STATISTICAL ANALYSIS PLAN

A Multicenter, Prospective, Active Controlled, Real World, Phase 4 Study of EXPAREL® in Multimodal Regimens Compared with Standard of Care for Postsurgical Pain Management in Subjects Undergoing Lumbar Posterior Spine Surgeries (FUSION)

Protocol No.:	402-C-413
IND No.:	Not applicable
Study Phase:	4
Study Drug:	EXPAREL® (bupivacaine liposome injectable suspension)
Date/Version:	19 October 2020/Version 1.0
Prepared by:	Ashley Pajak, MS Pacrira Pharmaceuticals, Inc.
Sponsor:	Pacira Pharmaceuticals, Inc. 5 Sylvan Way Parsippany, NJ 07054 Tel: 973-254-3560

SIGNATURE PAGE

Approved by:	DocuSigned by: Don Manning Signer Name: Don Manning Signing Reason: I approve this document Signing Time: 21-Oct-2020 | 04:15 AM EDT E092D856DC394A9B80AB96BC2794DF0F Donald Manning, MD, PhD Chief Medical Officer, Clinical Operations	21-Oct-2020 Date
Approved by:	DocuSigned by: Michael Rozycki Signer Name: Michael Rozycki Signing Reason: I approve this document Signing Time: 19-Oct-2020 | 11:47:01 AM PDT B4308C39715A4ED49144E886EF300CA3 Michael Rozycki, PhD Vice President, Regulatory Affairs	19-Oct-2020 Date
Approved by:	DocuSigned by: Gary Nevins Signer Name: Gary Nevins Signing Reason: I approve this document Signing Time: 20-Oct-2020 | 04:46 PM EDT 558D44F13780486C86D569374F58CB46 Gary Nevins, DC Executive Medical Director, Clinical Operations	20-Oct-2020 Date
Approved by:	DocuSigned by: Vincent Yu Signer Name: Vincent Yu Signing Reason: I approve this document Signing Time: 19-Oct-2020 | 12:16:02 PM PDT 381A73A2808A488ABDBCE0932644F2EC Vincent Yu, PhD Vice President, Biometrics	19-Oct-2020 Date

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

Abbreviation	Description
ADL	Activities of daily living
AE	Adverse event
AICC	Corrected Akaike information criterion
ASA	American Society of Anesthesiology
ATC	Anatomical therapeutic class
AUC	Area under the curve
BIC	Schwarz's Bayesian information criterion
BLOQ	Below the limit of quantification
BMI	Body mass index
BPI-sf	Brief Pain Inventory – short form
bpm	Beats per minute
CAS	Color Analog Scale
CI	Confidence interval
CMP	Complete metabolic panel
CRF	Case report form
CSR	Clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
CV	Coefficient of variation
EMA	European Medicines Agency
ER	Emergency room
GM	Geometric mean
HADS	Hospital Anxiety and Depression Scale
HCl	Hydrochloride
hr, h	Hour
ICF	Informed consent form
ICH	International Council for Harmonisation
IM	Intramuscular
IV	Intravenous
LIA	Local infiltration analgesia
LOS	Length of stay
MCID	Minimum clinically important difference
MedDRA	Medical dictionary for regulatory affairs
min	Minutes

Abbreviation	Description
mg MED	Morphine equivalent dose in mg
mg	Milligram
MPADSS	Modified Post-Anesthesia Discharge Scoring System
n	Number of subjects
NCI	National Cancer Institute
NRS	Numerical Rating Scale
OCC	5-item Opioid Compliance Checklist
ORAE	Opioid-related adverse events
OR-SDS	Opioid Related-Symptoms Distress Scale
PACU	Post-Anesthesia Care Unit
PO	Oral
PT	Preferred Term
SAE	Serious adverse event
SAP	Statistical analysis plan
SC	Subcutaneous
SD	Standard deviation
SOC	Standard of care
SOPA	Survey of Pain Attitudes
TEAE	Treatment-emergent adverse event
TLF	Tables, listings and figures
USFDA	United States Food and Drug Administration
WHO	World Health Organization
WHO-DD	World Health Organization – Drug Dictionary

1. INTRODUCTION

This Statistical Analysis Plan (SAP) describes the planned statistical analysis and reporting of the clinical study 402-C-413 titled "A Multicenter, Prospective, Active Controlled, Real World, Phase 4 Study of EXPAREL® in Multimodal Regimens Compared with Standard of Care for Postsurgical Pain Management in Subjects Undergoing Lumbar Posterior Spine Surgeries (FUSION)". This study is intended to evaluate postsurgical opioid consumption in adult subjects receiving EXPAREL and undergoing posterior lumbar spine surgeries.

This study was prematurely terminated by the sponsor. At the time of termination, the study has enrolled 65 subjects.

The purpose of this SAP is to outline how the collected data will be summarized and presented for the abbreviated study report.

The following documents were reviewed in preparation of this SAP:

- Amendment 1 of Protocol 402-C-413 issued on 25 February 2019.
- Case Report Form (CRF) final version 4.0 issued on 06 July 2020.
- 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 the collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analyses.

2. STUDY OBJECTIVES

2.1 Primary Objective

The primary objective of this study is to compare postsurgical opioid consumption through 72 hours postsurgery in patients receiving local infiltration analgesia (LIA) with EXPAREL and bupivacaine hydrochloride (HCl; EXPAREL group) with that of patients receiving standard of care (SOC; Control group) in adult subjects undergoing posterior lumbar spine surgeries where both groups are receiving a multimodal pain regimen.

2.2 Secondary Objectives

The secondary objectives are to:

1. Compare safety and effectiveness outcomes following LIA with EXPAREL and bupivacaine HCl versus SOC in adult subjects undergoing posterior lumbar spine surgeries through 72 hours, including time to first opioid, opioid-related adverse events (ORAEs).
2. Compare health outcomes following LIA with EXPAREL and bupivacaine HCl versus SOC in adult subjects undergoing posterior lumbar spine surgeries, including discharge readiness, hospital (or other facility) length of stay (LOS), discharge disposition, hospital readmissions, and health service utilization.

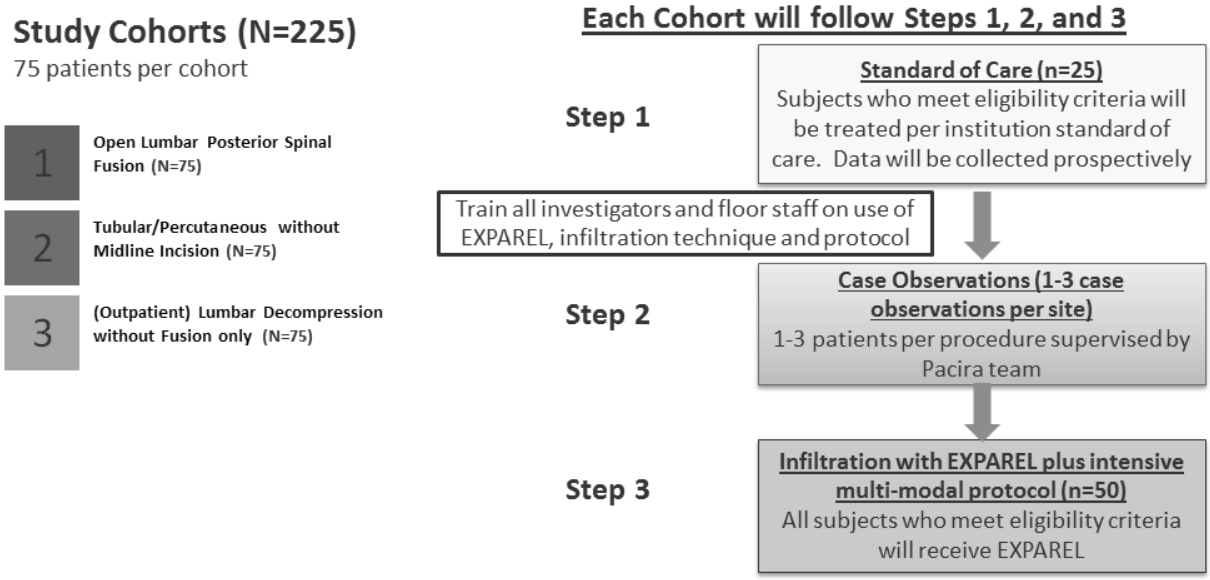
3. STUDY OVERVIEW

This is a Phase 4, multicenter, prospective, active-controlled, real-world study in approximately 225 adult subjects undergoing posterior lumbar spine surgeries under general anesthesia. This will be an open-label study and neither subjects nor investigators will be blinded for study group allocation. This study will include three cohort groups: cohort 1 – open lumbar spinal fusion technique ("open" cohort); cohort 2 – minimally invasive tubular and/or percutaneous pedicle screw insertion for lumbar decompression with or without fusion ("tubular/percutaneous without midline incision" cohort); and cohort 3 – lumbar decompression surgery (LDS) without fusion (discectomy or laminectomy cohort) outpatient cohort.

The initial sample size in each study cohort (i.e., cohort 1, cohort 2 and cohort 3) is estimated at 75 subjects (50 subjects with EXPAREL and 25 subjects with Control group), for a total of 225 subjects in all three cohorts. Within each assigned cohort, subjects will be allocated in a 2:1 ratio to the EXPAREL (50 subjects) and Control group (25 subjects).

The following sequence will be carried out for all cohorts: First, the subjects who meet eligibility criteria will be treated according to the institution's SOC. Their data will be collected prospectively. Next, at each investigational center, the administration of EXPAREL and bupivacaine HCl to the first 1 to 3 subjects in each cohort will be observed to ensure that the correct procedure for infiltration as described in the infiltration guide is being followed. If the infiltration was performed correctly, the subject will be included in the study. If the infiltration was performed incorrectly, the subject will continue in the study but will be removed from statistical analysis and will be replaced to ensure at least 50 evaluable EXPAREL patients are enrolled per cohort. If subjects are discontinued for other reasons, they will be replaced such that a total sample size of 75 fully evaluable subjects is obtained in each study cohort, with 50 in the EXPAREL group and 25 in the Control group. Criteria for being fully evaluable will be defined in detail in Section 5.

Figure 1 Study Schema



Source: Protocol, Amendment 1, 25 February 2019

4. DEFINITIONS

Study Day

Study Day is calculated as the date of the event minus the date of the start of surgery plus one (1), if the date of event is on or after the date of the start of surgery. If the date of the event is before the date of the start of surgery, study day is the date of the event minus the date of the start of surgery.

Time 0 (zero)

Time 0 is defined as the date and time of the end of surgery.

Treatment-emergent Adverse Events

Treatment-emergent adverse events (TEAEs) are those with onset between the end date and time of surgery, and the end of the study (Study Day 30 or until termination from the study).

Baseline

Baseline measurement or assessment is defined as the last available non-missing measurement or assessment prior to the start of surgery.

5. ANALYSIS SETS

All Subjects: all the listings presented in this SAP will be based on all enrolled subjects. Includes the following subjects who enrolled but did not undergo surgery; 101-01-0013, 101-03-0034, 109-02-0001, 113-03-0039.

6. STATISTICAL METHODS

6.1 General Principles

Only listings of subject data collected during the study will be provided. All listings will be sorted by treatment group, site ID, subject ID, and, if applicable, collection date and time.

6.1.1 Handling Missing Values

Data will be included in the listing as is. No imputed values will be included in the listings. However, in order to provide the drug safety profile, the missing or partial date/time will be imputed only for the determination of treatment emergency or prior/concomitant status.

6.1.1.1 Exposure, Surgery, and Rescue Opioid Medication Date or Time

It is expected that all necessary information on study drug exposure and surgery (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.

6.1.1.2 Adverse Event or Concomitant Medications Dates or Time.

For adverse events (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 year of the start of surgery.
- If the month is unknown, then:
  - If the year matches the year of start of surgery, then the month and day of the dose of study drug date will be used to impute the missing month and corresponding day.
  - Otherwise, ‘January’ will be assigned.
- If the day is unknown, then:
  - If the month and year match the month and year of the dose of start of surgery, then the day of the start of surgery date will be imputed.
  - Otherwise, ‘01’ will be assigned.
- If the time is unknown, then:
  - If the date (day, month, and year) matches the date of the start of surgery, then the end time of the surgery will be imputed.
  - Otherwise, ’00:00’ will be assigned.

For partial stop date/time:

- If the year is unknown, then the date will be assigned the year that subject had surgery, and time will be set to the last time of the day (‘23:59’).
- If the month is unknown, then month of start of surgery 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’), with the exception of end times for epoch in any CDISC dataset, where next day and ’00:00’ would be assigned.

6.2 Subject Disposition

A listing of subject disposition will be provided, which will include information on study completion status among others.

6.3 Description of Demographics and Baseline Characteristics

6.3.1 Demographics

Listing of demographic data will include:

- Initals
- Date of Birth (DOB)
- Age (years)
- Sex
- Ethnicity
- Race

6.3.2 Baseline Characteristics

Listing of baseline characteristic data will include:

- Screening Survey of Pain Attitudes (Single-item SOPA)
- Screening Hospital Anxiety and Depression Scale (HADS)
- Screening 5-item Opioid Compliance Checklist (OCC)
- Height (cm)
- Weight (kg)
- Body mass index (BMI;kg/m^2)

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 meters using the conversion factor of 0.0254 meters to 1 inch.

6.4 Surgery Characteristics and Prior Staged Procedure

Surgery characteristics include duration of surgery, total incision length, and type of procedure. Duration of surgery is calculated as the difference between the end of surgery and start of surgery times and reported in hours. Surgical characteristics will be included in data listings.

Prior staged procedue characteristics will be included in data listings.

6.5 Intraoperative, Prior, Concomitant, and Other Mediciations

Intraoperative, prior, and concomitant medications will be coded using the World Health Organization Drug Dictionary (WHODrug version: march 2019 B3) and will be classified according to the default anatomical therapeutic chemical (ATC 4) classification term and preferred term (PT).

Intraoperative medications are defined as medications given as part of the surgical procedure. These may include anesthesia, opioids or other medications and are collected on the intraoperative medication page of the case report form.

Prior medications are defined as medications with a stop date and time prior to the start of surgery and reported on the prior/concomitant medication page of the case report form.

Concomitant medications are defined as medications taken after the start of surgery (i.e., started prior to the start of surgery and continued after or started after the start of surgery) and reported on the prior/concomitant medication page of the case report form.

Data listings will be created for all medications, with separate listings for intraoperative, prior, concomitant, multimodal pain pre-operative, multimodal pain post-operative, prescription daily pain, and rescue medications.

A listing mapping the ATC class and PT to verbatim term will be presented.

6.6 Medicial History

Relevant medicial history and surgery will be presented in a by-subject listing.

6.7 Measurements of Treatment Compliance

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

6.8 Study Drug Exposure

A listing of study drug exposure, which includes volume of injection administered will be provided.

6.9 Efficacy Analysis

Listing of the following efficacy assessments will be provided:

- Pain intensity score using the NRS
- OR-SDS at 24, 48, and 72 hours postsurgery, at discharge, and at 14 days
- Brief Pain Inventory – Short Form at screening/baseline, 24 hours, 48 hours, and 72 hours, at discharge, and at 14 days

6.10 Health Outcomes Assessments

Listing of the following health outcome assessments will be provided:

- Post-Anesthesia Care Unit (PACU)- The date and time of admission and discharge, and the hours spent in the PACU will be provided in a listing. The hours spent in PACU will be computed as the date and time of discharge from PACU minus the date and time of admission to PACU.
- Surgical Facility- The date and time of admission and discharge, and the hours spent in the step-down and surgical facility will be provided in a listing.
- Modified Post-Anesthesia Discharge Scoring System (MPADSS) at 24, 48, and 72 hours, or at discharge, or until the subject attains a score of 9, whichever occurs first.
- Discharge Disposition
- Day 14 Call to doctor and office visits related to pain
- Day 30 Call to doctor and ER visits related to pain, and pain-related/all-casue 30-day readmissions

6.11 Safety Analyses

Safety assessments in this study consist of AEs. Adverse events will be collected from the time of informed consent through to the final Day 30 visit.

6.11.1 Adverse Events

All AEs will be mapped to PTs and related system/organ class using the Medical Dictionary for Regulatory Activities (MedDRA Version 22.0).

An AE will be considered TEAE if the onset date and time is between the end time and date of surgery and the final Day 30 visit. An AE will be considered related to study drug if “Possible”, “Probable” and “Definite.

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 time of surgery). If an AE has a missing relationship it will be assumed to be “Related”.

A listing of all AEs will be provided, with a flag indicating TEAEs.

6.12 Interim Analysis

Interim analysis may be conducted to adjust to variability. Adaptive study design (i.e., adjustment of sample size, cohort sequence, type of surgical procedure, endpints, etc.) will be used.

7. SAMPLE SIZE REVIEW

The sample size for this study was based on the primary outcome measure of postsurgical opioid use in mg MED PO from the end of surgery (closure of wound/incision) until 72 hours postsurgery. Based on preliminary data, the coefficient of variation (CV) is approximately 60%. The minimum clinically important difference (MCID) for this outcome was estimated at 40%.

With these parameters and a beta of 0.2 (i.e., 80% power), an alpha of 0.05, a 2-sided test, and allocating subjects in a 2:1 ratio to the EXPAREL group or Control group to minimize barriers to enrollment for an approved and marketed medication, a total sample size of 75 fully evaluable subjects is required in each study cohort, with 50 subjects in the EXPAREL group and 25 subjects in the Control group. The same assumptions are made across all cohorts. Subjects who undergo the planned surgery and whose infiltration is performed correctly and who are not discontinued early from the study for any other reasons will be fully evaluable. Not fully evaluable subjects should be replaced. Given that this study will have a case observation period for the first few subjects in EXPAREL group, if observation is deemed correct and infiltration was performed correctly, subject can be included in the study. If observation is deemed incorrect and infiltration was performed incorrectly, subject will continue in the study but will be removed from statistical analysis and will be replaced to ensure at least 50 evaluable EXPAREL arm patients are enrolled per cohort. The total number of subjects in all three cohorts will be 225, with 150 in the EXPAREL group and 75 in the Control group. This is subject to adjustment per interim analysis if necessary.

8. 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. Rubin, DB. (1987). Multiple Imputation for Nonresponse in Surveys. New York: John Wiley & Sons.
3. 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.
4. Royal Statistical Society. The Royal Statistical Society: Code of Conduct, August 1993. http://www.rss.org.uk/about/conduct.html.

9. TIME AND EVENTS SCHEDULE OF STUDY PROCEDURES

9.1 Part 1

Study Procedure	Screening/ Baseline (1-30 days prior to surgery)	Pre-op	Intra-op	PACU	Post-op
Screening and Baseline					
Obtain signed ICF[a]	X				
Record medical and surgical history	X				
Record medication history[b]	X				
Record demographics and baseline characteristics	X				
Record opioid use in last 30 days to determine mg MED PO/day average	X				
Record height, weight, and BMI	X				
Confirm eligibility	X				
Urine pregnancy test (UPT) (for women of childbearing potential)	X				
NRS for pain at the pre-surgical area	X				
Survey of Pain Attitudes (Single-item SOPA)	X				
Brief Pain Inventory – short form (BPI-sf)	X				
Hospital Anxiety and Depression Scale (HADS)	X				
5-item Opioid Compliance Checklist (OCC)[c]	X				
Record AEs and medications to treat AEs from the time ICF was signed	←	—	—	—	→
Day of surgery					
Confirm eligibility; UPT does not need to be repeated		X			
Administer scheduled presurgical medications		X			
Record surgery start and stop times			X		
Prepare study drug			X		
Administer study drug; record start and stop times			X		
Record intraoperative opioids administered and doses, and all concomitant medications			X		
Record times and doses of all opioid and non-opioid rescue medications administered			X		
Post-surgery[d]					
Record date, time, and dose of rescue postsurgical analgesics					X
Record date, times, and doses of all multimodal scheduled medications administered					X
Record date, time of admission to, and time of discharge from different hospital units (PACU, step-down)				X	
Record concomitant medications		←	—	—	→

Abbreviations: AE = Adverse event; BMI = Body mass index; BPI-sf = Brief Pain Inventory – short form; HADS = Hospital Anxiety and Depression Scale; ICF = Informed consent form; MED = Morphine equivalent dosing; OCC = 5-item Opioid Compliance Checklist (Jamison 2014; Jamison 2016); PACU = Post-anesthesia care unit; PO = per os (oral); SOC = standard of care; SOPA = Survey of Pain Attitude; UPT = urine pregnancy test.

[a] No more than 30 days should pass between signing of the ICF and performance of the surgery. Subjects will be screened within 30 days prior to surgery; screening on the day of surgery will be allowed but is discouraged. If a subject can only be screened on the day of surgery, the informed consent process must still be started at least 24 hours prior to the conduct of any screening procedures that are not considered SOC at the institution and such procedures may not be performed until written informed consent is provided. All screening procedures that are not SOC must be performed and documented within the 30-day time window (inclusive of the day of surgery for those subjects who can only be screened on the day of surgery) as described here. During the screening visit, subjects will be assessed for any past or present medical conditions that in the opinion of the investigator would preclude them from study participation.

[b] Record any medications for the condition for which the procedure is being performed that were administered within 30 days prior to screening.

[c] Sources for 5-item OCC are Jamison 2014 and Jamison 2016.

[d] All assessments conducted after baseline (prior to the study drug administration) will be timed from the end of surgery. Postsurgical is defined as a period after the end of surgery. End of surgery is defined as the time (when the last incision/wound is closed).

9.2 Part 2- After PACU Arrival

	From End of Surgery 6-72 Hours[a]									Discharge	Phone call or Visit[a]	Phone call[b]
Time Point ± Time window	6 hrs ±1 hr	12 hrs ±1 hr	18 hrs ±1 hr	24 hrs ±1 hr	30 hrs ±2 hr	36 hrs ±2 hr	42 hrs ±2 hr	48 hrs ±2 hr	72 hrs ±4 hr[b]		14 days ±3 days[a]	30 days ±3 days
Study Procedure												
NRS for pain at surgical site	X	X	X	X	X	X	X	X	X	X	X	
BPI-sf				X				X	X	X	X	
Record date and time of all opioid and non-opioid rescue medications[a]	←	—	—	—	—	—	—	—	—	—	→	
OR-SDS				X				X	X	X	X	
MPADSS[c]				X				X	X	X[c]		
Record date and time of discharge										X		
Record subject discharge disposition										X		
Document any unscheduled phone calls or office visits related to pain											X	
Document any requests for refills for opioid medication											X	
Record persistent opioid use by asking the subject "Are you currently taking opioid medication to manage pain from your spine surgery?"												X
Document any hospital readmissions related to pain												X
Document hospital readmissions for any cause												X
Document any unscheduled visits to the ER related to pain												X
Record date and time of AEs and medications to treat AEs (with dosage)	←	—	—	—	—	—	—	—	—	—	—	→

Abbreviations: AE=adverse event; BPI-sf = Brief Pain Inventory – short form; ER = Emergency room; hr/hrs = hour(s); MPADSS = Modified Post-Anesthesia Discharge Scoring System; NRS=numeric rating scale; OR-SDS = Opioid-Related Symptom Distress Scale.

[a] Subjects are to record their responses to subject questionnaires on an electronic device (eDiary) at screening, while in the hospital (or other facility), and at Day 14. Every day from discharge through Day 14, subjects are to record in the eDiary any pain medication (date, time, and dose) taken in the prior 24 hours in addition to recording questionnaire responses. Subjects who were lent an eDiary will have to return to the site at 14 days at which time they are to return the device. Subjects who used their own device will have a follow-up phone call at Day 14. All subjects will have a follow up call at 30 days after the surgery.

[b] For all subjects, if discharge occurs prior to 72 hours postsurgery, all Discharge assessments are to be performed at the time of discharge. After discharge, all scheduled assessments should be performed at the scheduled time points (i.e., NRS pain assessments at 6, 12, 18, 24, 30, 36, 42, 48, and 72 hours postsurgery; BPI-sf and OR-SDS at 24, 48, and 72 hours; and date, time, and dose of all opioid and non-opioid rescue medications) and recorded in the eDiary.

[c] Discharge readiness via the MPADSS will be assessed at 24, 48, and 72 hours and/or discharge or until the subject attains a score of 9, whichever occurs first.

Note: Early Termination: Whenever possible, subjects discontinuing the study should complete end of study (EoS) assessments. Subjects discontinuing prior to 72 hours are to complete the 72 hour assessments as EoS assessments. If early termination occurs after discharge but prior to Day 14, Day 14 assessments are to be completed as EoS assessments. If early termination occurs after Day 14 but prior to Day 30, Day 30 assessments are to be completed as EoS assessments.

10. LAYOUT OF LISTINGS

Listings will have 10-point font size. The listing will have Times New Roman, Courier New, or SAS Monospace type face. All final listings will be provided in both PDF and Word (or RTF) file formats.

Titles on the Listings should appear as following:

```
Listing 16.2-1.1.1
Subject Disposition- All Subjects
Cohort: Cohort 1; Treatment: EXPAREL
```

The text "Cohort: Cohort 1; Treatment: EXPAREL" refers to the cohort and treatment group. There should be a page break between the cohort and treatment group and should be presented in the order of:

```
Cohort: Cohort 1; Treatment: SOC
Cohort: Cohort 1; Treatment: EXPAREL
Cohort: Cohort 1; Treatment: NOT TREATED
Cohort: Cohort 2; Treatment: SOC
Cohort: Cohort 2; Treatment: EXPAREL
Cohort: Cohort 2; Treatment: NOT TREATED
Cohort: Cohort 3; Treatment: SOC
Cohort: Cohort 3; Treatment: EXPAREL
Cohort: Cohort 3; Treatment: NOT TREATED
```

Listings should be generally ordered by Cohort, Treatment, Site, Subject and Date where applicable. If data is missing in a column, the column may be populated with "-" for reading ease.

11. TABLE OF CONTENTS FOR LISTING MOCK-UPS

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-1.1: Subject Disposition- All Subjects

Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Date of the Start of the Last Visit	Date of Last Contact	End of Study Status	Primary Reason for Early Termination	If Other, Specify	Additional Early Termination Details
XXX	XX-YYYY	DDMONYYYY	DDMONYYYY	XXXXXXXX	XXXXXX	XXXXX	XXXXXXX

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

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-2: Enrollment- All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Informed Consent Date (Day)	Is the Subject Enrolled?	Enrollment Date/Time (Day)	Enrollment Cohort
XXX	XX-YYYY	DDMONYYYY (XX)	XXX	DDMONYYYYTHH:MM (XX)	XXXXX

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

SAS X.Y Program: program_name

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-3: Inclusion/ Exclusion Criteria- Failures Subjects

Cohort: -; Treatment: SCREEN FAILURES

Site	Subject	Informed Consent Date	Protocol Version Enrolled Under	Criteria ID Failed
XXX	XX-YYYY	DDMONYYYY	Version 1	XXXXXXXXX, XXXXXXXX

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

SAS X.Y Program: program_name

Programmer Note: column “Criteria ID Failed” should read “Inclusion 09” for example. progra

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-4.1: Demographics – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name;*

Site	Subject	Initials	DOB	Age (yrs)	Sex	Ethnicity	Race
XXX	XX-YYYY	AMZ	DDMONYYYY	XX	X	XXXXXXXXX	XXXXXXXXX
XXX	XX-YYYY	AMZ	DDMONYYYY	XX	X	XXXXXXXXX	XXXXXXXXX

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

SAS X.Y Program: program_name

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

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-4.2: Demographics – Screen Failures
Cohort: *cohort;* TREATMENT: Screen Failures*;*

Site	Subject	Initials	DOB	Age (yrs)	Sex	Ethnicity	Race
XXX	XX-YYYY	AMZ	DDMONYYYY	XX	X	XXXXXXXXX	XXXXXXXXX
XXX	XX-YYYY	AMZ	DDMONYYYY	XX	X	XXXXXXXXX	XXXXXXXXX

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

SAS X.Y Program: program_name

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

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-4.3: Demographics – Subject Enrolled but No Surgery
Cohort: *cohort;* TREATMENT: Screen Failures*;*

Site	Subject	Initials	DOB	Age (yrs)	Sex	Ethnicity	Race
XXX	XX-YYYY	AMZ	DDMONYYYY	XX	X	XXXXXXXXX	XXXXXXXXX
XXX	XX-YYYY	AMZ	DDMONYYYY	XX	X	XXXXXXXXX	XXXXXXXXX

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

SAS X.Y Program: program_name

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

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-5.1: Baseline Characteristics (Survey of Pain Attitudes (SOPA))– All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Date (Day)	Data Type	Data
XXX	XX-YYYY	DDMONYYYY (XX)	Q1: There is little I can do to ease my pain	0 = This is very untrue for me
			Q2: My pain does not stop me from leading a physically active life	0 = This is very untrue for me
			Q3: The pain I feel is a sign that damage is being done	0 = This is very untrue for me
			Q4: There is a connection between my emotions and my pain level	0 = This is very untrue for me
			Q5: I will probably always have to take pain medications	0 = This is very untrue for me
			Q6: When I am hurting, I deserve to be treated with care and concern	0 = This is very untrue for me
			Q7: I trust that doctors can cure my pain	0 = This is very untrue for me

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

SAS *X.Y* *Program: program_name*

Programmer Note: For column "Data Type" please display as verbatim in the shell not as what is presented in QS.QSTEST

Listing 16.2-5.2: Baseline Characteristics (Hospital Anxiety and Depression Score (HADS))- All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Date (Day)	Data Type	Data
XXX	XX-XXX	DDMONYYYY (XX)	(A) I feel tense or 'wound up'	Very often
			(D) I still enjoy the things I used to enjoy	Very often
			(A) I get a sort of frightened feeling as if something awful is about to happen	Very often
			(D) I can laugh and see the funny side of things	Very often
			(A) Worrying thoughts go through my mind	Very often
			(D) I feel cheerful	Very often
			(A) I can sit at ease and feel relaxed	Very often
			(D) I feel as if I am slowed down	Very often
			(A) I get a sort of frightened feeling like "butterflies" in the stomach	Very often
			(D) I have lost interest in my appearance	Very often
			(A) I feel restless as if I have to be on the move	Very often
			(D) I look forward with enjoyment of things	Very often
			(A) I get sudden feelings of panic	Very often
			(D) I can enjoy a good book or radio or TV Program	Very often
			Total Score Anxiety	9
			Total Score Depression	9

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

SAS *X.Y* *Program:program_name*

Programmer Note: For column "Data Type" please display as verbatim in the shell not as what is presented in QS.QSTEST

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-5.3: Baseline Characteristics (5-Item Opioid Compliance Checklist (OCC) – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Date (Day)	Data Type	Data
XXX	XX-XXX	DDMONYYYY (XX)	Over the past month have you:	
			1. Lost or misplaced your opioid medications?	Yes
			2. Run out of your pain medication early?	Yes
			3. Missed any scheduled medical appointments?	Yes
			4. Used any illegal or unauthorized substances?	Yes
			5. Been completely honest about your personal drug use?	Yes

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

SAS X.Y *Program:program_name*

Programmer Note: For column "Data Type" please display as verbatim in the shell not as what is presented in QS.QSTEST

Pacira Pharmaceuticals, Inc (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-6.1: Pregnancy test- All Female Subects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Is subject of child bearing potential?	If Yes, Was Urine Pregnancy Test done?	Test Result
XXX	XX-YYYY	X	X	XXXXX

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

Pacira Pharmaceuticals, Inc (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-6.2: Pregnancy test- Female Screen Fails

Site	Subject	Is subject of child bearing potential?	If Yes, Was Urine Pregnancy Test done?	Test Result
XXX	XX-YYYY	X	X	XXXXX

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

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-7.1: Admission and Discharge- Post-Anesthesia Care Unit (PACU) – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Admission Date/Time (Day)	Discharge Date/Time (Day)	Total length of stay (hours)
XXX	XX-YYYY	DDMONYYYYTHH:MM (XX)	DDMONYYYYTHH:MM (XX)	XXX.X

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

SAS X.Y Program: *program_name*

Programmer Note: For column "Total length of stay (hours)" please populate with the numeric number not as P0DT1H24M as displayed in SDTM.HO.HODUR

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-413
EXPAREL

Listing 16.2-7.2: Admission and Discharge – Surgical Facility – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Admission Date/ Time (Day)	Discharge Date/ Time (Day)	Total length of stay in step-down (hours)	Total length of stay in hospital/facility (hours)
XXX	XX-YYYY	DDMONYYYYTHH:MM (XX)	DDMONYYYYTHH:MM (XX)	XX	XX

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

SAS X.Y Program: *program_name*

Programmer Note: For column "Total length of stay in hospital/facility (hours)" please populate with the numeric number not as P0DT1H24M as displayed in SDTM.HO.HODUR

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-8.1: Surgery Characteristics- Procedure – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Start Date/ Time (Day)/ End Date/Time (Day)/ Duration [1]	Procedure Name	Surgery Performed by	Incision Length (cm)
XXX	XX-YYYY	DDMONYYYYTHH:MM (XX)/ DDMONYYYYTHH:MM (XX)/ XXXX	XXXXXX/ Subtypes	XXX	3

[1] Duration of surgery is calculated as the difference between the end of surgery and start of surgery times and reported in hours

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

Pacira Pharmaceuticals, Inc (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-8.2: Surgery Characteristics- Anesthesia- All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Surgery Start Date (Day)	Anesthsia Start Time	Anesthsia End Time	Type of Anesthesia
XXX	XX-YYYY	DDMONYYYY (XX)	HH:MM	HH:MM	XXXXX

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

SAS X.Y Program: program_name

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

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-8.3: Surgery Characteristics- Autograft- All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Surgery Start Date (Day)	Was an Autograft Taken?	If Yes, Harvest Site
XXX	XX-YYYY	DDMONYYYY (XX)	Yes	Other: XXXXXX

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

SAS X.Y Program: program_name

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-8.4: Surgery Characteristics-Prior Staged Procedure – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Surgery part of a staged procedure?	Staged Procedure Type	Start Date/Time (Day)	Stop Date/Time (Day)
XXX	XX-YYYY	XXX	XXXXXXXX	DDMONYYYYTHH:MM (XX)	DDMONYYYYTHH:MM (XX)

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

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-9: Medical/Surgical History – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Medical History Number	Data Type	Data
XXX	XX-YYYY	XX	Start Date	DDMONYYYY
			Stop Date	DDMONYYYY
			System Organ Class	XXXXXXXXXXXXXXXXXX
			Preferred	XXXXXXXXXXXXXXXXXXXX
			Verbatim	XXXXXXXXXXXXXXXXXXXXXX

Note: Only subjects with relevant medicial history or surgery are included in this listing.

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

Note to programmer: *If condition is ongoing, put ONGOING in stop row. Do not split a condition across pages. Insert a page break between subjects. The column "Medicial History Number" should correspond to MHSEQ*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-10: Study Drug Administration – All EXPAREL Subjects
Cohort: *cohort;* TREATMENT: EXPAREL

Site	Subject	Case Obs Correctly?	Start Date/Time (Day)/ End Date/Time (Day	Total Volume (mL)	Study Drug Administered by
XXX	XX-YYYY	XXX	DDMONYYYYTHH:MM (XX)/ DDMONYYYYTHH:MM (XX)	XXX	XXX

Note: Only subjects in Cohort 3 were administered EXPAREL.

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

SAS X.Y Program: program_name

Note to programmer: *If Not Done is checked then text should read 'Not Done: reason-text'.*

Pacira Pharmaceuticals, Inc. (Page X of Y) Protocol: 402-C-413
EXPAREL

Listing 16.2-11.1: All Adverse Events – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	TEAE	Data Type	Data
XXX	XX-YYYY	N	Start Date/ Time (Day)	DDMONYYYYTHH:MM (XX)
			Stop Date/ Time (Day)	DDMONYYYYTHH:MM (XX)
			AE Number	X
			System Organ Class	XXXXXXXXXXXXXXXXXX
			Preferred	XXXXXXXXXXXXXXXXXXX
			Verbatim	XXXXXXXXXXXXXXXXXXXXX
			Severity	XXXXXXXX
			Relationship to Study Drug	XXXXXXXX
			Action Taken with Subject	XXXXXXXXXXXXXXXXXXX
			Outcome	XXXXXXXXXXXXXX
			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: 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.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-413
EXPAREL

Listing 16.2-11.2.1: All Treatment Emergent Adverse Events – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Data Type	Data
XXX	XX-YYYY	Start Date/ Time (Day)	DDMONYYYYTHH:MM (XX)
		Stop Date/ Time (Day)	DDMONYYYYTHH:MM (XX)
		AE Number	X
		System Organ Class	XXXXXXXXXXXXXXXXXX
		Preferred	XXXXXXXXXXXXXXXXXXX
		Verbatim	XXXXXXXXXXXXXXXXXXXXX
		Severity	XXXXXXXX
		Relationship to Study Drug	XXXXXXXX
		Action Taken with Subject	XXXXXXXXXXXXXXXXXXXX
		Outcome	XXXXXXXXXXXXXX
		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.*

Pacira Pharmaceuticals, Inc. (Page X of Y) Protocol: 402-C-413
EXPAREL
Listing 16.2-11.2.2: All Treatment Emergent Adverse Events Related to Study Drug – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Data Type	Data
XXX	XX-YYYY	Start Date/ Time (Day)	DDMONYYYYTHH:MM (XX)
		Stop Date/ Time (Day)	DDMONYYYYTHH:MM (XX)
		AE Number	X
		System Organ Class	XXXXXXXXXXXXXXXXXX
		Preferred	XXXXXXXXXXXXXXXXXXX
		Verbatim	XXXXXXXXXXXXXXXXXXXXX
		Severity	XXXXXXXX
		Relationship to Study Drug	XXXXXXXX
		Action Taken with Subject	XXXXXXXXXXXXXXXXXXXX
		Outcome	XXXXXXXXXXXXXX
		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.*

Pacira Pharmaceuticals, Inc. (Page X of Y) Protocol: 402-C-413
EXPAREL

Listing 16.2-11.3.1: All Serious Adverse Events – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	TEAE	Data Type	Data
XXX	XX-YYYY	N	Start Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
			Stop Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
			AE Number	X
			System Organ Class	XXXXXXXXXXXXXXXXXX
			Preferred	XXXXXXXXXXXXXXXXXXX
			Verbatim	XXXXXXXXXXXXXXXXXXXXX
			Severity	XXXXXXXX
			Relationship to Study Drug	XXXXXXXX
			Action Taken	XXXXXXXXXXXXXXXXXXX
			Outcome	XXXXXXXXXXXXXX
			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.*

Pacira Pharmaceuticals, Inc. (Page X of Y) Protocol: 402-C-413
EXPAREL

Listing 16.2-11.3.2: All Non-serious Adverse Events – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	TEAE	Data Type	Data
XXX	XX-YYYY	N	Start Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
			Stop Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
			AE Number	X
			System Organ Class	XXXXXXXXXXXXXXXXXX
			Preferred	XXXXXXXXXXXXXXXXXXX
			Verbatim	XXXXXXXXXXXXXXXXXXXXX
			Severity	XXXXXXXX
			Relationship to Study Drug	XXXXXXXX
			Action Taken	XXXXXXXXXXXXXXXXXXX
			Outcome	XXXXXXXXXXXXXX
			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.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 402-C-413
EXPAREL, Inc.

Listing 16.2-11.4.1: All Treament Emergent Serious Adverse Events – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Data Type	Data
XXX	XX-YYYY	Start Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
		Stop Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
		AE Number	X
		System Organ Class	XXXXXXXXXXXXXXXXXX
		Preferred	XXXXXXXXXXXXXXXXXXX
		Verbatim	XXXXXXXXXXXXXXXXXXXXX
		Severity	XXXXXXXX
		Relationship to Study Drug	XXXXXXXX
		Action Taken	XXXXXXXXXXXXXXXXXXXX
		Outcome	XXXXXXXXXXXXXX
		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.*

Pacira Pharmaceuticals, Inc. (Page X of Y) Protocol: 402-C-413
EXPAREL

Listing 16.2-11.4.2: All Treatment Emergent Non-serious Adverse Events – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Data Type	Data
XXX	XX-YYYY	Start Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
		Stop Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
		AE Number	X
		System Organ Class	XXXXXXXXXXXXXXXXXX
		Preferred	XXXXXXXXXXXXXXXXXXX
		Verbatim	XXXXXXXXXXXXXXXXXXXXX
		Severity	XXXXXXXX
		Relationship to Study Drug	XXXXXXXX
		Action Taken	XXXXXXXXXXXXXXXXXXXX
		Outcome	XXXXXXXXXXXXXX
		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.*

Pacira Pharmaceuticals, Inc. (Page X of Y) Protocol: 402-C-413
EXPAREL
Listing 16.2-11.5: All Treament Emergent Study Drug Related Serious Adverse Events – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Data Type	Data
XXX	XX-YYYY	Start Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
		Stop Date/ Time (XX)	DDMONYYYYTHH:MM (XX)
		AE Number	X
		System Organ Class	XXXXXXXXXXXXXXXXXX
		Preferred	XXXXXXXXXXXXXXXXXXX
		Verbatim	XXXXXXXXXXXXXXXXXXXXX
		Severity	XXXXXXXX
		Relationship to Study Drug	XXXXXXXX
		Action Taken	XXXXXXXXXXXXXXXXXXXX
		Outcome	XXXXXXXXXXXXXX
		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.*

Pacira Pharmaceuticals, Inc. (Page X of Y) Protocol: 402-C-413
EXPAREL

Listing 16.2-12: Vital Signs – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Done?	Date/Time (Day)	Height (cm)	Weight (kg)	BMI
XXX	XX-YYYY	Yes	DDMONYYYYTHH:MM (XX)	XX	XX	XX
XXX	XX-YYYY	Yes	DDMONYYYYTHH:MM (XX)	XX	XX	XX
XXX	XX-YYYY	Yes	DDMONYYYYTHH:MM (XX)	XX	XX	XX
XXX	XX-YYYY	No, XXXXXX	DDMONYYYYTHH:MM (XX)	-	-	-

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

SAS X.Y Program:program_name

Note to programmer: *If Not Done is checked then text should read 'Not Done: reason-text'. If data is missing populate with "-".*

Pacira Pharmaceuticals, Inc. (Page X of Y) Protocol: 402-C-413
EXPAREL

Listing 16.2-13: Numeric Rating Scale (NRS) Pain Intensity Score – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Time Point / Asleep During Time Point [1]	Date/Time (Day)	NRS Pain Intensity Score
XXX	XX-YYYY	Screening	DDMONYYYYTHH:MM (XX)	-
		48 hours / No	DDMONYYYYTHH:MM (XX)	XXX
		Discharge	DDMONYYYYTHH:MM (XX)	XXX
		14 days	DDMONYYYYTHH:MM (XX)	XXX

[1] Asleep During Time Point only used for schelduled 6 – 72 hours.

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

SAS X.Y Program: program_name

Note to programmer: *Include all NRS scores. For colum* "Time Point / Asleep During Time Point [1]" a subject is considered to be asleep during an assessment if SDTM.QS.qscat=" NRS-R Pain Intensity" and QSREASND="ASLEEP"

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-14: Opioid Related Symptoms Distress Scale (ORSDS) – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Time Point	Date/Time (Day)	Symptom	Did Have	# Episodes	Often	Severe	Distress or Bother
XXX	XX-YYYY	24 hrs	DDMONYYYYTHH:MM (XX)	Fatigue	N		-		
				Drowsiness	-		Occasionally	Slight	A little bit
				Concentrate	N				
				Nausea	N				
				Dizziness	N				
				Constipation	N				
				Itching	N				
				Urination	N				
				Confusion	N				
				Retching/vomiting	N				

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

SAS X.Y Program: program_name

Note to programmer: *Add in all applicable visits.*

Pacira Pharmaceuticals (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-15: BPI-sf – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Timepoint	Date of Assessment	Data Type	Data
XXX	XX-YYYY	Screening	DDMONYYYYTHH:MM	Have you had pain, other than everyday pain kinds of pain today?	Yes
				Area where you feel pain	Front leg, Back Leg
				Area where it hurts the most	Front Leg
				Rate your pain that describes your pain at its worst in the last 24 hours	1
				Rate your pain that describes your pain at its least in the last 24 hours	2
				Rate your pain that describes your pain on average	3
				Rate your pain that describes your pain right now	2
				In the last 24 hours, how much relief have pain medications provided? (Percentage)	1
				During the past 24 hours pain has interfered with: General Activity	2
				During the past 24 hours pain has interfered with: Mood	3
				During the past 24 hours pain has interfered with: Walking Abililty	4
				During the past 24 hours pain has interfered with: Normal Work	2
				During the past 24 hours pain has interfered with: Relationships	1
				During the past 24 hours pain has interfered with: Sleep	1
				During the past 24 hours pain has interfered with: Enjoyment of life	3

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

SAS X.Y

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-16: Health Outcomes Assessments – MPADSS - All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Timepoint	Done?	Date/ Time (Day)	Data Type	Data
XXX	XX-YYYY	24 Hours	Yes	DDMONYYYYTHH:MM (XX)	Vital Signs	2 = <=20% of preoperative value
					Ambulation	2 = Steady gait/no dizziness
					Nausea/Vomiting	2 = Minimal
					Pain	2 = Minimal
					Surgical Bleeding	2 = Minimal
					Score	10
XXX	XX-YYYY	48 Hours	No, XX	DDMONYYYYTHH:MM (XX)		

MPADSS= Modified Post-Anesthesia Discharge Scoring System;

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

SAS X.Y

Note to programmer: *If Not Done is checked then text should read 'Not Done: reason-text'.*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-17: Health Outcomes Assessments- Discharge Disposition – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Where will the Subject be Discharged?
XXX	XX-YYYY	Home
XXX	XX-YYYY	Home
XXX	XX-YYYY	Home
XXX	XX-YYYY	Home

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

SAS X.Y Program: program_name

Programmer Note: if column "Where will the Subject be Discharged?" is Other, it should read "Other:*text*".

Pacira Pharmaceuticals, Inc (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-18.1: Phone Call / In Person Visit Day 14 (Pain Visits) - All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Completed?	Phone Call or In Person Visit?	Date of Visit (Day)	How Many Times Called Physician About Pain Related to Your Surgery?	Any Unscheduled Pain-Related Visits Since Discharge?	If Yes, Number of Pain-related Visits
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX	XXX
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX	XXX
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX	XXX
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX	XXX
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX	XXX

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

SAS X.Y Program: program_name

Note to programmer: *If Was Day 14 Visit Completed? is 'No' then text should read 'No: reason-text'.*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-18.2: Phone Call / In Person Visit Day 14 (Medication)- All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Completed?	Phone Call or In Person Visit?	Date of Visit (Day)	Any Requests for Refills for Opioid Medication?	If Yes, Number of Refill Requests
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX
XXX	XX-YYYY	XXX	XXX	DDMONYYYY(XX)	XXX	XXX

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name
Note to programmer: *If Was Day 14 Visit Completed? is 'No' then text should read 'No: reason-text'.*

Pacira Pharmaceuticals, Inc (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-19.1: Phone Call / In Person Visit Day 30 (Pain Visits) - All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Was Phone Call Made to the Subject?	Date of Phone Contact (Day)	Any Hospital/ Facility Readmissions Since Discharge? (Number)	If Yes, Of the Total Readmissions, How Many Were Related to Pain	Any ED Visits Since Subject Discharge? (Number)
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX (xx)	XXX	XXX (xx)
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX (xx)	XXX	XXX (xx)
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX (xx)	XXX	XXX (xx)
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX (xx)	XXX	XXX (xx)
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX (xx)	XXX	XXX (xx)

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

SAS X.Y Program: program_name

Note to programmer: *If Was Day 30 Visit Completed? is 'No' then text should read 'No: reason-text'.*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-19.2: Phone Call / In Person Visit Day 30 (Medications) - All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Was Phone Call Made to the Subject?	Date of Phone Contact (Day)	Currently Taking Opioid Medications?
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX
XXX	XX-YYYY	XXX	DDMONYYYY (XX)	XXX

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

SAS X.Y Program: program_name

Note to programmer: *If Was Day 30 Visit Completed? is 'No' then text should read 'No: reason-text'.*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-20.1: Multimodal Pain Medication – Pre-Operative – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Medication	Was Medication Taken?	Date/ Time (Day)	Dose (units)	Route
XXX	XX-YYYY	Tylenol (PO)	XXX	DDMONYYYYTHH:MM (XX)	XX(XXXX)	XX
		Gabapentin (PO)	XXX	DDMONYYYYTHH:MM (XX)	XX(XXXX)	XX
		Robaxin (PO)	XXX	DDMONYYYYTHH:MM (XX)	XX(XXXX)	XX
		Pregabalin (PO)	XXX	DDMONYYYYTHH:MM (XX)	XX(XXXX)	XX

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

SAS X.Y Program: program_name

Note to programmer: *If Mediciation is not taken then text should read 'No: reason-text'.*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-20.2: Multimodal Pain Medication – Post-Operative – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Medication	Was Medication Taken?	Date/ Time (Day)	Dose (units)	Route
XXX	XX-YYYY	Tylenol (PO)	XXX	DDMONYYYYTHH:MM (XX)	XX(XXXX)	XX
		Gabapentin (PO)	XXX	DDMONYYYYTHH:MM (XX)	XX(XXXX)	XX
		Robaxin (PO)	XXX	DDMONYYYYTHH:MM (XX)	XX(XXXX)	XX
		Pregabalin (PO)	XXX	DDMONYYYYTHH:MM (XX)	XX(XXXX)	XX

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

SAS X.Y Program: program_name

Note to programmer: *If Mediciation is not taken then text should read 'No: reason-text'.*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-20.3: Intraoperative Medications – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Data Type	Data
XXX	XX-YYYY	Start Date/ Time	DDMONYYYYTHH:MM
		End Date/ Time	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
		Dose	XXXXXXXX
		Unit	XXXXXXXX
		Route	XXXXXXXX
		Associated AE #	XXX AE # XX, XX

ATC=Anatomical therapeutic class

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

SAS *X.Y* Program: program_name

Note to programmer: *If medication has unknown end time, put 'Unknown' after date in End row. Do not split a medication across pages. The AE number should correspond SDTM.AE.AESEQ*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-20.4: Prescription Daily Pain Medications – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Data Type	Data
XXX	XX-YYYY	Start Date/ Time	DDMONYYYYTHH:MM
		Medication Number	X
		ATC Level 1	XXXXXXXXXXXXXXXXXX
		ATC Level 2	XXXXXXXXXXXXXXXXXXXX
		ATC Level 3	XXXXXXXXXXXXXXXXXXXXX
		ATC Level 4	XXXXXXXXXXXXXXXXXXXX
		Preferred Name	XXXXXXXXXXXXXXXXXXXX
		Verbatim	XXXXXXXXXXXXXXXXXXXX
		Dose	XXXXXXXX
		Unit	XXXXXXXX
		Route	XXXXXXXX

ATC=Anatomical therapeutic class

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

SAS *X.Y* Program: *program_name*

Note to programmer: *If medication has unknown end time, put 'Unknown' after date in End row. Do not split a medication across pages. If Unit or Route is 'Other', text should read 'Other: specify-text'. Insert a page break between subjects.*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-20.5: Rescue Medication – All Subjects
Cohort: *cohort;* TREATMENT: *treatment-name*

Site	Subject	Medication	Date/ Time (Day)	Dose (unit)	Route
XXX	XX-YYYY	XXXXXXXXXXXX	DDMONYYYYTHH:MM (XX)	XX(mg)	XXXXXXX
		XXXXXXXXXXXX	DDMONYYYYTHH:MM (XX)	XX(mg)	XXXXXXX
		XXXXXXXXXXXX	DDMONYYYYTHH:MM (XX)	XX(mg)	XXXXXXX
		XXXXXXXXXXXX	DDMONYYYYTHH:MM (XX)	XX(mg)	XXXXXXX

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

SAS X.Y Program: program_name

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-20.6: Prior Medications – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Reason for Use	Data Type	Data
XXX	XX-YYYY	XXXXXXXX	Start Date and Time	DDMONYYYYTHH:MM
			End Date and Time	DDMONYYYYTHH:MM
			Medication Number	X
			ATC Level 1	XXXXXXXXXXXXXXXXXX
			ATC Level 2	XXXXXXXXXXXXXXXXXXXX
			ATC Level 3	XXXXXXXXXXXXXXXXXXXXX
			ATC Level 4	XXXXXXXXXXXXXXXXXXX
			Preferred Name	XXXXXXXXXXXXXXXXXXXX
			Verbatim	XXXXXXXXXXXXXXXXXXX
			Dose (Unit)	XXXXXXXX (XXXXXXXX)
			Route	XXXXXXXX
			Frequency	XXXXXXXX
			Given for AE or MH?	XXXXXXXXXXXXXXXX AE # XX *(or MH # XX)*

ATC=Anatomical therapeutic class

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

SAS *X.Y* Program: *program_name*

Programmer Note: AE and MH number should correspond to AESEQ and MHSEQ

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-20.7: Concomitant Medications – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Reason for Use	Data Type	Data
XXX	XX-YYYY	XXXXXXXX	Start Date and Time	DDMONYYYYTHH:MM
			End Date and Time	DDMONYYYYTHH:MM
			Medication Number	X
			ATC Level 1	XXXXXXXXXXXXXXXXXX
			ATC Level 2	XXXXXXXXXXXXXXXXXXXX
			ATC Level 3	XXXXXXXXXXXXXXXXXXXXX
			ATC Level 4	XXXXXXXXXXXXXXXXXXX
			Preferred Name	XXXXXXXXXXXXXXXXXXXX
			Verbatim	XXXXXXXXXXXXXXXXXXX
			Dose (Unit)	XXXXXXXX (XXXXXXXX)
			Route	XXXXXXXX
			Frequency	XXXXXXXX
			Given for AE or MH?	XXXXXXXXXXXXXXX AE # XX *(or MH # XX)*

ATC=Anatomical therapeutic class

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

SAS *X.Y* *Program: program_name*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-21: Protocol Deviations – All Subjects
Cohort: *cohort;* Treatment: treatment-name

Site	Subject	Category	Date and Time	Description
XXX	XX-YYYY	XXX	DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXXXX

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

SAS X.Y Program: *program_name*

Note to programmer: *Subjects may have multiple deviations. Sort deviations by cohort, treatment, center, subject.*

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-22: 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 version 22.0

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

SAS X.Y Program: *program_name*

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

Pacira Pharmaceuticals, Inc. (Page X of Y) 402-C-413
EXPAREL

Listing 16.2-23: 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 Version March 2019 B3

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

SAS X.Y Program: *program_name*

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