebo.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Locations to appear on this table, in order, are 'Shoulder', 'Forearm', '5th finger', 'Middle finger' and 'Thumb'. If a subject meets the loss criteria at any timepoint, the subject will be counted in 'loss ever' category; otherwise the subject will be counted in 'loss never' category. Note time to last loss will only be provided if more than 10% of the subjects in a treatment arm have more than 1 sensation loss-return cycle.*

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Table 14.3-5.4.1: Analysis of Time to First Sensation Return – Safety Analysis Set

Location: *location-name*		EXPAREL			
		133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]
Sensation	Statistic	n (%)	n (%)	n (%)	n (%)
Loss Ever	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Return					
Ever	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Never*	n (%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Time to First Return (hrs)					
Quartiles [1]					
First (25%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Median (50%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Third (75%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Minimum	Observed	xx.xx	xx.xx	xx.xx	xx.xx
Maximum	Observed	xx.xx*	xx.xx*	xx.xx	xx.xx
p-value [2]		0.xxxx	0.xxxx	0.xxxx	

Loss: absence of at least one of cold, pinprick or light touch sensation. * = censored
Return: all 3 (cold, pinprick and light touch) sensations are present after loss of sensation
Time to sensation return is the time from first sensation loss to first sensation return.
[1] Estimates from Kaplan-Meier analysis.
[2] p-value from log-rank test comparing EXPAREL to placebo.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Locations to appear on this table, in order, are 'Shoulder', 'Forearm', '5th finger', 'Middle finger' and 'Thumb'. This table based on only those subjects who lost sensation (ie, the loss ever row is the population appearing in analyses).*

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Table 14.3-5.4.2: Analysis of Time to Last Sensation Return – Safety Analysis Set

Location: *location-name*		EXPAREL			
		133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]
Sensation	Statistic	n (%)	n (%)	n (%)	n (%)
Time to Last Return (hrs)					
Quartiles [1]					
First (25%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Median (50%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Third (75%)	Estimate	xx.xx	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Minimum	Observed	xx.xx	xx.xx	xx.xx	xx.xx
Maximum	Observed	xx.xx*	xx.xx*	xx.xx	xx.xx
p-value [2]		0.xxxx	0.xxxx	0.xxxx	

Loss: absence of at least one of cold, pinprick or light touch sensation. * = censored
Return: all 3 (cold, pinprick and light touch) sensations are present after loss of sensation
Time to sensation return is the time from first sensation loss to first sensation return.
[1] Estimates from Kaplan-Meier analysis.
[2] p-value from log-rank test with terms for treatment comparing EXPAREL to placebo.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Locations to appear on this table, in order, are 'Shoulder', 'Forearm', '5th finger', 'Middle finger' and 'Thumb'. 'Loss Ever' counts on this table should agree with 'loss ever' counts on Table 14.3-5.1.1. If a subject meets the return criteria at any time, the subject will be counted in 'return ever' category; otherwise the subject will be counted in the 'return never' category. The sum of 'return ever' and 'return never' should add up to 'loss ever'; subjects who did not experience a loss of sensation cannot have a return of sensation. Only subjects experiencing a 'loss ever' will contribute to the body of this table. Note time to last return will only be provided if more than 10% of the subjects in a treatment arm have more than 1 sensation loss-return cycle.*

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Table 14.3-5.5: Summary of Duration (hrs) of Sensation Loss – Safety Analysis Set

Location: *location-name*		EXPAREL			
		133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]
	Statistic	n (%)	n (%)	n (%)	n (%)
Total Duration	n	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx
Cycle 1	n	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx
Etc.	n	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx

Duration is the time between loss and return of sensation.
Total duration is the sum, within a subject, of all sensation loss-return cycles.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Locations to appear on this table, in order, are 'Shoulder', 'Forearm', '5th finger', 'Middle finger' and 'Thumb'. Only subjects experiencing a sensation loss will contribute to the body of this table. Note summaries of cycles will only be provided if more than 10% of the subjects in a treatment arm have more than 1 sensation loss-return cycle.*

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Table 14.3-5.6: Summary of the Number of Sensation Loss-Return Cycles - Safety Analysis Set

Location: *location-name*		EXPAREL			
	Statistic	133 mg [N=XX]	266 mg [N=XX]	All EXPAREL [N=XX]	Placebo [N=XX]
Count Summary	n	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Median	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx
Count Distribution					
0	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
5	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
U	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Locations to appear on this table, in order, are 'Shoulder', 'Forearm', '5th finger', 'Middle finger' and 'Thumb'. Distribution should present all counts up to the highest number of loss-return cycles in the data (U). Only subjects experiencing a sensation loss will contribute to the body of this table. This table will only be provided if at least 1 subject has more than 1 sensation loss-return cycle.*

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Table 14.3-6.1: Summary of Motor Function Loss and Return by Timepoint – Safety Analysis Set

	EXPAREL				
Timepoint	133 mg [N=XXX] n (%)	266 mg [N=XXX] n (%)	All EXPAREL [N=XXX] n (%)	Placebo [N=XXX] n (%)	Total [N=XXX] n (%)
At Any Time					
Loss					
Thumb abduction (radial nerve)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Thumb adduction (ulnar nerve)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Thumb opposition (median nerve)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Elbow flexion (musculocutaneous nerve)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Return					
Elbow flexion (musculocutaneous nerve)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Thumb adduction (ulnar nerve)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Thumb opposition (median nerve)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Elbow flexion (musculocutaneous nerve)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Loss: Lovett scale score < 3 in at least one of the motor function assessments
Return: Lovett scale score returns to 3 or more in any motor function assessment.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Locations to appear on this table, in order, are Thumb abduction (radial nerve), Thumb adduction (ulnar nerve), Thumb opposition (median nerve), and Elbow flexion (musculocutaneous nerve). Timepoints to appear on this table are, in order, are: At Any Time, 15, 30 and 45 minutes and 6, 9, 12, 18, 24, 36, 48, 60, and 72 hours.*

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Table 14.3-6.2: Analysis of Time to Onset of Motor Function Loss - Efficacy Analysis Set

Location: *location-name (nerve name)*	Statistic	EXPAREL 133 mg [N=XX]	EXPAREL 266 mg [N=XX]	Placebo [N=XX]
Number of Subjects with				
Motor Function Loss	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No Motor Function Loss	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Time to Loss				
Quartiles [1]				
First (25%)	Estimate	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Median (50%)	Estimate	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Third (75%)	Estimate	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Minimum	Observed	xx.xx	xx.xx	xx.xx
Maximum	Observed	xx.xx*	xx.xx*	xx.xx
p-value [2]		0.xxxx	0.xxxx	

Locations to appear on this table, in order, are Thumb abduction (radial nerve), Thumb adduction (ulnar nerve), Thumb opposition (median nerve), and Elbow flexion (musculocutaneous nerve).
Loss: Lovett scale score < 3 in at least one of the motor function assessments

* indicates censored observation CI = confidence interval
[1] Estimates from Kaplan-Meier analysis.
[2] p-value from log-rank test comparing EXPAREL to placebo.
Source: *list SAS datasets used to create table* *DDMONYYYYTHH:MM*
SAS X.Y *program_name*

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Table 14.3-6.3: Analysis of Time to Return of Motor Function - Efficacy Analysis Set

Location: *location-name (nerve name)*	Statistic	EXPAREL 133 mg [N=XX]	EXPAREL 266 mg [N=XX]	Placebo [N=XX]
Number of Subjects with				
Motor Function Return	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No Motor Function Return	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Time to Return				
Quartiles [1]				
First (25%)	Estimate	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Median (50%)	Estimate	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Third (75%)	Estimate	xx.xx	xx.xx	xx.xx
	(95% CI)	(xx.xx,xx.xx)	(xx.xx,xx.xx)	(xx.xx,xx.xx)
Minimum	Observed	xx.xx	xx.xx	xx.xx
Maximum	Observed	xx.xx*	xx.xx*	xx.xx
p-value [2]		0.xxxx	0.xxxx	

Locations to appear on this table, in order, are Thumb abduction (radial nerve), Thumb adduction (ulnar nerve), Thumb opposition (median nerve), and Elbow flexion (musculocutaneous nerve).
Return: Lovett scale score returns to 3 or more in any motor function assessment.
* indicates censored observation CI = confidence interval
[1] Estimates from Kaplan-Meier analysis.
[2] p-value from log-rank test with terms for treatment comparing EXPAREL to placebo.
Source: *list SAS datasets used to create table* *DDMONYYYYTHH:MM*
SAS X.Y *program_name*

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Table 14.3-6.4: Summary of Motor Function Assessments by Timepoint – Safety Analysis Set

Active Flexion (degrees)			EXPAREL				
Timepoint	Value	Statistic	133 mg [N=XXX]	266 mg [N=XXX]	All EXPAREL [N=XXX]	Placebo [N=XXX]	Total [N=XXX]
Baseline	Actual	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx
15 min	Baseline [1]	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx
	Actual	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx
	Change	n	xx	xx	xx	xx	xx
		Mean	xx.x	xx.x	xx.x	xx.x	xx.x
		SD	x.xx	x.xx	x.xx	x.xx	x.xx
		Minimum	xx	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x	xx.x
		Maximum	xx	xx	xx	xx	xx

[1] Baseline (prior to surgery) for subjects with data at the timepoint.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM

SAS X.Y program_name

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Table 14.3-7.1.1: Overview of Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set

	EXPAREL				
Number of	133 mg [N=XX] n (%)	266 mg [N=XX] n (%)	All EXPAREL [N=XX] n (%)	Placebo [N=XX] n (%)	Total [N=XX] n (%)
Subjects with Any TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Maximum Severity of Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Maximum Severity of Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Maximum Severity of Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At least one Related	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At least one Serious	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects Discontinued due to TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Died on Study	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Related TEAEs are those AEs indicated as 'possible', 'probable' or 'definite' related by the investigator on the AE CRF.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM

SAS X.Y program_name

Note to programmer: *Only present overall sites.* All categories on this table should appear, even if not present in the data.

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Table 14.3-7.1.2: Summary of Incidence of Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set

System Organ Class Preferred Term	EXPAREL 133 mg [N=XX] n (%)	EXPAREL 266 mg [N=XX] n (%)	EXPAREL All EXPAREL [N=XX] n (%)	Placebo [N=XX] n (%)	Total [N=XX] n (%)
Subjects with at least one TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT1.1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT1.2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT2.1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT2.2	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)	xx (xx.x)
ETC.					

Adverse events coded using the Medical Dictionary for Regulatory Activities (MedDRA TBD).
Sorted by descending total incidence by system organ class and preferred term within system organ class.
Subjects experiencing the same TEAE more than once are counted only once at each summary level.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Only present overall sites. Use mock-up Table 14.3-2.1.2 for the following tables:*

Table 14.3-7.1.3: Summary of Incidence of Study Drug-Related Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set
Table 14.3-7.1.4: Summary of Incidence of Treatment-Emergent Adverse Events (TEAEs) Leading to Study Withdrawal - Safety Analysis Set
Table 14.3-7.1.5: Summary of Incidence of Study Drug-Related Treatment-Emergent Adverse Events (TEAEs) Leading to Study Withdrawal - Safety Analysis Set

For related tables add the following footnote to the table:
Related TEAEs are those AEs indicated as 'possible', 'probable' or 'definite' related by the investigator on the AE CRF.

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Table 14.3-7.1.6: Summary of Incidence of Treatment-Emergent Adverse Events (TEAEs) by Severity - Safety Analysis Set

System Organ Class Preferred Term	Severity	EXPAREL 133 mg [N=XX] n (%)	EXPAREL 266 mg [N=XX] n (%)	EXPAREL All EXPAREL [N=XX] n (%)	Placebo [N=XX] n (%)	Total [N=XX] n (%)
Subjects with at least one TEAE	Mild	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)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC1	Mild	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)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT1.1	Mild	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)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Adverse events coded using the Medical Dictionary for Regulatory Activities (MedDRA TBD).
Sorted by descending total incidence by system organ class and preferred term within system organ class.
Subjects experiencing the same TEAE more than once are counted only once at each summary level.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

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Table 14.3-7.1.7: Summary of Incidence of Treatment-Emergent Adverse Events (TEAEs) by Relationship to Study Drug - Safety Analysis Set

System Organ Class Preferred Term	Relation	EXPAREL 133 mg [N=XX] n (%)	EXPAREL 266 mg [N=XX] n (%)	EXPAREL All EXPAREL [N=XX] n (%)	Placebo [N=XX] n (%)	Total [N=XX] n (%)
Subjects with at least one TEAE	Unrelated	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Unlikely	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Possible	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Probable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Definite	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC1	Unrelated	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Unlikely	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Possible	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Probable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Definite	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT1.1	Unrelated	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Unlikely	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Possible	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Probable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Definite	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Adverse events coded using the Medical Dictionary for Regulatory Activities (MedDRA TBD).
Sorted by descending total incidence by system organ class and preferred term within system organ class.
Subjects experiencing the same TEAE more than once are counted only once at each summary level.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Only present overall sites. For related tables add the following footnote to the table, "Related TEAEs are those AEs indicated as 'possible', 'probable' or 'definite' related by the investigator on the AE CRF." Use indicated mock-up for the following tables:*

Use mock-up 14.7-1.1
Table 14.3-7.2.1: Overview of Serious Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set
Use mock-up 14.7-1.2
Table 14.3-7.2.2: Summary of Incidence of Serious Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set
Use mock-up 14.7-1.3
Table 14.3-7.2.3: Summary of Incidence of Study Drug-Related Serious Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set
Use mock-up 14.7-1.4
Table 14.3-7.2.4: Summary of Incidence of Serious Treatment-Emergent Adverse Events (TEAEs) Leading to Study Withdrawal - Safety Analysis Set
Use mock-up 14.7-1.5
Table 14.3-7.2.5: Summary of Incidence of Study Drug-Related Serious Treatment-Emergent Adverse Events (TEAEs) Leading to Study Withdrawal - Safety Analysis Set
Use mock-up 14.7-1.6
Table 14.3-7.2.6: Summary of Incidence of Serious Treatment-Emergent Adverse Events (TEAEs) Resulting in Death - Safety Analysis Set
Use mock-up 14.7-1.7
Table 14.3-7.2.7: Summary of Incidence of Study Drug-Related Serious Treatment-Emergent Adverse Events (TEAEs) Resulting in Death - Safety Analysis Set

Use mock-up 14.7-1.1
Table 14.3-7.3.1: Overview of Treatment-Emergent Adverse Events (TEAEs) of Special Interest - Safety Analysis Set
Use mock-up 14.7-1.2
Table 14.3-7.3.2: Summary of Incidence of Treatment-Emergent Adverse Events (TEAEs) of Special Interest - Safety Analysis Set
Use mock-up 14.7-1.3
Table 14.3-7.3.3: Summary of Incidence of Study Drug-Related Treatment-Emergent Adverse Events (TEAEs) of Special Interest - Safety Analysis Set
Use mock-up 14.7-1.4
Table 14.3-7.3.4: Summary of Incidence of Treatment-Emergent Adverse Events (TEAEs) of Special Interest Leading to Study Withdrawal - Safety Analysis Set
Use mock-up 14.7-1.5

Table 14.3-7.3.5: Summary of Incidence of Study Drug-Related Treatment-Emergent Adverse Events (TEAEs) of Special Interest Leading to Study Withdrawal - Safety Analysis Set

Use mock-up 14.7-1.6

Table 14.3-7.3.6: Summary of Incidence of Treatment-Emergent Adverse Events (TEAEs) of Special Interest Resulting in Death - Safety Analysis Set

Use mock-up 14.7-1.7

Table 14.3-7.3.7: Summary of Incidence of Study Drug-Related Treatment-Emergent Adverse Events (TEAEs) of Special Interest Resulting in Death - Safety Analysis Set

Note to programmer: *Use mock-up 14.1-4.1 for tables:*

Table 14.3-8.1: Incidence of Prior Medications – Safety Analysis Set.

On this table change the footnote 'Intraoperatives medications are those indicated as such by the investigator' to read 'Prior medications are those stopped before start of study drug administration.'

Table 14.3-8.2: Incidence of Concomitant Medications – Safety Analysis Set.

On this table change the footnote 'Intraoperatives medications are those indicated as such by the investigator' to read 'Concomitant medications are those taken between the start of study drug administration and discharge from study and are not designated intraoperative medications.'

Note to programmer: *For the following tables, only present US and ROW regions; there is no overall regions group. All of the following mock-ups will put the region as a by-line title in the table.*

Use mock-up 14.3-5.1 for table:

Table 14.3-9.1.1: Region Tabulation of Sensation Tests – Safety Analysis Set

Use mock-up 14.3-5.2 for table:

Table 14.3-9.1.2: Region Summary of Sensation Loss and Return by Timepoint – Safety Analysis Set

Use mock-up 14.3-5.3 for table:

Table 14.3-9.1.3: Region Analysis of Time to Sensation Loss – Safety Analysis Set

Use mock-up 14.3-5.4 for table:

Table 14.3-9.1.4: Region Analysis of Time to Sensation Return – Safety Analysis Set

Use mock-up 14.3-5.5 for table:

Table 14.3-9.1.5: Region Summary of Duration (hrs) of Sensation Loss – Safety Analysis Set

Use mock-up 14.3-6.1 for table:

Table 14.3-9.2.1: Region Summary of Active Motor Function Loss and Return by Timepoint – Safety Analysis Set

Use mock-up 14.3-6.2 for table:

Table 14.3-9.2.2: Region Analysis of Time to Onset of Motor Function Loss - Efficacy Analysis Set

Use mock-up 14.3-6.3 for table:
Table 14.3-9.2.3: Region Analysis of Time to Return of Motor Function - Efficacy Analysis Set

Use mock-up 14.3-6.4 for table:

Table 14.3-9.2.4: Region Summary of Motor Function Assessments by Timepoint – Safety Analysis Set

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Table 14.3-9.3.1: Region Overview of Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set

Region: US	EXPAREL				
	133 mg [N=XX]	266 mg [N=XX]	All EXPAREL [N=XX]	Placebo [N=XX]	Total [N=XX]
Number of	n (%)	n (%)	n (%)	n (%)	n (%)
Subjects with Any TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Maximum Severity of Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Maximum Severity of Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Maximum Severity of Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At least one Related	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At least one Serious	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects Discontinued due to TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Died on Study	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Only present US and ROW regions; there is no overall regions group. All categories on this table should appear, even if not present in the data.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Table 14.3-9.3.2: Region Summary of Incidence of Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set

Region:	EXPAREL				
System Organ Class Preferred Term	133 mg [N=XX] n (%)	266 mg [N=XX] n (%)	All EXPAREL [N=XX] n (%)	Placebo [N=XX] n (%)	Total [N=XX] n (%)
Subjects with at least one TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT1.1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT1.2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT2.1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT2.2	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)	xx (xx.x)
ETC.					

Adverse events coded using the Medical Dictionary for Regulatory Activities (MedDRA TBD).
Sorted by descending total incidence by system organ class and preferred term within system organ class.
Subjects experiencing the same TEAE more than once are counted only once at each summary level.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Only present US and ROW regions; there is no overall regions group. Use this template for table:*

Table 14.3-9.3.3: Region Summary of Incidence of Serious Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set

15. TABLE OF CONTENTS FOR LISTING MOCK-UPS

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-1: Subject Disposition – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Date of Last Visit	End of Study Status	Specify
XXX	XXX-YYYY	DDMONYYYY		

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *End of study status for subject who early terminated from the study is the primary reason for termination. If subject discontinued due to an AE then the reason should read 'ADVERSE EVENT, AE # X'. If subject discontinued due to death the reason should read 'DEATH ON DDMONYYYY'. For those reasons that also collected a specify text, that text belongs in the specify column.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-2: Randomization and Analysis Sets – All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

		Randomization		Protocol	Analysis Set		
Site	Subject	Date and Time	Number	Amendment	Safety	Efficacy	Per-protocol
XXX	XXX-YYYY	DDMONYYYYTHH:MM	XXXXX	X	X	X	X

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Analysis set will by 'Y' if subject in set, blank otherwise.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-3: Demographics – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject Number	Subject Init.	Birth Date	Age (yrs)	Sex	Dominant Hand	Race	Ethnicity	ASA Class	Region	Country
XXX	XXX-YYYY	AMZ	DDMONYYYY	XX	X	XXXXX	XXXXXXXXXXX	XXXXXXXXX	X	XXX	XXXXXXX

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *If race is 'other' then race should be 'Other: other-specify-text'.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-4: Height and Weight – All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Height and Weight Collection Date	Height (cm)	Weight (kg)	Body Mass Index (kg/m^2)
XXX	XXX-YYYY	DDMONYYYYTHH:MM	XXX.X	XXX.X	XX.X

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-5: Surgery – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Date	Start Time	Stop Time	Duration (hrs)	Location	Incision Length (cm)	Anesthesia Type
XXX	XXX-YYYY	DDMONYYYY	HH:MM	HH:MM	X.X	XXXXX	XX.X	XXXXXXXXXXXXXXXXXXX

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *If anesthesia type is 'other' then text should read 'other: specify-text'.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-6: Visual Analog Scale (VAS) – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Date Time	Time From Dose: Scheduled (hr)	Time From Dose: Actual (hr)	Time From Dose: Deviation (hrs)	VAS (cm)	Pain-Free
XXX	XXX-YYYY	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y

Pain-free is VAS ≤ 1.5 cm and no prior rescue medication use.
VAS: 0=No pain to 10=Worst Pain Imaginable ND=Not Done NA=Not Applicable
* = out of window
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by VAS collection date and time. If VAS was taken due to rescue medication dosing, put RESCUE in scheduled column and hours from dose in actual column – leave deviation column blank. Do not split a subject's data across pages if it can be avoided. Pain-free will have Y if VAS ≤ 1.5 otherwise blank. An asterisk (*) will be placed next to the deviation if an assessment is out of window. See Table of Time and Events for windows.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-7.1: Rescue Medication Total Dose (MED mg) and Opioid-free Status - All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	48 hrs	24 hrs	72 hrs	24-48hrs	48-72hrs	Opioid-Free
XXX	XXX-YYYY	XXXX.X	XXXX.X	XXXX.X	XXXX.X	XXXX.X	NO
XXX	XXX-YYYY	-	-	-	-	-	YES

Total dose is dose from end of surgery through timepoint.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *If medication is 'Other', text should read 'Other: specify-text'. Sort by date and time within subject.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-7.2: Rescue Medication – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Date and Time	Time to Rescue (hr)	Medication	Dose (units)	Conversion Factor	Dose (MED mg)	Route
XXX	XXX-YYYY	DDMONYYYYTHH:MM	XXX.X	XXXXXXXXXXXX	XX(XXXX)	X.XX	XXX.X	XXXXXXX
		DDMONYYYYTHH:MM	XXX.X	XXXXXXXXXXXX	XX(XXXX)	X.XX	XXX.X	XXXXXXX
		DDMONYYYYTHH:MM	XXX.X	XXXXXXXXXXXX	XX(XXXX)	X.XX	XXX.X	XXXXXXX
		DDMONYYYYTHH:MM	XXX.X	XXXXXXXXXXXX	XX(XXXX)	X.XX	XXX.X	XXXXXXX

Time to rescue is time from end of surgery to rescue medication dose.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *If medication is 'Other', text should read 'Other: specify-text'. Sort by date and time within subject.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-8: Overall Benefit of Analgesia – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

		Assessment			Question							
Site	Subject	Date and Time	Schedule (hrs)	Actual (hrs)	Deviation (hrs)	1	2	3	4	5	6	7	Total Score
XXX	XXX-YYYY	DDMONYYYYTHH:MM	24	XX.X	XX.X	X	X	X	X	X	X	X	XX
		DDMONYYYYTHH:MM	72	XX.X	XX.X	X	X	X	X	X	X	X	XX
		DDMONYYYYTHH:MM	240 (D10)	XXX.X	XX.X	X	X	X	X	X	X	X	XX

Total score = sum of questions 1 to 6 scores minus question 7 score plus 4.
1) Please rate your current pain at rest on a scale between 0=minimal pain and 4=maximum imaginable pain
2) Please grade any distress and bother from vomiting in the past 24 h (0=not at all to 4=very much)
3) Please grade any distress and bother from itching in the past 24 h (0=not at all to 4=very much)
4) Please grade any distress and bother from sweating in the past 24 h (0=not at all to 4=very much)
5) Please grade any distress and bother from freezing in the past 24 h (0=not at all to 4=very much)
6) Please grade any distress and bother from dizziness in the past 24 h (0=not at all to 4=very much)
7) How satisfied are you with your pain treatment during in the past 24 h (0=not at all to 4=very much)
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-9: Subject Satisfaction with Post-Surgical Pain Control – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Assessment	Date and Time	Rating	Score
XXX	XXX-YYYY	24 hr	DDMONYYYYTHH:MM	EXTREMELY DISSATISFIED	1
		72 hr	DDMONYYYYTHH:MM	DISSATISFIED	2
		Day 10	DDMONYYYYTHH:MM	NEITHER SATISFIED NOR DISSATISFIED	3
XXX	XXX-YYYY	24 hr	DDMONYYYYTHH:MM	SATISFIED	4
		72 hr	DDMONYYYYTHH:MM	EXTREMELY SATISIFIED	5
		Day 10	DDMONYYYYTHH:MM	EXTREMELY SATISIFIED	5

Etc.

Time to rescue is time from end of surgery to rescue medication dose.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-10: Modified Post-Anesthesia Discharge Scoring System (MPADSS)– All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

		Assessment			Question					
Site	Subject	Date and Time	Schedule (hrs)	Actual (hrs)	Deviation (hrs)	1	2	3	4	5	Total Score
XXX	XXX-YYYY	DDMONYYYYTHH:MM	24	XX.X	XX.X	X	X	X	X	X	XX
		DDMONYYYYTHH:MM	72	XX.X	XX.X	X	X	X	X	X	XX
		DDMONYYYYTHH:MM	240 (D10)	XXX.X	XX.X	X	X	X	X	X	XX

*=out of window
Total score = sum of scores.
1) Vital signs: 2 = ≤ 20%; 1 = 20-40%; 0 = >40% of preoperative value.
2) Ambulation: 2 = steady gait/no dizziness; 1 = with assistance; 0 = none/dizziness
3) Nausea and Vomiting: 2 = minimal; 1 = moderate; 0 = severe
4) Pain: 2 = minimal; 1 = moderate; 0 = severe
5) Surgical bleeding: 2 = minimal; 1 = moderate; 0 = severe
Source: list SAS datasets used to create table DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-11: Day 29 Phone Call – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Date	Schedule (days)	Actual (days)	Deviation (days)	Number of pain-related Phone Calls	Visits	Total
XXX	XXX-YYYY	DDMONYYYY	29	XX.X	XX.X	XX	XX	XXXX
XXX	XXX-YYYY	DDMONYYYY	29	XX.X	XX.X	XX	XX	XXXX
XXX	XXX-YYYY	DDMONYYYY	29	XX.X	XX.X	XX	XX	XXXX

Total = sum of calls and visits.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-12: Hematology – All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Visit	Date and Time	Analyte (units)	Normal Range Low	Normal Range High	Result	Change	Flag
XXX	XXX-YYYY	Screening	DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	-	H
				XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	-	
				XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	-	L
				XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	-	
				…					
		Baseline	DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	-	
				XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	-	
				XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	-	L
				XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	-	
				…					
		Day 10	DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	XX.X	
				XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	XX.X	
				XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	XX.X	L
				XXXXXXXXXXXXXXXX (units)	xxx.xx	xxx.xx	xxx.xx	XX.X	

Flag: L=below normal range; H=above normal range.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject and analyte alphabetically within date. Change is only calculated for Day 10 visit. Use this mock-up for the following listings:*

Listing 16.2-13: Chemistry – All Subjects
Listing 16.2-14.1: Urinalysis – Numeric Results – All Subjects

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-14.2: Urinalysis – Character Results – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Visit	Date and Time	Analyte	Normal Criteria	Result	Flag
XXX	XXX-YYYY	Screening	DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	A
				XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	
				XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	
				XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	
				…			
		Baseline	DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	A
				XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	
				XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	
				XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	
				…			
		Day 10	DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	
				XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	
				XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	
				XXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXX	

Flag: A = abnormal.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject and analyte alphabetically within date.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-15: Vital Signs Assessment – All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

			Assessment			Heart Rate (bpm)		Blood Pressure (mmHg) Systolic		Blood Pressure (mmHg) Diastolic	
Site	Subject	Date and Time	Schedule (hrs)	Actual (hrs)	Dev. (hrs)	Actual	Change	Actual	Change	Actual	Change
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Screening	-	-	XX	-	XXX	-	XX	-
		DDMONYYYYTHH:MM	Baseline	-	-	XX	-	XXX	-	XX	-
		DDMONYYYYTHH:MM	PACU	-	-	XX	XX	XXX	-X	XX	X
		DDMONYYYYTHH:MM	6	XXX.XX	XXX	XX	-XX	XXX	X	XX	-X
		DDMONYYYYTHH:MM	12	XXX.XX	XXX	XX	XX	XXX	X	XX	X
		DDMONYYYYTHH:MM	24	XXX.XX	XXX	XX	XX	XXX	-X	XX	X
		DDMONYYYYTHH:MM	36	XXX.XX	XXX	XX	XX	XXX	X	XX	X
		DDMONYYYYTHH:MM	48	XXX.XX	XXX	XX	-XX	XXX	X	XX	-X
		DDMONYYYYTHH:MM	60	XXX.XX	XXX	XX	XX	XXX	-X	XX	X
		DDMONYYYYTHH:MM	66	XXX.XX	XXX	XX	XX	XXX	-X	XX	-X
		DDMONYYYYTHH:MM	72	XXX.XX	XXX	XX	-XX	XXX	X	XX	X
		DDMONYYYYTHH:MM	120 (D5)	XXX.XX	XXX	XX	XX	XXX	X	XX	-X
		DDMONYYYYTHH:MM	240 (D10)	XXX.XX	XXX	XX	-XX	XXX	-X	XX	X

*=out of window
Change is change from baseline (Preop).
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject. An asterisk (*) will be placed next to the deviation if an assessment is out of window. See Table of Time and Events for windows.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-16: Electrocardiogram Findings – Investigator Assessment – All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

		Assessment				
Site	Subject	Date and Time	Schedule (hrs)	Actual (hrs)	Deviation (hrs)	Finding
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Screening	-	-	Normal
		DDMONYYYYTHH:MM	Preop	-	-	Abnormal, clinically significant
		DDMONYYYYTHH:MM	PACU	-	-	Abnormal, not clinically significant
		DDMONYYYYTHH:MM	6	XXX.XX	XXX	Normal
		DDMONYYYYTHH:MM	12	XXX.XX	XXX	Normal
		DDMONYYYYTHH:MM	24	XXX.XX	XXX	Normal
		DDMONYYYYTHH:MM	36	XXX.XX	XXX	Normal
		DDMONYYYYTHH:MM	48	XXX.XX	XXX	Normal
		DDMONYYYYTHH:MM	60	XXX.XX	XXX	Normal
		DDMONYYYYTHH:MM	66	XXX.XX	XXX	Normal
		DDMONYYYYTHH:MM	72	XXX.XX	XXX	Normal
		DDMONYYYYTHH:MM	120 (D5)	XXX.XX	XXX	Normal
		DDMONYYYYTHH:MM	240 (D10)	XXX.XX	XXX	Normal

*=out of window

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject. An asterisk (*) will be placed next to the deviation if an assessment is out of window. See Table of Time and Events for windows.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-17: Neurological Assessment – All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

		Assessment				Question					
Site	Subject	Date and Time	Schedule (hrs)	Actual (hrs)	Deviation (hrs)	1	2	3	4	5	6
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Screening	-	-	X	X	X	X	X	X
		DDMONYYYYTHH:MM	Preop	-	-	X	X	X	X	X	X
		DDMONYYYYTHH:MM	PACU	-	-	X	X	X	X	X	X
		DDMONYYYYTHH:MM	6	XXX.XX	XXX	X	X	X	X	X	X
		DDMONYYYYTHH:MM	12	XXX.XX	XXX	X	X	X	X	X	X
		DDMONYYYYTHH:MM	24	XXX.XX	XXX	X	X	X	X	X	X
		DDMONYYYYTHH:MM	36	XXX.XX	XXX	X	X	X	X	X	X
		DDMONYYYYTHH:MM	48	XXX.XX	XXX	X	X	X	X	X	X
		DDMONYYYYTHH:MM	60	XXX.XX	XXX	X	X	X	X	X	X
		DDMONYYYYTHH:MM	66	XXX.XX	XXX	X	X	X	X	X	X
		DDMONYYYYTHH:MM	72	XXX.XX	XXX	X	X	X	X	X	X
		DDMONYYYYTHH:MM	120 (D5)	XXX.XX	XXX	X	X	X	X	X	X
		DDMONYYYYTHH:MM	240 (D10)	XXX.XX	XXX	X	X	X	X	X	X

*=out of window
1) Is subject oriented?
2) Do you have numbness of the lips, the tongue or around the mouth?
3) Do you have a metallic taste in your mouth?
4) Are you having problems with your hearing not related to the use of a hearing aid?
5) Are you having problems with your vision not related to the use of eye glasses?
6) Are your muscles twitching?

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject. An asterisk (*) will be placed next to the deviation if an assessment is out of window. See Table of Time and Events for windows.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-18.1: Sensory Function Assessment – All Subjects (Part 1 of 3)

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

			Assessment			Axillary Nerve			Musculocutaneous Nerve		
Site	Subject	Date and Time	Schedule (hrs)	Actual (hrs)	Dev. (hrs)	Cold	Pin-prick	Light Touch	Cold	Pin-prick	Light Touch
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Screening	-	-	+	+	+	+	+	+
		DDMONYYYYTHH:MM	Baseline	-	-	+	+	+	+	+	+
		DDMONYYYYTHH:MM	PACU	-	-	+	+	+	+	+	+
		DDMONYYYYTHH:MM	6	XXX.XX	XXX	+	+	+	+	+	+
		DDMONYYYYTHH:MM	9	XXX.XX	XXX	-L	+	+	+	+	+
		DDMONYYYYTHH:MM	12	XXX.XX	XXX	-	+	+	+	+	+
		DDMONYYYYTHH:MM	18	XXX.XX	XXX	-	+	+	+	+	+
		DDMONYYYYTHH:MM	24	XXX.XX	XXX	-	+	+	+	+	+
		DDMONYYYYTHH:MM	36	XXX.XX	XXX	-	-L	+	+	+	+
		DDMONYYYYTHH:MM	48	XXX.XX	XXX	+R	+R	+	+	+	+
		DDMONYYYYTHH:MM	60	XXX.XX	XXX	+	+	+	+	+	+
		DDMONYYYYTHH:MM	72	XXX.XX	XXX	+	+	+	+	+	+
		DDMONYYYYTHH:MM	120 (D5)	XXX.XX	XXX	+	+	+	+	+	+
		DDMONYYYYTHH:MM	240 (D10)	XXX.XX	XXX	+	+	+	-L	+	+
		DDMONYYYYTHH:MM	Unsched.	-	-	+	+	+	-	+	+

*=out of window '-/+'=Absent/Present; L/R=Loss/Return of sensation Unsched=Unscheduled
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject. An asterisk (*) will be placed next to the deviation if an assessment is out of window. See Table of Time and Events for windows.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-18.1: Sensory Function Assessment – All Subjects (Part 2 of 3)

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

			Assessment			Median Nerve			Ulnar Nerve		
Site	Subject	Date and Time	Schedule (hrs)	Actual (hrs)	Dev. (hrs)	Cold	Pin-prick	Light Touch	Cold	Pin-prick	Light Touch
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Screening	-	-	+	+	+	+	+	+
		DDMONYYYYTHH:MM	Baseline	-	-	+	+	+	+	+	+
		DDMONYYYYTHH:MM	PACU	-	-	+	+	+	+	+	+
		DDMONYYYYTHH:MM	6	XXX.XX	XXX	+	+	+	+	+	+
		DDMONYYYYTHH:MM	9	XXX.XX	XXX	-L	+	+	+	+	+
		DDMONYYYYTHH:MM	12	XXX.XX	XXX	-	+	+	+	+	+
		DDMONYYYYTHH:MM	18	XXX.XX	XXX	-	+	+	+	+	+
		DDMONYYYYTHH:MM	24	XXX.XX	XXX	-	+	+	+	+	+
		DDMONYYYYTHH:MM	36	XXX.XX	XXX	-	-L	+	+	+	+
		DDMONYYYYTHH:MM	48	XXX.XX	XXX	+R	+R	+	+	+	+
		DDMONYYYYTHH:MM	60	XXX.XX	XXX	+	+	+	+	+	+
		DDMONYYYYTHH:MM	72	XXX.XX	XXX	+	+	+	+	+	+
		DDMONYYYYTHH:MM	120 (D5)	XXX.XX	XXX	+	+	+	+	+	+
		DDMONYYYYTHH:MM	240 (D10)	XXX.XX	XXX	+	+	+	-L	+	+
		DDMONYYYYTHH:MM	Unsched.	-	-	+	+	+	-	+	+

*=out of window '-/+'=Absent/Present; L/R=Loss/Return of sensation Unsched=Unscheduled
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject. An asterisk (*) will be placed next to the deviation if an assessment is out of window. See Table of Time and Events for windows.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-18.1: Sensory Function Assessment – All Subjects (Part 3 of 3)

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

			Assessment			Radial Nerve		
Site	Subject	Date and Time	Schedule (hrs)	Actual (hrs)	Dev. (hrs)	Cold	Pin-prick	Light Touch
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Screening	-	-	+	+	+
		DDMONYYYYTHH:MM	Baseline	-	-	+	+	+
		DDMONYYYYTHH:MM	PACU	-	-	+	+	+
		DDMONYYYYTHH:MM	6	XXX.XX	XXX	+	+	+
		DDMONYYYYTHH:MM	9	XXX.XX	XXX	-L	+	+
		DDMONYYYYTHH:MM	12	XXX.XX	XXX	-	+	+
		DDMONYYYYTHH:MM	18	XXX.XX	XXX	-	+	+
		DDMONYYYYTHH:MM	24	XXX.XX	XXX	-	+	+
		DDMONYYYYTHH:MM	36	XXX.XX	XXX	-	-L	+
		DDMONYYYYTHH:MM	48	XXX.XX	XXX	+R	+R	+
		DDMONYYYYTHH:MM	60	XXX.XX	XXX	+	+	+
		DDMONYYYYTHH:MM	72	XXX.XX	XXX	+	+	+
		DDMONYYYYTHH:MM	120 (D5)	XXX.XX	XXX	+	+	+
		DDMONYYYYTHH:MM	240 (D10)	XXX.XX	XXX	+	+	+
		DDMONYYYYTHH:MM	Unsched.	-	-	+	+	+

*=out of window '-/+'=Absent/Present; L/R=Loss/Return of sensation Unsched=Unscheduled
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject. An asterisk (*) will be placed next to the deviation if an assessment is out of window. See Table of Time and Events for windows.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-18.2: Time to Loss and Return of Sensory Function – All Subjects

TREATMENT: *treatment-name*

		Loss-Return			Date and Time of		Time to (hrs)	
Site	Subject	Cycle Number	Location	Dose	Loss	Return	Loss [1]	Return [2]
XXX	XXX-YYYY	1	*XXXXXXX*	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	XXX.X	XXX.X
		2		-	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	XXX.X	XXX.X
		…		-	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	XXX.X	XXX.X
		n		-	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM*	XXX.X	XXX.X*
		Total		-	-	-	-	D.D

[1] Time to loss is the time from start of study drug administration to loss of sensation
[2] Time to return is time the time from most recent loss of sensation to return of sensation
*=Censored return (time of last sensory assessment)Source: *list SAS datasets used to create table* DDMONY
SAS X.Y program_name

Note to programmer: *Locations are axillary, musculo., median, ulnar and radial. Sort by date and time within subject. In total row, L is the total number of times subject lost sensation, R is total number of times subject had return of sensation; and D.D is sum of durations from all cycles. Some subjects may have more losses of sensation than returns.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-19.1: Motor Function Assessment – All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

			Assessment			Thumb			
Site	Subject	Date and Time	Schedule (hrs)	Actual (hrs)	Dev. (hrs)	Abduct	Adduct	Oppos	Elbow Flexion
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Screening	-	-	X	-	X	-
		DDMONYYYYTHH:MM	Baseline	-	-	X	-	X	-
		DDMONYYYYTHH:MM	PACU	-	-	X	X	X	X
		DDMONYYYYTHH:MM	6	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	9	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	12	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	18	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	24	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	36	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	48	XXX.XX	XXX	XL	X	X	X
		DDMONYYYYTHH:MM	60	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	72	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	120 (D%)	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	240 (D10)	XXX.XX	XXX	X	X	X	X
		DDMONYYYYTHH:MM	Unsched.	-	-	X	X	X	X

*=out of window L=Loss of function/R=Return of function Unsched=Unscheduled
Abduct=Abduction Adduct=adduction Oppos=opposition
0=no evidence of contractility; 1=evidence of slight contractility;
2=complete range of motion without gravity; 3=complete range of motion with gravity;
4=complete range of motion against gravity with some resistance;
5=complete range of motion against gravity with full resistance.
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Sort by date and time within subject. An asterisk (*) will be placed next to the deviation if an assessment is out of window. See Table of Time and Events for windows.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Listing 16.2-19.2: Time to Loss and Return of Motor Function – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

		Loss-Return		Date and Time of			Time (hrs) to	
Site	Subject	Cycle Number	Assessment	Dose	Loss	Return	Loss [1]	Return [2]
XXX	XXX-YYYY	1	Abduct	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	XXX.X	XXX.X
		2	Flexion	-	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	XXX.X	XXX.X
		…		-	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	XXX.X	XXX.X
		n		-	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM*	XXX.X	XXX.X*
		Total		-	-	-	-	D.D

[1] Time to loss is the time from start of study drug administration to loss of motor function
[2] Time to return is time the time from most recent loss of to return of motor function
Total Return is the time from first loss to last return of motor function.
*=Censored return (time of last motor assessment)
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Note to programmer: *Assessments are Abduct, Adduct, Oppos and Flexion. Sort by date and time within subject. In total row, D.D is the time from first loss of motor function to last return of motor function Some subjects may have more losses of motor function than returns.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-20.1: All Adverse Events – All Subjects
Treatment: treatment-name
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	TEAE	Data Type	Data
XXX	XXX-YYYY	N	Start	DDMONYYYYTHH:MM
			Stop	DDMONYYYYTHH:MM
			AE Number	X
			System Organ Class	XXXXXXXXXXXXXXXXXX
			Preferred	XXXXXXXXXXXXXXXXXXXX
			Verbatim	XXXXXXXXXXXXXXXXXXXXXX
			Severity	XXXXXXXX
			Relationship to Study Drug	XXXXXXXX
			Action Taken	XXXXXXXXXXXXXXXXXXXX
			Outcome	XXXXXXXXXXXXX
			Serious	XXX
			Serious Cause(s)	XXXXXXXXXXXXX
				XXXXXXXXXXXXXXXXXXXXX

TEAE: Treatment-emergent AE (Y=TEAE/N=Not TEAE)
Source: *list SAS datasets used to create listing* *DDMONYYYYTHH:MM*
SAS *X.Y* *program_name*

Note to programmer: *If AE is ongoing, put ONGOING in stop row. Do not split an AE across pages. Insert a page break between subjects. Use this template for the following listings:*
Listing 16.2-20.2.1: Treatment-emergent Adverse Events – All Subjects
Listing 16.2-20.2.2: Treatment-emergent Study Drug Related Adverse Events – All Subjects
Listing 16.2-20.3: All Serious Adverse Events – All Subjects
Listing 16.2-20.4.1: Treatment-emergent Serious Adverse Events – All Subjects
Listing 16.2-20.4.2: Treatment-emergent Study Drug Related Serious Adverse Events – All Subjects
Listing 16.2-20.5.1: Treatment-emergent Adverse Events of Special Interest – All Subjects
Listing 16.2-20.5.2: Treatment-emergent Study Drug Related Adverse Events of Special Interest – All Subjects

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-21.1: All Prior and Concomitant Medications – All Subjects
Treatment: treatment-name
Surgery: surgery-type
Nerve Block: nerve-block type

Site	Subject	Category	Data Type	Data
XXX	XXX-YYYY		Start	DDMONYYYYTHH:MM
			Stop	DDMONYYYYTHH:MM
			Medication Number	X
			ATC Level 1	XXXXXXXXXXXXXXXXXX
			ATC Level 2	XXXXXXXXXXXXXXXXXXX
			ATC Level 3	XXXXXXXXXXXXXXXXXXXXX
			ATC Level 4	XXXXXXXXXXXXXXXXXXX
			Preferred Name	XXXXXXXXXXXXXXXXXXX
			Verbatim	XXXXXXXXXXXXXXXXXXX
			Route	XXXXXXXX
			Frequency	XXXXXXXX
			Given for AE or MH?	XXXXXXXXXXXXXXXXXXXX AE # XX *(or MH # XX)*

ATC=Anatomical therapeutic class
Source: *list SAS datasets used to create listing* *DDMONYYYYTHH:MM*
SAS *X.Y* *program_name*

Note to programmer: *If medication is ongoing, put ONGOING in stop row. Do not split a medication across pages. Insert a page break between subjects. Values for category column are: CONCOMITANT; SURGICAL/ANESTHESIA; NON-MEDICATION; PRIOR. Use this template for the following listings:*

Listing 16.2-21.2: Prior Medications – All Subjects
Listing 16.2-21.3: Concomitant Medications – All Subjects

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-22: Medical History – All Subjects
Treatment: treatment-name
Surgery: surgery-type
Nerve Block: nerve-block type

Site	Subject	Data Type	Data
XXX	XXX-YYYY	Start	DDMONYYYY
		Stop	DDMONYYYY
		System Organ Class	XXXXXXXXXXXXXXXXXX
		Preferred	XXXXXXXXXXXXXXXXXXXX
		History Verbatim	XXXXXXXXXXXXXXXXXXXXX
		Start	DDMONYYYY
		Stop	DDMONYYYY
		System Organ Class	XXXXXXXXXXXXXXXXXX
		Preferred	XXXXXXXXXXXXXXXXXXXX
		History Verbatim	XXXXXXXXXXXXXXXXXXXXX

Source: list SAS datasets used to create listing DDMONYYYYTHH:MM
SAS X.Y program_name

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-23: Intraoperative Medications – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Administered	Name	Dose	Unit	Route
XXX	XXX-YYYY	YES	*OPIOID-NAME*	XXX.XX	(UNITS)	XXXX
XXX	XXX-YYYY	NO				

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-24: Study Drug Administration – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Date	Start Time	Stop Time	Total Volume (mL)
XXX	XXX-YYYY	DDMONYYYY	HH:MM	HH:MM	XXX

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327

Listing 16.2-25: Urine Drug Screen, Alcohol Blood Test and Pregnancy Test – All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Visit	Urine Drug	Blood Alcohol	Pregnancy
XXX	XXX-YYYY	Screening	XXXXXXXX	XXXXXXXX	XXXXXXXX
		Day 0 (Preop)	XXXXXXXX	XXXXXXXX	XXXXXXXX
XXX	XXX-YYYY	Screening	XXXXXXXX	XXXXXXXX	XXXXXXXX
		Day 0 (Preop)	XXXXXXXX	XXXXXXXX	XXXXXXXX
XXX	XXX-YYYY	Screening	XXXXXXXX	XXXXXXXX	XXXXXXXX
		Day 0 (Preop)	XXXXXXXX	XXXXXXXX	XXXXXXXX
XXX	XXX-YYYY	Screening	XXXXXXXX	XXXXXXXX	XXXXXXXX
		Day 0 (Preop)	XXXXXXXX	XXXXXXXX	XXXXXXXX

Source: list SAS datasets used to create table DDMONYYYYTHH:MM
SAS X.Y program_name

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-26: Admission and Discharge – All Subjects

TREATMENT: *treatment-name*
Surgery*: surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Date and Time	
		Admission	Discharge
XXX	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM
XXX	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM
XXX	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM

*=out of window
Total score = sum of scores.
1) Vital signs: 2 = ≤ 20%; 1 = 20-40%; 0 = >40% of preoperative value.
2) Ambulation: 2 = steady gait/no dizziness; 1 = with assistance; 0 = none/dizziness
3) Nausea and Vomiting: 2 = minimal; 1 = moderate; 0 = severe
4) Pain: 2 = minimal; 1 = moderate; 0 = severe
5) Surgical bleeding: 2 = minimal; 1 = moderate; 0 = severe
Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-27: Unique Adverse Events Terms and Associated Coded Terms

MedDRA Terms SOC Preferred Term	Verbatim(s)
SOC1	XXXXXXXXXXXXXXXXXXXXXXXXXX
PT1.1	XXXXXXXXXXXXXXXXXXXXXXXXXX
	XXXXXXXXXXXXXXXXXXXXXXXXXX
	XXXXXXXXXXXXXXXXXXXXXXXXXX
PT1.2	XXXXXXXXXXXXXXXXXXXXXXXXXX
	XXXXXXXXXXXXXXXXXXXXXXXXXX
SOC2	
PT2.1	XXXXXXXXXXXXXXXXXXXXXXXXXX
	XXXXXXXXXXXXXXXXXXXXXXXXXX

Coded using MedDRA
Source: *list SAS datasets used to create listing* *DDMONYYYYTHH:MM*
SAS X.Y *program_name*

Note to programmer: *Sort by SOC and preferred term in alphabetical order.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-28: Unique Medication Terms and Associated Coded Terms

Who Drug Dictionary Terms ACT1 ACT2 ACT3 ACT4 Preferred name	Verbatim(s)
ATC1	
ATC1.2	
PN1.2.1	XXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXX
PN1.2.2	XXXXXXXXXXXXXXXXXXXXXXXXX
ATC2	
ATC2.2	
ATC2.3	
ATC2.4	
PN2.2.3.4.1	XXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXX

Coded using Who Drug Dictionary
Source: *list SAS datasets used to create listing* *DDMONYYYYTHH:MM*
SAS X.Y *program_name*

Note to programmer: *Sort by ATC1, ATC2, ATC3, ATC4 and preferred name in alphabetical order*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-327
Listing 16.2-29: Protocol Deviations – All Subjects

TREATMENT: *treatment-name*
Surgery: *surgery-type*
Nerve Block: *nerve-block type*

Site	Subject	Important	Date	Description
XXX	XXX-YYYY	XXX	DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXXXX
			DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXXXX

Categories: Important, might significantly impact; Not-Important, none to minimal impact on study outcomes.
Important:
Source: *list SAS datasets used to create listing* *DDMONYYYYTHH:MM*
SAS X.Y *program_name*

Note to programmer: *Subjects may have multiple deviations. Sort deviations by treatment, surgery type, nerve block type, site, subject, then category 'Important' followed by 'Not-Important' and finally important ('YES' then 'NO'). Date may or may not include time.*

16. TABLE OF CONTENTS FOR FIGURE MOCK-UPS

Figure Mock-up 1

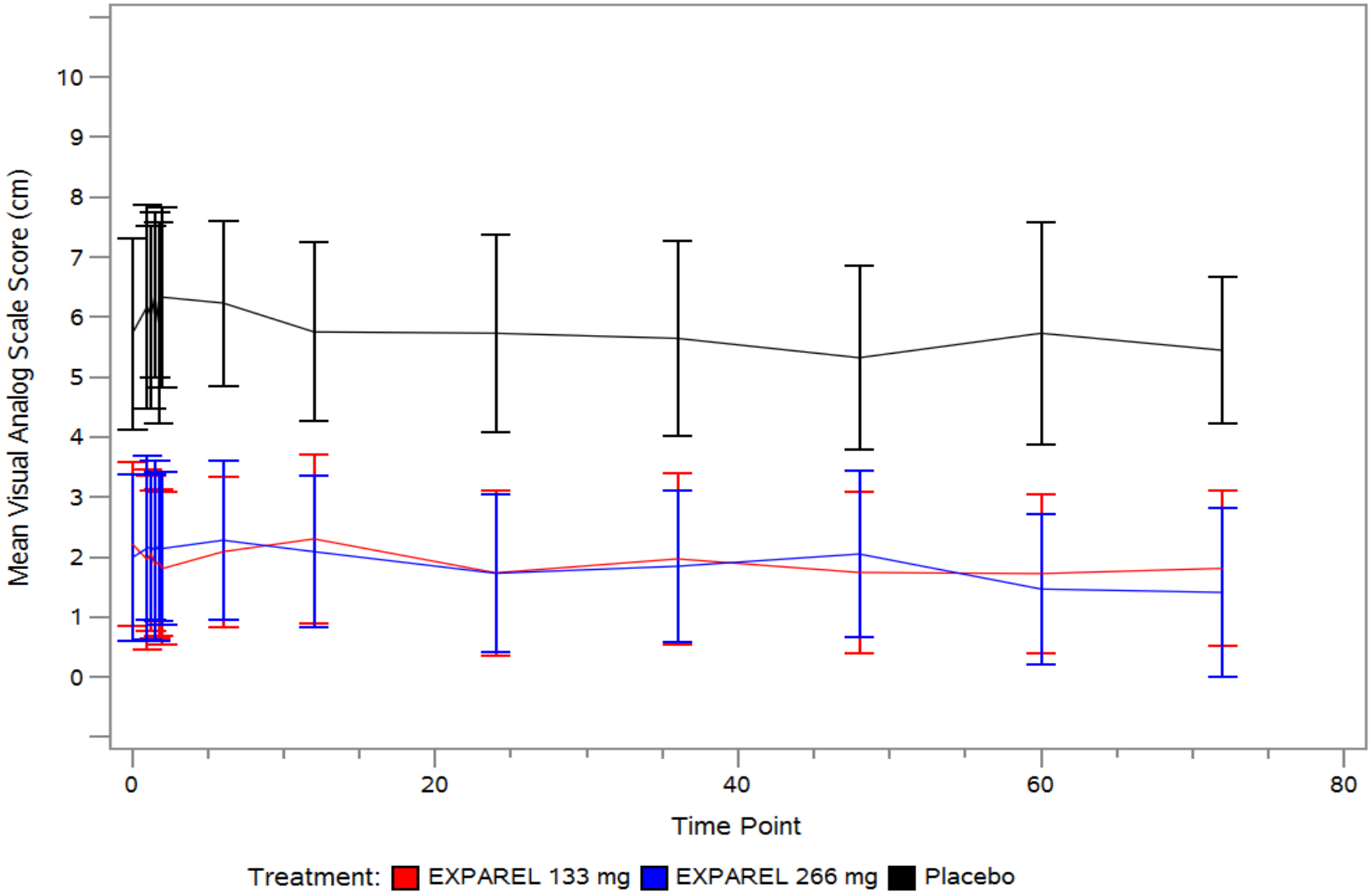


Figure Mock-up 2

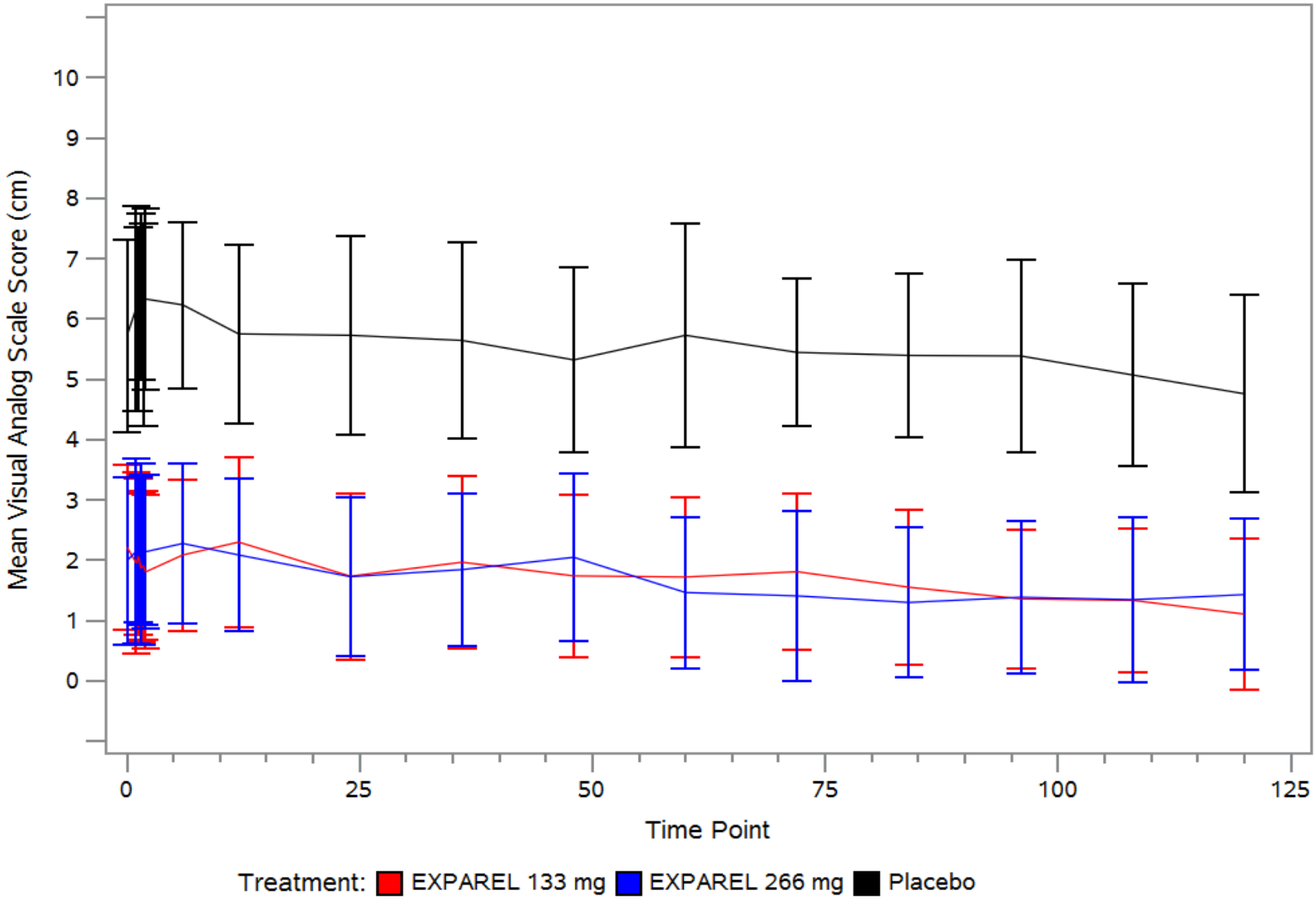
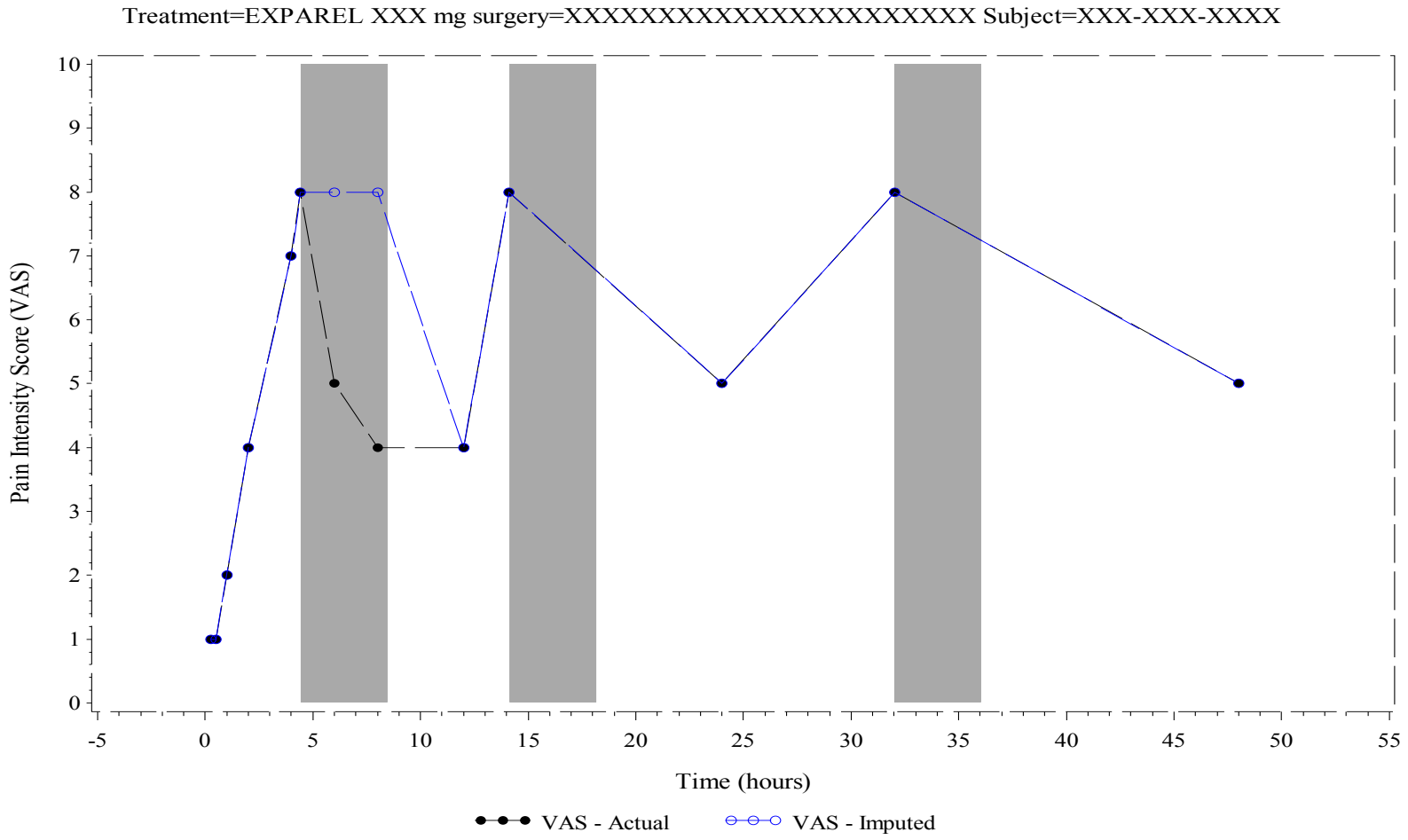
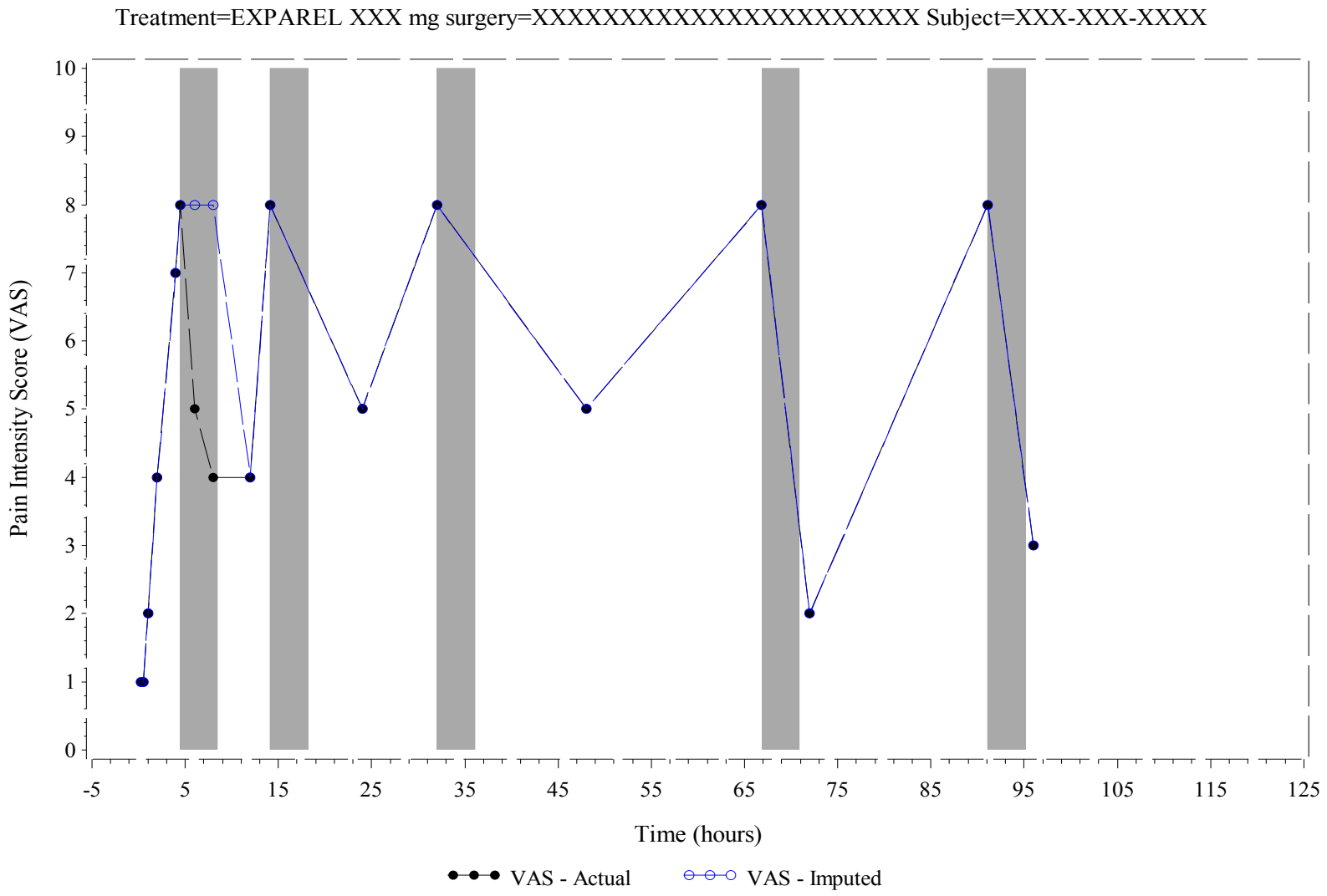


Figure Mock-up 3



Gray bars indicate rescue medication windows

Figure Mock-up 4



Gray bars indicate rescue medication windows

Note to programmers: *Note the colors and symbols used in the figure mock-ups are not correct per the SAP description; all figures created should use the SAP defined colors and symbols. In figure mock-ups 3 and 4: the gray bars highlight the rescue medication windows for that subject; the time axes are set to ensure the entire period is captured and doesn't end at the limits of the figure. Use the indicated figure mock-up for the following figures.*

Use Figure mock-up 1 for the following (do not include EXPAREL 266 mg):

Figure 1.1: Plot of Mean Pain Intensity Score (VAS) vs Time through 48 hours – Efficacy Analysis Set
Figure 1.2: Plot of Mean Pain Intensity Score (VAS) vs Time through 48 hours – Per-protocol Analysis Set

Use Figure mock-up 2 for the following (do not include EXPAREL 266 mg and the x-axis should track through 76 hours):

Figure 2.1: Plot of Mean Pain Intensity Score (VAS) vs Time through 72 hours – Efficacy Analysis Set
Figure 2.2: Plot of Mean Pain Intensity Score (VAS) vs Time through 72 hours – Per-protocol Analysis Set

Use Figure mock-up 3 for the following (do not include EXPAREL 266 mg subjects, use actual hours since the end of surgery and not scheduled hours, include all VAS scores collected, include the following footnote "RCR = Rotator Cuff Repair; TSA = Total Shoulder Arthoplasty;"):

Figure 3.1: Plot of Individual Subject Pain Intensity Score (VAS) vs Time through 48 hours – Efficacy Analysis Set
Figure 3.2: Plot of Individual Subject Pain Intensity Score (VAS) vs Time through 48 hours – Per-Protocol Analysis Set

Use Figure mock-up 4 for the following (do not include EXPAREL 266 mg subjects, use actual hours since the end of surgery and not scheduled hours, include all VAS scores collected, the x-axis should track through 76 hours, include the following footnote "RCR = Rotator Cuff Repair; TSA = Total Shoulder Arthoplasty;"):

Figure 4.1: Plot of Individual Subject Pain Intensity Score (VAS) vs Time through 72 hours – Efficacy Analysis Set
Figure 4.2: Plot of Individual Subject Pain Intensity Score (VAS) vs Time through 72 hours – Per-Protocol Analysis Set