STATISTICAL ANALYSIS PLAN

A Randomized, Single-Blind, Active-Controlled, Dose-Ranging Study to Evaluate the Pharmacokinetics, Safety, and Efficacy of Local Administration of DepoTXA for Reduced Postsurgical Bleeding in Subjects Undergoing Total Knee Arthroplasty

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1. SIGNATURE PAGE

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1. SIGNATURE PAGE

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2. TABLE OF CONTENTS

3. LIST OF ACRONYMS/ABBREVIATIONS

Acronym/Abbreviation	Description
AE	Adverse event
AESI	Adverse event of special interest
ATC	Anatomical therapeutic class
AUC	Area under the curve
BLOQ	Below the limit of quantification
BMI	Body mass index
BV	Blood volume
CRF	Case report form
CSR	Clinical study report
CV	Coefficient of variation
D1 Preop	Day 1 pre-operation
ECG	Electrocardiogram
EMA	European Medicines Agency
FDA	Food and Drug Administration
GMR	Geometric Mean Ratio
Hct	hematocrit
Hb	hemoglobin
ICF	Informed consent form
ICH	International Conference on Harmonization
IV	Intravenous
MedDRA	Medical dictionary for regulatory affairs
n	Number of subjects
NRS	Numeric Rating Scale
PACU	Post-anesthesia care unit
PK	Pharmacokinetics
PT	Preferred Term
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SE	Standard error
SOC	System Organ Class
SWAS	Surgical Wound Aspect Score
TEAE	Treatment-emergent adverse event
TKA	Total knee arthroplasty
TLF	Tables, listings and figures
TUG	Timed Up-and-Go
TXA	Tranexamic Acid
WHO-DD	World Health Organization - Drug Dictionary Enhanced

4. INTRODUCTION

This Statistical Analysis Plan (SAP) describes the planned statistical analysis and reporting of the clinical study 404-C-201 titled "A Randomized, Single-Blind, Active-Controlled, Dose-Ranging Study to Evaluate the Pharmacokinetics, Safety, and Efficacy of Local Administration of DepoTXA for Reduced Postsurgical Bleeding in Subjects Undergoing Total Knee Arthroplasty". The primary objective of this study is to evaluate pharmacokinetics of DepoTXA compared to intravenous (IV) tranexamic acid (TXA).

The structure and content of this SAP provides 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 (US Federal Register, 1998). All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association (American Statistical Association, 1999) and the Royal Statistical Society (Royal Statistical Society, 1993), 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 regarding 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 2 of Protocol 404-C-201 issued on 27SEP2017.
- CRF issued on 01MAR2017.
- 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 pharmacokinetics of DepoTXA compared to IV TXA.

5.2. Secondary Objectives

The secondary objectives of this study are to evaluate (1) the safety of DepoTXA, (2) the efficacy of DepoTXA (over 5 days) compared to IV TXA, and (3) a potential dose-related response to DepoTXA at 400, 800, and 1200 mg (33 mg/mL).

6. STUDY OVERVIEW

This is a Phase 2, randomized, single-blind, active-controlled dose-ranging study in patients scheduled to undergo total knee arthroplasty (TKA). Approximately 60 subjects (15 per treatment group) are planned for enrollment. Subjects will be randomized in a 1:1:1:1 ratio to receive DepoTXA 400 mg, DepoTXA 800 mg, DepoTXA 1200 mg, or IV TXA (Cyklokapron® 1 gram).

Blood samples for PK analysis will be obtained at baseline (prior to study drug administration); at 5, 15, and 30 minutes; and at 1, 2, 4, 6, 8, 12, 16, and 24 hours after study drug administration for all treatment groups. Additional blood samples will be collected at 36, 48, 60, 72, and 96 hours after study drug administration for DepoTXA-treated subjects.

Postsurgical efficacy assessments will include measurement of blood loss (as assessed by hemoglobin [Hb] and hematocrit [Hct] levels), transfusion requirement, knee flexion, timed up-and-go (TUG) test, knee and thigh measurements, numeric rating scale (NRS_ pain scores), days to independent ambulation, and the surgical wound aspect score (SWAS).

Postsurgical safety assessments will include vital signs, neurological assessment, clinical laboratory testing (hematology, chemistry, and coagulation), 12-lead electrocardiogram (ECG), and adverse event (AE) monitoring. Subject monitoring will include, but not be limited to, changes in vision, neurologic function, or renal function; and occurrence of hematoma, wound dehiscence/disruption, surgical site infection (per Centers for Disease Control and Prevention definition), nausea, vomiting, and diarrhea.

Adverse events of special interest (AESI) include changes in color vision, venous thromboembolism or pulmonary embolism, and oliguria. If an AESI or serious AE (SAE) occurs during the study, an unscheduled PK blood sample must be collected. In addition, vital signs, the neurological assessment, and clinical laboratory tests must be conducted, as appropriate. If a subject experiences changes in color vision, an ophthalmological consultation must be ordered.

7. DEFINITIONS

Study Day

Study Day 1 is defined as the day of surgery. 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 study drug administration have negative values while those on or after the date of surgery have positive values.

Treatment-emergent Adverse Events

A TEAE will be any adverse event or pre-existing medical condition that worsens in intensity after the start of study drug and within 30 days of the last dose.

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 in the Protocol for individual timepoint windows). Various time frames that are dependent on these windows are used in the data analyses. Table 1 defines the actual elapsed times with allowance for the windows that can be included in the window.

Table 1: Time Periods

Defined time frame	Acceptable elapsed times
5 min	3-7 min
15 min	12-18 min
30 min	25-35 min
1h	50-70 min
2h	105-135 min
4h	225-255 min
6h	345-375 min
8h	450-510 min
12h	690-750 min
16h	15-17h
24h	23-25h
36h	34-38h
48h	46-50h
60h	57-63h
72h	68-76h
96h	90-102h
120h	114-126h
Study Day 7	Study Day 6-8
Study Day 14	Study Day 13-15
Study Day 30 Call	Study Day 27-33
Study Day 60 Call	Study Day 57-63

If there are two or more data points that fit the time window the data point that occurs the closest, in absolute value, to the scheduled observation will be used.

Baseline

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

8. ANALYSIS SETS

The safety analysis set will include all subjects who received study drug. Subjects in the safety analysis set will be assessed according to the actual treatment they received.

The efficacy analysis set will include all subjects who received study drug and underwent the planned surgery. Subjects in the efficacy analysis set will be assessed according to their randomized treatment, regardless of the actual treatment they received.

The PK analysis set will include all subjects who received study drug, provided sufficient samples to allow for calculation of PK parameters ($AUC_{[0\text{-}tlast]}$ and global, C_{max} and T_{max}) required for analysis, and who do not have significant protocol deviations that may invalidate or bias the results. Subjects in the PK analysis set will be assessed according to the actual treatment they received.

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 and categorical variables will be tabulated with the 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 presenting multiple treatments,

- IV TXA will be represented in black with solid lines and dots;

  SAS Code: symbol interpol=spline width=1 value=dot line=1 c=black;
- DepoTXA 400 will be represented in red with solid lines and hollow triangles;

  SAS Code: symbol interpol=spline width=1 value=triangle line=1 c=red;
- DepoTXA 800 will be represented in green with solid lines and hollow circles;

  SAS Code: symbol interpol=spline width=1 value=circle line=1 c=green;
- DepoTXA 1200 will be represented in purple with solid lines and hollow squares;

  SAS Code: symbol interpol=spline width=1 value=square line=1 c=purple.

Figures presenting a single subject will be represented in black with solid lines and dots.

All tables will present DepoTXA 400 mg, DepoTXA 800 mg, DepoTXA 1200 mg, and IV TXA as separate columns, in this order.

9.1.1. Handling Missing Values

9.1.1.1. Post-baseline Cummulative Blood Loss

It is expected that all necessary information to calculate post-baseline cumulative blood loss 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. There will be no hypothesis testing and it is assumed that missing data on cumulative blood loss will be rare or non-existent, thus a single imputation method is expected to provide useful enough information to plan for the next phase of DepoTXA development. The following single imputation procedures will be used:

a) A simple linear imputation will be used for a missing value from the closest observed values prior and post for non-monotone missing data.

b) If the missing data are monotone, then last observed carried forward will be used.

It is currently assumed that approximately 84% of the total cumulative blood loss will occur within 12 hours post-surgery and approximately 94% of the total cumulative blood loss will occur within 24 hours post-surgery (Kumar, 2005).

9.1.1.2. Adverse Event Date or Time

It is expected that all necessary information on adverse events and the surgeries (start and stop date and time) will be complete. Unless an adverse event can be excluded as a treatment emergent by the known start and stop date/time, the adverse event should be considered treatment emergent.

9.1.1.3. Concomitant Medications Date or Time

It is expected that all necessary information on medications and surgeries (start and stop date and time) will be complete. Unless a medication can be excluded as a concomitant by the known start and stop date/time, the medication should be considered concomitant.

9.1.1.4. Adverse Event Severity or Relationship to Study Drug

If severity of an AE is not reported, then for tables of AEs by severity, the missing severity will not be imputed, but will be described in the footnote for the table. 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 or defined as 'definite' when no investigtor assessment is made.

9.1.2. Multiplicity Adjustments

Not applicable.

9.2. Subject Disposition

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

- Screened,
  - Screen failure
  - Reasons for screen failure (Did not meet Inclusion #1, ect.)
- Randomized
  - Randomized not treated
  - Randomized treated
  - Randomized did not undergo surgery
  - Randomized underwent surgery
- In the safety analysis set
- In the efficacy analysis set
- In the PK analysis set
- Completed the study as planned
- Discontinued from the study
- By reason for discontinuation from the study.

Percentages will be reported for the screen failures and enrolled subjects using the number of subjects screened as the denominator and for the safety, efficacy and PK analysis sets, completed study, discontinued from study, and reasons for discontinuation with the number of subjects

randomized as denominator. The percentages for the safety analysis set will use the number of subjects randomized and treated as the denominator.

Safety and PK analysis sets 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 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 (%)
- ASA classification – n (%)
- Country – n (%)

Age is calculated from the date the subject signed the informed consent form (ICF) and birth date. It is presented as the number of years between, rounding down to the nearest integer year. The following macro will be used to derive age:

```
%macro age_integer (dob=,eventdate=);
   floor((intck('month',&dob.,&eventdate.) - (day(&eventdate.)<day(&dob.)))/12);
%mend age_integer;
```

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. Summaries will be provided for all (safety, efficacy, and PK) 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:

- Total Blood Volume (BV; in mL)
- 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 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 and across treatment groups (Total). Summaries will be provided for all (safety, efficacy and PK) analysis sets. This summary table will show summaries across all sites and for each site separately.

Descriptive statistics (n, mean, standard deviation [SD], median, minimum and maximum) will be provided for total blood volume, height, weight, and BMI.

9.4. Surgery Characteristics

The following surgery characteristics will be summarized: duration of surgery, length of incision, trouniquet use, duration of tourniquet use, maximum pressure of tourniquet, and type of anesthesia.

9.5. Medical and Surgical History

Medical and surgical history recorded at the screening visit will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1 or higher. Medical and surgical history will be listed by treatment and subject as well as summarized by system organ class (SOC) and preferred term (PT).

9.6. Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary Enhanced (WHO-DD) September 2016 and will be classified according to the default anatomical therapeutic chemical (ATC) classification system term and PT.

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 within 30 days after the start of study drug administration).

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 PT for the safety analysis set. Subjects may have more than one medication per ATC category and PT. 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 PT to verbatim term will be presented.

9.7. Measurements of Treatment Compliance

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

9.8. Efficacy Analysis

No formal statistical hypothesis testing will be performed. The following endpoints will be summarized using descriptive statistics:

- Total blood loss as measured by Hb and Hct levels upon arrival at the post-anesthesia care unit (PACU) and at 6, 12, 24, 48, 72, 120 hours, and Day 7
- Incidence of transfusion (number of units/subject, number of subjects transfused)

- Time to 90˚ passive and active knee flexion at 24, 48, and 72 hours for patients enrolled prior to Amendment 2 and by AM/PM at 24, 48, and 72 hours for patients enrolled on Amendment 2
- Time to complete TUG test once on study day 1 (postsurgical day 0), twice a day on study day 2 (6:00 - 10:00 and 18:00 - 22:00), at hospital discharge, and on study day 7
- Change in knee and thigh measurements on the morning of postsurgical day 2 and at the day 7 follow-up visit
- NRS Pain Scores upon arrival at the PACU, at each in-hospital vital sign assessment beginning with the 48-hour assessment, and at the Day 7 follow-up visit
- Days to Independent Ambulation assessed beginning at Day 7 follow-up visit
- Surgical Wound Aspect Score (SWAS) on the morning of postsurgical day 2 and on day 7

9.8.1. Total Blood Loss

Total loss will be calculated separately using two separate methods. The first method is based on Hct and the second method is based upon Hb. Total blood loss will be calculated at 6, 12, 24, 48, 72, 120 hours, and Day 7 postsurgery for each subject. Descriptive statistics summarizing the total blood loss will be summarized by postsurgical timepoint and treatment group for the efficacy analysis population for each method. Baseline is considered the last value measured before the surgery.

Total BV in mL will be calculated using the Nadler formula (Nadler 1962) at baseline by

$$BV_{baseline} = (a * h^3 + b * w + c)$$

where h = height (m), w = baseline weight (kg), {a=0.3669, b=0.03219, c=0.6041} for males and {a=0.3561, b=0.03308, c=0.1833} for females. The $BV_{baseline}$ is used in methods 1 and 2 to determine blood loss.

Method 1 (Gibon 2013):

Total RBC loss is in mL calculated by the following formula:

$$RBC_{lost} = BV_{baseline} * \left(Hct_{baseline} - Hct_{postop\ hour}\right) + BV_{transfused}$$

where $Hct_{baseline}$ is measured as the volume percentage of red blood cells in the blood at baseline, $Hct_{post-op\ hour}$ is measured as the volume percentage of red blood cells in the blood at the specified postsurgical timepoint in hours, total $BV_{baseline}$ is measured in mL, and $BV_{transfused}$ is the mL volume of blood transfused to the subject.

Method 2 (Gao et al, 2015):

Another method of calculating blood loss is presented by Gao as follows:

Hb_{loss} [g] = $BV_{baseline}$ [mL] · ($Hb_{baseline}$ [g/L] – Hb_{postop} [g/L]) · 0.001 [L/mL] + Hb_t [g],

Hb_t = $BV_{transfused}$ [Unit] · 52 [g/Unit], and

RBC_{lost} [mL] = 1000 x Hb_{loss} [g] / $Hb_{baseline}$ [g/L],

where Hb_{loss} is the total loss of hemoglobin in gram, $BV_{baseline}$ is the presurgery blood volume in mL, $Hb_{baseline}$ and Hb_{postop} are the presurgery and post surgery hemoglobin concentration in g/L, Hb_t is the amount of hemoglobin transfused in gram, $BV_{transfused}$ is the banked blood transfused in Unit, and RBC_{lost} is the total volume of RBC lost. The above formulae can be simplified as

$$RBC_{lost} = \frac{BV_{baseline}*(Hb_{baseline}-Hb_{postop})+BV_{transfused}*52000}{Hb_{baseline}}.$$

Total blood loss upon arrival at the PACU and at 6, 12, 24, 48, 72, 120 hours, and Day 7 will be summarized using descriptive statistics [n, mean, SD, minimum, median, and maximum] for method 1 and method 2 serperately. When both methods are presented together on the same graph, method 1 will be represented using a solid line (line=1) and method 2 will be represented using a dashed line (line 2).

9.8.2. Incidence of transfusion

The incidence of transfusion (number of units/subject and number of subjects transfused) will be tabulated by postsurgical timepoint and treatment group for the efficacy analysis population with number and percentage of subjects. Percentages will be based on the number of subjects in the treatment group within the efficacy population.

9.8.3. Time to 90^o Passive and Active Knee Flexion

The proportion of subjects capable of 90˚ passive and active knee flexion, separately, at 24, 48, and 72 hours will be tabulated with the number and percentage of subjects by postsurgical timepoint and treatment group for the efficacy analysis population. For patients enrolled after on/after Protocol Amendment 2, the summary table will be broken down by time of the day (AM or PM) of the assessment. The time to 90˚ knee flexion, for both passive and active separately, will be summarized using Kaplan-Meier estimates (n, 25th percentile, median, and 75th percentile). The actual time of assessment will be used for this calculation.

9.8.4. Time to Complete TUG Test

The time (seconds) to complete TUG test on study day 1 (postsurgical day 0), twice a day on study day 2 (6:00am - 10:00 am and 6:00pm - 10:00pm), at hospital discharge, and on study day 7 will be summarized by postsurgical timepoint and treatment group for the efficacy analysis population using descriptive statistics (n, mean, SD, minimum, median, and maximum). In addition, the amount of physical assistance required to complete the TUG test at each time point will be tabulated with the number and percentage of subjects in each category.

9.8.5. NRS Pain Scores

The NRS pain scores will be summarized using descriptive statistics (n, mean, SD, minimum, median, and maximum) at each scheduled timepoint. In addition, the AUC from the time a subject is admitted to the PACU through 72 hours will be calculated and summarized by treatment group for the efficacy analysis population using descriptive statistics (n, mean, SD, minimum, median, and maximum).

9.8.6. Change in Knee and Thigh Circumferences

Prior to Protocol Amendment 2, knee and thigh circumferences were collected for both surgical and non-surgical legs. Protocol Amendment 2 requires the collection only for the surgical leg. As such, for subjects enrolled prior to Amendment 2, the circumferences for the surgical and non surgical legs, the differences between the two, and their changes from baseline within subject will be summarized separately for the knee and thigh by treatment group for the efficacy analysis population using descriptive statistics (n, mean, SD, minimum, median, and maximum) for postsurgical day 2 (study day 3) and study day 7. For subjects enrolled after Amendment 2, only the circumferences of the surgical legs and their changes from baseline will be summarized.

9.8.7. Days to First Independent Ambulation

The number of days until the first independent ambulation will be summarized using Kaplan-Meier estimates (n, 25^{th} percentile, median, and 75^{th} percentile).

9.8.8. Surgical Wound Aspect Score (SWAS)

The SWAS will be tabulated by treatment group for the efficacy analysis population with number and percentage of subjects for the score of wound oozing, erythema, ecchymosis, and blisters for postsurgical day 2 (study day 3) and study day 7. In addition, the sum of the wound oozing, erythema, ecchymosis, and blister scores will also be tabulated by treatment group for the efficacy analysis population for postsurgical day 2 (study day 3) and study day 7. Percentages will be based on the number of subjects in the treatment group within the efficacy population.

9.9. Safety Analyses

The following safety assessments will be summarized:

- 12-lead ECGs at day 1 Preop (D1 Preop), and 1 hour and 12 hours after study drug administration.
- Vital signs (resting heart rate and blood pressure) at Baseline, and 5min, 15min, 30min, 1hr, 2hr, 4hr, 6hr, 8hr, 12hr, 16hr, 24hr, 36hr, 48hr, 60hr, 72hr, and 96hr after study drug administration.
- Neurological assessment at D1 Preop and at 12, 24, 36, 48, 60, 72, and 96 hours after study drug administration.
- Clinical laboratory testing (hematology [including fibrinogen and fibrin split products, lipid profile] and chemistry) at D1 Preop, at 48 hours, and at day 7.
- Creatinine clearance measurement at 48 hours and at day 7.
- Reoperations due to hematoma or wound dehiscence.
- Adverse events through study day 60.

No inferential statistics are planned for any of the safety assessments.

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

9.9.2. 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 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.

9.9.3. Neurological Assessments

The neurological assessments summary will include the proportion of subjects who are oriented, and proportion of subjects who have any of the neurologic events (answered "Yes" to any of the additional questions regarding numbness, taste, hearing, vision, or twitching). Percentages will be based on the number of subjects in the treatment group. The number and percentage of subjects will be tabulated by treatment group at each assessment timepoint.

9.9.4. Clinical Laboratory Assessments

Clinical laboratory assessments are collected at D1 Preop and at 48 hours after study drug administration. Laboratory results will be summarized by treatment group at each assessment timepoint. Summaries will present both actual results and change from baseline results for each clinical laboratory parameter. Baseline statistics will also be presented for each clinical laboratory parameter.

Tabulations of the number and percentage of subjects with values outside the normal range will be provided by treatment group at baseline 48 hours, and day 7 for each parameter.

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 48 hour categories for the rows. Each treatment group separately and all DepoTXA subjects, in the safety analysis set, will be presented. Each cell will present the number and percentage of subjects in that cell. Due to the width of these tables, only one treatment will be presented per page.

Creatine clearance will be summarized for study day 7 in a similar manner as the other laboratory parameters at 48 hours.

9.9.5. Reoperation Due to Hematoma or Wound Dehiscence

The number and percentage of subjects with reoperations due to hematoma or wound dehiscence will be tabulated by treatment group and for All DepoTXA.

9.9.6. Adverse Events

Adverse events will be coded using MedDRA version 19.1 or higher.

A TEAE will be any adverse event with the onset date and time on or after the start date and time of study drug administration and within 30 days of the dose, or a pre-existing medical condition that worsens in intensity after the start of study drug (date and time) and within 30 days of the dose.

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 TEAE, 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 TEAEs 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
- At least one related serious TEAE
- Subjects discontinued because of a TEAE
- Died during the 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
- All Nonserious TEAEs (CT.gov only)
- 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 death

If 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' or if no investigator assessment is provided.

Treatment emergent AESIs include changes in color vision, venous thromboembolism or pulmonary embolism, and oliguria.

A listing of the mapping of the SOC and PTs to verbatim terms will be presented.

9.10. Pharmacokinetic Analysis

9.10.1. Sample Collections for Pharmacokinetic Analysis

Blood samples for the PK analysis will be obtained at baseline (prior to study drug administration); at 5, 15, and 30 minutes; and at 1, 2, 4, 6, 8, 12, 16, and 24 hours after study drug administration for all treatment groups. Additional blood samples will be collected at 36, 48, 60, 72, and 96 hours after study drug administration for DepoTXA-treated subjects.

9.10.2. Pharmacokinetic Parameter Calculation Methods

Pharmacokinetic parameters will be calculated by a noncompartmental analysis method from concentration-time data using WinNonlin Professional (Version 5.2 or later) or SAS following these guidelines:

- Actual sampling times relative to study drug administration will be used for all calculations of the PK parameters. If there is any doubt as to the actual time a sample was taken, then the scheduled time will be used. Descriptive statistics will be used to summarize the PK parameters.
- Concentrations from unscheduled PK blood samples will be used in the analysis of the parameters.
- There will be no imputation of missing data.

For the calculation of AUC from PK concentrations, concentration below the limit of quantification (BLOQ) will be handled as follows:

- Pre-dose values will be set to zero.
- All remaining BLOQ values will be set to missing.

Pharmacokinetic parameters will be estimated according to the following guidelines:

- The maximum observed plasma concentration (C_{max}) will be obtained directly from the concentration-time data.
- Time to maximum concentration (T_{max}) is the time at which C_{max} is observed.
- The apparent terminal elimination rate constant (λ_Z) will be estimated at terminal phase by linear regression after log-transformation of the concentrations:
    - Only those data points that are judged to describe the terminal log-linear decline will be used in the regression.
    - A minimum number of three data points in the terminal phase will be used in calculating λ_z with the line of regression starting at post-C_{max} data point (C_{max} should not be part of the regression slope) and including C_{last} and t_{last}.
    - The adjusted correlation coefficient (R^2 adjusted) in general should be greater than 0.90. Any value less than 0.90 may be used according to the pharmacokineticist's best knowledge and judgment.
    - An appropriate number of decimal places should be used for λ_z for an precise calculation of the of half-life ($t_{½}$).
- Half-life ($t_{1/2}$) will be calculated as $\ln(2)/\lambda_Z$.
- AUC will be calculated as follows:
    - The linear trapezoidal method will be employed for all incremental trapezoids arising from increasing concentrations and the logarithmic trapezoidal method will be used for those arising from decreasing concentrations.
    - $AUC_{(0-t)} = \int_0^t C(t)dt$
    - $AUC_{(O-\infty)} = \int_0^t C(t)dt + \int_t^\infty C(t)dt = AUC_{(0-t)} + C_t / \lambda_z$
- C_t is last observed quantifiable concentration.

9.10.3. Pharmacokinetic Concentrations and Variables

The analysis of the PK data will be based on the PK analysis set.

TXA plasma concentrations will be listed by treatment group, subject, nominal time, and actual time. Concentrations that are BLOQ will be indicated by BLOQ in this listing.

Plasma concentrations will be summarized by treatment at each time point. The following descriptive statistics will be presented for plasma concentrations obtained at each nominal time point: n, arithmetic mean, SD, coefficient of variation (%CV), geometric mean, median, minimum and maximum.

Pharmacokinetic parameters will be summarized for each treatment group. Descriptive statistics for calculated PK parameters will include: n, arithmetic mean, SD, %CV, geometric mean,

median, minimum and maximum values. Geometric mean will not be presented for T_{max}. Values of %AUC extrapolated > 20% will be flagged in the listings.

Individual plasma concentration versus actual times will be plotted by treatment in linear and semi-logarithmic scale.

The geometric mean ratios (GMRs) for DepoTXA 400 mg, DepoTXA 800 mg, and DepoTXA 1200 mg to IV TXA will be presented separately along with their corresponding 95% confidence intervals for AUC_{0-t} and C_{max}.

9.11. Interim Analysis

No Interim analyses are planned.

10. SAMPLE SIZE CALCULATION

The sample size was not based on statistical considerations.

11. REFERENCES

American Statistical Association. Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, 07 August 1999.
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Gao F, Li Z, Zhang K, et al. Four methods for calculating blood-loss after total knee arthroplasty. Chin Med J. 2015;128(21):2856-2860.

Senthil Kumar G, Von Arx OA, Pozo JL. Rate of blood loss over 48 hours following total knee replacement. Knee 2005;12:307-9.

Nadler SB, Hidalgo JU, Bloch T. Prediction of blood volume in normal human adults. Surgery. 1962 Feb;51(2):224-32.
Royal Statistical Society. The Royal Statistical Society: Code of Conduct, August 1993.
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12. TIME AND EVENTS SCHEDULE OF STUDY PROCEDURES

	Screen Visit[1]	D1 Preop	OR	PACU Arrival	5 min	15 min	30 min	1h	2h	4h	6h	8h	12h	16h	24h	36h	48h	60h	72h	96h	120h	Day 7	D14 Call	D30 Call	D60 Call
Time Window	**Within 30 days**				**±2 min**	**±3 min**	**±5 min**	**±10 min**	**±15 min**	**±15 min**	**±15 min**	**±30 min**	**±30 min**	**±1h**	**±1h**	**±2h**	**±2h**	**±2h**	**±4h**	**±6h**	**±6h**	**±1d**	**±1d**	**±3d**	**±3d**
Obtain signed ICF	X																								
Assess/confirm eligibility	X	X																							
Record medical and surgical history	X	X																							
Record demographics and baseline characteristics	X																								
Conduct pregnancy test for WOCBP	X	X																							
Perform physical examination	X																X								
Clinical labs (hematology, chemistry)[2]	X	X															X					X			
Coagulation (fibrinogen and fibrin split products)	X	X															X					X			
Creatinine clearance calculation[2]		X															X					X			
Hemoglobin and hematocrit[2]	X	X		X							X		X		X		X		X		X	X			
Perform neurological assessment[3]	X	X											X		X	X	X	X	X	X					
Perform 12-lead ECG recordings[4]		X						X[4]					X[4]												
Measure vital signs[5]	X	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X						
Collect NRS-R pain score		X		X					X	X	X	X	X	X	X	X	X		X			X			
Collect knee and thigh measurements (both legs)		X															X[6]		X[6]			X[6]			
Assess surgical wound for SWAS parameters[7]																	X		X			X			
Collect PK blood sample from all treatment groups; record date and time[8]		X			X	X	X	X	X	X	X	X	X	X	X										
Collect additional PK blood samples for DepoTXA treatment groups; record date and time																X	X	X	X	X					
Randomize patient, prepare study drug		X																							
Administer study drug			X																						
Record start and end time of tourniquet use and max pressure (mm Hg) used			X																						
Record surgery start and stop times			X																						
Perform knee flexion assessment[13]	X											◄	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	►				
Perform TUG test; record date and time[11]	X											◄	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	[11] ►	X			
Record date and time of discharge																	◄	- - -	- - -	- - -	- - -	►			
Record any blood transfusion data (eg, start and stop times, units)				◄	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	►				
Record any reoperations due to hematoma or wound dehiscence				◄	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	►	
Record prior and concomitant medications[12]	◄	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	►	
Record whether patient has achieved independent ambulation																						◄	- - -	►	
Record AEs beginning at time ICF is signed[2,3,5,8,10]	◄	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	►

Abbreviations: AE = adverse event; d = day; D = day; ECG = electrocardiogram; h = hours; ICF = informed consent form; max = maximum; min = minutes; OR = operating room; PACU = post-anesthesia care unit; PK = pharmacokinetic; Preop = preoperative; TUG = timed up-and-go; WOCBP = women of childbearing potential.

* Postsurgical assessments will be conducted at the timepoints specified after the beginning of study drug administration.

[1] The screening visit must take place at least 1 day prior to surgery.

[2] Also conduct clinical laboratory tests if a patient experiences an AE of special interest or a serious AE (SAE), if appropriate; see footnote 10.

[3] Also conduct a neurological assessment if a patient experiences an AE of special interest or an SAE, if appropriate; see footnote 10.

[4] Postsurgical 12-lead ECGs will be performed at 1 hour (±15 minutes) and 12 (±2) hours after study drug administration

[5] Vital signs will be measured after the patient has rested in a supine position for at least 5 minutes. Also measure vital signs if a patient experiences an AE of special interest or an SAE, if appropriate; see footnote 10.

[6] Collect knee and thigh measurements (both legs) on the morning of postsurgical Day 2.

[7] The surgical wound will be assessed for the SWAS parameters (wound oozing, erythema, ecchymosis, and blisters) at the time of knee measurements on the morning of postsurgical Day 2 and on Day 7.

[8] Also collect a PK sample if a patient experiences an AE of special interest or an SAE; see footnote 10.

[9] Record date and time of all medications starting at least 30 days prior to study drug administration through 120 hours after study drug administration. Record medications administered for treatment of an AE through Day 60 (±3 days).

[10] Adverse events of special interest include changes in color vision, VTE or PE, and oliguria. If an AE of special interest or serious AE (SAE) occurs during the study, an unscheduled PK blood sample must be collected. In addition, vital signs, the neurological assessment, and clinical laboratory tests should be conducted, as appropriate. If a patient experiences changes in color vision, an ophthalmological consultation must be ordered.

[11] Postsurgical "Timed Up-and-Go" will be assessed once on the day of the surgery; at approximately 8:00 am and 8:00 pm (±2 hours) daily from Day 2 through hospital discharge; and on Day 7.

[12] Each institution may follow its standard protocol for the control of postsurgical pain; however, patient-controlled analgesia is not permitted.

[13] Each institution may follow its standard protocol for the control of postsurgical pain; however, patient-controlled analgesia is not permitted.

13. TABLE OF CONTENTS FOR TABLES

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Table 14.1-1: Tabulation of Subject Disposition – All Screened Subjects
Site: Overall

	DepoTXA 400 [N=XX] n (%)	DepoTXA 800 [N=XX] n (%)	DepoTXA 1200 [N=XX] n (%)	IV TXA [N=XX] n (%)	Total [N=XX] n (%)
Screened					xx
Screen Failure					xx (xx.x)
Did Not Meet Inclusion #1					xx (xx.x)
Did Not Meet Inclusion #2					xx (xx.x)
…					xx (xx.x)
Randomized [2]	xx	xx	xx	xx	xx
Not Treated	xx	xx	xx	xx	xx
Treated	xx	xx	xx	xx	xx
Underwent Surgery	xx	xx	xx	xx	xx
Did Not Undergo Surgery	xx	xx	xx	xx	xx
Safety Analysis Set [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Efficacy Analysis Set [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PK Analysis Set [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	NA	NA
Completed Study [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Discontinued from Study [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reasons for Discontinuation					
Death [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Adverse Event [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lack of Efficacy [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to Follow-up [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal by Subject [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] As treated
[2] As randomized
Number of subjects randomized is used as denominator for all percentages except screened. Screen Failure and the associated reasons reported uses the number of subjects screened as the denominator.

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. If no subjects were mistreated, then no footnote will be needed; otherwise list all subjects who were mistreated in this study by site and subject number in the footnotes of each applicable table.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Table 14.1-2.1: Tabulation of Subject Demographics - Safety Analysis Set
Site: Overall

	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [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
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x	xx.x
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 or Alaska Native	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black or 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 or Pacific Islander	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
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)
Country						
United States of America	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: *Use table 14.1-2.1 as a template for the following tables:*
Table 14.1-2.2: Tabulation of Subject Demographics – Efficacy Analysis Set
Table 14.1-2.3: Tabulation of Subject Demographics - PK Analysis Set

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201

Table 14.1-3.1: Summary of Subject Baseline Characteristics - Safety Analysis Set

Site: Overall

	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]	Total [N=XX]
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
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx	xx	xx
	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
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x	xx.x
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
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x	xx.x
Total Blood Volume (mL)	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.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x	xx.x

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

Note to programmer: *Use table 14.1-3.1 as a template for the following tables:*
Table 14.1-3.2: Summary of Subject Baseline Characteristics – Efficacy Analysis Set
Table 14.1-3.3: Summary of Subject Baseline Characteristics - PK Analysis Set

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201

Table 14.1-4.1: Summary of Surgery Characteristics - Safety Analysis Set

Site: Overall

Characteristics	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]	Total [N=XX]
Duration of Surgery (hrs)	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.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x	xx.x
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.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x	xx.x
Tourniquet Used	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Tourniquet Duration (hrs)	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.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x	xx.x
Tourniquet Maximum 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
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x	xx.x
Type of Anesthesia						
General	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Spinal	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	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: *Use this template also for table:*
Table 14.1-4.2: Summary of Surgery Characteristics – Efficacy Analysis Set
Table 14.1-4.3: Summary of Surgery Characteristics– PK Analysis Set

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Table 14.1-5.1: Tabulation of Medical History - Safety Analysis Set
Site: Overall

System Organ Class Preferred Term	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)	Total [N=XXX] n(%)
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					
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)
ETC.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Medical History coded using the Medical Dictionary for Regulatory Activities (MedDRA version 19.1 or higher). Sorted by descending total incidence by system organ class and preferred term within system organ class. Subjects with the same Medical History reported 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 Medical History. Use mock-up Table 14.1-5.1 for the following tables:*
Table 14.1-5.2: Tabulation of Medical History - Efficacy Analysis Set
Table 14.1-5.3: Tabulation of Medical History - PK Analysis Set

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201

Table 14.2-1.1: Summary of Total Blood Volume (mL) by Scheduled Timepoint (Method 1 Hct)–Efficacy Analysis Set

Site: Overall

Timepoint	Value	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
Baseline	Actual	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
5 min	Actual	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
	Blood Loss	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

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

Note to programmer: *This table should include the PACU, 6, 12, 24, 48, 72, 120 hour, and Day 7 timepoints. Use this template for the following table:*

Table 14.2-1.2: Summary of Total Blood Loss (mL) by Scheduled Timepoint (Method 2 Hb)– Efficacy Analysis Set

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Table 14.2-2: Summary of Incidence of Transfusion – Efficacy Analysis Set

Site: Overall

	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
Number of Units/Subject	n	xx	xx	xx	xx
	Mean	x.x	x.x	x.x	x.x
	SD	x.xx	x.xx	x.xx	x.xx
	Median	x.x	x.x	x.x	x.x
	Minimum	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x
Subjects Transfused	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*

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Table 14.2-3.1a: Summary of Time to 90° Active Knee Flexion (for Subjects Enrolled Prior to Protocol Amendment 2) – Efficacy Analysis Set

Site: Overall

Timepoint	90° Knee Flexion	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
Day 1	Yes	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Censored	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 2	Yes	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Censored	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 3	Yes	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Censored	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
KM Estimates of Time to 90° Knee Flexion						
		Minimum	xx.x	xx.x	xx.x	xx.x
		25th Percentile	xx.x	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x	xx.x
		75th Percentile	xx.x	xx.x	xx.x	xx.x
		Maximum	xx.x	xx.x	xx.x	xx.x

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

Note to programmer: *Use the mock-up from Table 14.2-3.1a for the following table:*
Table 14.2-3.2a: Summary of Time to 90° Passive Knee Flexion – Efficacy Analysis Set

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Table 14.2-3.1b: Summary of Time to 90° Active Knee Flexion (for Subjects Enrolled After Protocol Amendment 2) – Efficacy Analysis Set

Site: Overall

Timepoint	90° Knee Flexion	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
Day 1 AM	Yes	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Censored	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 1 PM	Yes	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Censored	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 2 AM	Yes	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Censored	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 2 PM	Yes	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Censored	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

(Continue through Day 5 PM)

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

Note to programmer: *Use the mock-up from Table 14.2-3.1b for the following table:*
Table 14.2-3.2b: Summary of Time to 90° Passive Knee Flexion – Efficacy Analysis Set

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Table 14.2-3.1c: Kaplan-Meier Estimate of Time to 90° Active Knee Flexion – Efficacy Analysis Set

Site: Overall

Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
Minimum	xx.x	xx.x	xx.x	xx.x
25th Percentile	xx.x	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x	xx.x
75th Percentile	xx.x	xx.x	xx.x	xx.x
Maximum	xx.x	xx.x	xx.x	xx.x

Note: + indicates a censored value; KM = Kaplan-Meier

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

Note to programmer: *Use the mock-up from Table 14.2-3.1c for the following table:*
Table 14.2-3.2c: Summary of Time to 90° Passive Knee Flexion – Efficacy Analysis Set

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Table 14.2-4.1: Summary of Time to Complete Timed Up-and-Go (TUG) Test - Efficacy Analysis Set

Site: Overall

Timepoint[1]	Value	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
Baseline	Actual	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
Study Day 1	Actual	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
	Change from Baseline	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

Note: Only subjects who completed the TUG test at a timepoint are included in the summary at that timepoint. All times are measured in seconds.
[1] Hospital Discharge only applies to the subjects enrolled after Protocol Amendment 2.

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

Note to programmer: *This table should include the Study Day 1, Study Day 2 morning and evening timepoints, hospital discharge (post amendment) and on Study Day 7.*

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Table 14.2-4.2: Tabulation of Physical Assistance Required to Complete the TUG Test - Efficacy Analysis Set

Site: Overall

Timepoint[1]	Category	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)
Baseline	Did Not Complete TUG Test	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Completed TUG Test	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total Assistance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Maximal Assistance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate Assistance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Minimal Assistance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Supervision	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Modified Independance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Complete Independence	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Was any Aid used for the test?	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	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)
	NA	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Unknown	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Study Day 1	Did Not Complete TUG Test	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Completed TUG Test	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total Assistance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Maximal Assistance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate Assistance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Minimal Assistance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Supervision	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Modified Independance	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Complete Independence	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Was any Aid used for the test?	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	…	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Hospital Discharge only applies to the subjects enrolled after Protocol Amendment 2.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name
Note to programmer: *Do not split study day across pages. This table should include the Baseline, Study Day 1, Study Day 2 morning and evening timepoints, and on Study Day 7.*

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Table 14.2-4.3: Shift Table of Physical Assistance Required to Complete the TUG Test - Efficacy Analysis Set

Site: Overall

		Baseline							
Timepoint[1]		1	2	3	4	5	6	7	8
Treatment		n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Study Day 1									
DepoTXA 400	1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	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)
	3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	5	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	6	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	7	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	8	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Study Day 1									
DepoTXA 800	1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	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)
	3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	5	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	6	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	7	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	8	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Study Day 1									
DepoTXA 1200	1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	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)
	3	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)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: 1- Did Not Complete TUG Test, 2- Total Assistance, 3- Maximal Assistance, 4- Moderate Assistance, 5- Minimal Assistance, 6- Supervision, 7- Modified Independence, and 8- Complete Independence.
[1] Hospital Discharge only applies to the subjects enrolled after Protocol Amendment 2.

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

Note to programmer: *Do not split study day and treatment across pages. This table should include the Baseline, Study Day 1, Study Day 2 morning and evening timepoints, hospital discharge, and on Study Day 7.*

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Table 14.2-5.1: Summary of NRS at Assessment Timepoints – Efficacy Analysis Set

Site: Overall

Timepoint	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
D1 Preop	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
PACU	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

PACU is Postanesthesia Care Unit
Number of subjects randomized is used as denominator for all percentages.

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, D1 Preop and PACU, 2, 4, 6, 8, 12, 16, 24, 36, and 48 hours, 72 hours (Amendment 2) and Study Day 7.*

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

Use mock-up 14.2-5.1:

Table 14.2-5.2: Summary of NRS AUC - Efficacy Analysis Set

AUC parameters for Table 14.2-5.2 are: AUC(0-24), AUC(0-48), AUC(0-72), AUC(24-48), and AUC(48-72).

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Table 14.2-6.1.1: Knee Circumference at Assessment Timepoints – Efficacy Analysis Set

Site: Overall

Timepoint	Statistic	DepoTXA 400 [N=XX]		DepoTXA 800 [N=XX]		DepoTXA 1200 [N=XX]		IV TXA [N=XX]	
		Surgical Leg	Non-Surgical Leg	Surgical Leg	Non-Surgical Leg	Surgical Leg	Non-Surgical Leg	Surgical Leg	Non-Surgical Leg
D1Preop									
	n	xx	xx	xx	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx
Postsurgical Day 2									
	n	xx	xx	xx	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx
Postsurgical Day 2 Change from Baseline									
	n	xx	xx	xx	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx

Note: Data for non-surgical legs were collected only from subjects enrolled prior to Protocol Amendment 2.

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, D1 Preop, Postsurgical Day 2, Postsurgical Day 2 from Baseline, Study Day 7, and Study Day 7 Change from Baseline.*

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Table 14.2-6.1.2: Leg Difference in Knee Circumference (for Subjects Enrolled Prior to Protocol Amendment 2) – Efficacy Analysis Set

Site: Overall

Timepoint	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
Postsurgical Day 2	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
Study Day 7	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

Leg difference in change from baseline is calculated by = (Operated Leg) – (Non-Operated Leg)

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

Note to programmer: *This table is only for pre-amendment.*

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

Use mock-up 14.2-6.1.2:

Table 14.2-6.1.3: Leg Difference in Change from Baseline in Knee Circumference (for Subjects Enrolled Prior to Protocol Amendment 2) – Efficacy Analysis Set
Change the footnote to: Leg difference in change from baseline is calculated by
= (Operated Leg Change from Baseline) – (Non-Operated Leg Change from Baseline)
Note to programmer: *this table is only for pre-amendment*

Table 14.2-6.1.4: Change from Baseline in Surgical Knee Circumference – Efficacy Analysis Set
Remove the footnote
Note to programmer: *this table is only for pre-amendment*

Use mock-up 14.2-6.1.1:

Table 14.2-6.2.1: Thigh Circumference at Assessment Timepoints – Efficacy Analysis Set
Note to programmer: *same comment as for knee*

Use mock-up 14.2-6.1.2:

Table 14.2-6.2.2: Leg Difference in Thigh Circumference (for Subjects Enrolled Prior to Protocol Amendment 2) – Efficacy Analysis Set

Table 14.2-6.2.3: Leg Difference in Change from Baseline in Thigh Circumference (for Subjects Enrolled Prior to Protocol Amendment 2) – Efficacy Analysis Set
Note to programmer: *same comment as for knee*

Use mock-up 14.2-6.1.2:

Table 14.2-6.2.4: Change from Baseline in Surgical Thigh Circumference – Efficacy Analysis Set
Note to programmer: *same comment as for knee*

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Table 14.2-7: Summary of Days to First Independent Ambulation – Efficacy Analysis Set

Site: Overall

	Statistic	DepoTXA 400 mg [N=XX]	DepoTXA 800 mg [N=XX]	DepoTXA 1200 mg [N=XX]	IV TXA [N=XX]
Number of subjects ambulating	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of subjects censored	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
KM Estimates of Days to First Independent Amulation	n	xx	xx	xx	xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	25th Percentile	xx.x	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x	xx.x
	75th Percentile	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x

Note: + indicates a censored value; KM = Kaplan-Meier

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

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Table 14.2-8: Tabulation of Surgical Wound Aspect Score on Postsurgical Day – Efficacy Analysis Set

Site: Overall

Study Day		DepoTXA 400 [N=XX] n (%)	DepoTXA 800 [N=XX] n (%)	DepoTXA 1200 [N=XX] n (%)	IV TXA [N=XX] n (%)
2	Wound Oozing				
	0: No signs of blood on the gauze	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: 1-2 spots of blood on the gauze	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: >2 spots of blood on the gauze	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Erythema				
	0: Erythema absent	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Erythema at wound edges	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Erythema beyond wound edges	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Ecchymosis				
	0: Ecchymosis absent	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Ecchymosis at wound edges	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Ecchymosis beyond wound edges	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Blisters				
	0: Blisters absent	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: 1-2 blisters of <2 cm each	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: >2 blisters of any size or ≥1 blister >2 cm	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Sum of Categories				
	0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	5	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	6	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	7	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	8	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Descriptive Statistics of the Sum of Categories				
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

Number of subjects randomized is used as denominator for all percentages.

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

Note to programmer: *Put study day 7 on the next page*

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Table 14.3-1.1: Tabulation of Electrocardiogram – Investigator Read - Safety Analysis Set

Site: Overall

Time Point	Interpretation	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)	Total [N=XXX] n(%)
D1 PreOp	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal, N.C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal, C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Any Post-Baseline	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal, N.C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal, C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1 hour	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal, N.C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal, C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
12 hours	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal, N.C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal, C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: C.S. is Clinically Significant and N.C.S is Not Clinically Significant.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name
Note to programmer: *Only present overall sites.*

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Table 14.3-1.2: Shift Table of Electrocardiogram – Investigator Read - Safety Analysis Set

Site: Overall

			D1PreOp		
Treatment Group	Time Point	Interpretation	Normal n(%)	Abnormal N.C.S n(%)	Abnormal C.S. n(%)
DepoTXA 400	Any Post-Baseline	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Abnormal, N.C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Abnormal, C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1 hour	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Abnormal, N.C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Abnormal, C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)
	12 hours	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Abnormal, N.C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Abnormal, C.S.	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: C.S. is Clinically Significant and N.C.S is Not Clinically Significant.

Source: *list SAS datasets used to create table* DDMONYYYYTHH:MM
SAS X.Y program_name
Note to programmer: *Present each treatment group and the Total on separate pages; DepoTXA 400, DepoTXA 800, DepoTXA 1200, IV TXA, and Total.*

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Table 14.3-2: Summary of Vital Signs – Safety Analysis Set

Site: Overall

Vital Sign: Resting Heart Rate (bpm)

Timepoint	Value	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]	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
5 min	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 from Baseline	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: *Only present overall sites. Vital signs are 'Resting Heart Rate (bpm)', 'Systolic Blood Pressure (mmHg)' and 'Diastolic Blood Pressure (mmHg)'. Timepoints to appear on this table are Baseline, 5min, 15min, 30min, 1hr, 2hr, 4hr, 6hr, 8hr, 12hr, 16hr, 24hr, 36hr, 48hr, 60hr, 72hr, and 96hr. Don't split timepoints across pages. See SAP section 9.9.2 for further details.*

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Table 14.3-3: Tabulation of Neurological Assessments by Timepoint- Safety Analysis Set

Site: Overall

Timepoint: Baseline

Assessment	Score	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)	Total [N=XXX] n(%)
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)
Numbness	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)

Note: Numbness referes to the numbness of the lips, tongue, and/or mouth.

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 anytime after baseline, 12, 24, 36, 48, 60, 72, 84 and 96 hours. Do not split a timepoint across pages. For the timepoint 'anytime after baseline' if there is at least one 'yes' at any timepoint but baseline, the subject will be a 'yes'.*

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Table 14.3-4.1: Summary of Clinical Laboratory Assessments - Safety Analysis Set

Site: Overall

Clinical Laboratory Parameter: Albumin (g/L)

Timepoint	Value	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]	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
48 Hours	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 from Baseline	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: *Only present overall sites. Each clinical labortory parameter (w/ unit) should have a unique page. Clinical labortory parameters should be presented in alphabetical order. Clinical Labs are collected at baseline, 48 hours, and day 7, with the exception of Creatine Clearance only at Baseline and Day 7.*

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Table 14.3-4.2: Tabulation of Incidence of Abnormal Clinical Laboratory Assessments - Safety Analysis Set

Site: Overall

Parameter	Timepoint	Range	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)	Total [N=XXX] n(%)
Albumin (g/L)	Baseline	Low	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)
		Above	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	48 hours	Low	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)
		Above	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Day 7	Low	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)
		Above	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Low indicates the the parameter was below the lower limit of the normal range, Normal indicates the the parameter was within the normal range, limits inclusive, and above indicates the the parameter was above the upper limit of the normal range.

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 and 48 hours and Day 7. Do not split a parameter across multiple pages.*

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Table 14.3-4.3: Shift Table of Clinical Laboratory Assessments - Safety Analysis Set

Site: Overall

Parameter: Albumin (g/L)

			Baseline		
			Low	Normal	Above
Timepoint	Treatment Group	Range	n(%)	n(%)	n(%)
48 hours	DepoTXA 400	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Above	xx (xx.x)	xx (xx.x)	xx (xx.x)
	DepoTXA 800	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Above	xx (xx.x)	xx (xx.x)	xx (xx.x)
	DepoTXA 1200	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Above	xx (xx.x)	xx (xx.x)	xx (xx.x)
	IV TXA	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Above	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Above	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Low indicates the the parameter was below the lower limit of the normal range, Normal indicates the the parameter was within the normal range, limits inclusive, and Above indicates the the parameter was above the upper limit of the normal range.

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

Note to programmer: *Present each Laboratory Parameter on a separate page, Day 7 parameters should occur after all parameters have been presented for 48 hours.*

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Table 14.3-5.1.1: Overview of Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set

Site: Overall

Number of	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)	Total [N=XXX] 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)
At least one Related 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 overall sites.*

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Table 14.3-5.1.2: Tabulation of Incidence of Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set

Site: Overall

System Organ Class Preferred Term	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)	Total [N=XXX] 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)
ETC.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
ETC.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
ETC.	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 version 19.1 or higher). 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 14.3-5.1.3: Tabulation of Incidence of Study Drug-Related Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set
Table 14.3-5.1.4: Tabulation of Incidence of Treatment-Emergent Adverse Events (TEAEs) Leading to Study Withdrawal - Safety Analysis Set
Table 14.3-5.1.5: Tabulation 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 or if no investigator assessment is provided.

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Table 14.3-5.1.6: Tabulation of Incidence of Treatment-Emergent Adverse Events (TEAEs) by Severity - Safety Analysis Set

Site: Overall

System Organ Class Preferred Term	Severity	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)	Total [N=XXX] 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)
PT1.2	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)
SOC2	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)
PT2.1	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)
ETC.						

Adverse events coded using the Medical Dictionary for Regulatory Activities (MedDRA version 19.1 or higher). 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 14.3-5.1.7: Tabulation of Incidence of Treatment-Emergent Adverse Events (TEAEs) by Relationship to Study Drug - Safety Analysis Set

Site: Overall

System Organ Class Preferred Term	Relation	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)	Total [N=XXX] 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)
	Not Reported	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC1	Unrelated					
	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)
	Not Reported	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)
	Not Reported	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PT1.2	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)
	Not Reported	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 version 19.1 or higher). 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 template 14.3-5.1.2 for the following tables:*
Table 14.3-5.2.1: Tabulation of Incidence of Serious Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set
Table 14.3-5.2.1.CT: Tabulation of Incidence of Non-Serious Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set
Table 14.3-5.2.2: Tabulation of Incidence of Study Drug-Related Serious Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set
Table 14.3-5.2.3: Tabulation of Incidence of Serious Treatment-Emergent Adverse Events (TEAEs) Leading to Study Withdrawal - Safety Analysis Set
Table 14.3-5.2.4: Tabulation of Incidence of Study Drug-Related Serious Treatment-Emergent Adverse Events (TEAEs) Leading to Study Withdrawal - Safety Analysis Set
Table 14.3-5.2.5: Tabulation of Incidence of Serious Treatment-Emergent Adverse Events (TEAEs) Resulting in Death - Safety Analysis Set
Table 14.3-5.2.6: Tabulation of Incidence of Study Drug-Related Serious Treatment-Emergent Adverse Events (TEAEs) Resulting in Death - Safety Analysis Set
Table 14.3-5.3.1: Tabulation of Incidence of Treatment-Emergent Adverse Events (TEAEs) of Special Interest - Safety Analysis Set
Table 14.3-5.3.2: Tabulation of Incidence of Study Drug-Related Treatment-Emergent Adverse Events (TEAEs) of Special Interest - Safety Analysis Set
Table 14.3-5.3.3: Tabulation of Incidence of Treatment-Emergent Adverse Events (TEAEs) of Special Interest Leading to Study Withdrawal - Safety Analysis Set
Table 14.3-5.3.4: Tabulation of Incidence of Study Drug-Related Treatment-Emergent Adverse Events (TEAEs) of Special Interest Leading to Study Withdrawal - Safety Analysis Set
Table 14.3-5.3.5: Tabulation of Incidence of Treatment-Emergent Adverse Events (TEAEs) of Special Interest Resulting in Death - Safety Analysis Set
Table 14.3-5.3.6: Tabulation of Incidence of Study Drug-Related Treatment-Emergent Adverse Events (TEAEs) of Special Interest Resulting in Death - Safety Analysis Set

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Table 14.3-6.1: Tabulation of Incidence of Prior Medications - Safety Analysis Set

Site: Overall

System Organ Class Preferred Term	DepoTXA 400 [N=XX] n(%)	DepoTXA 800 [N=XX] n(%)	DepoTXA 1200 [N=XX] n(%)	IV TXA [N=XX] n(%)	Total [N=XXX] 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)
ETC.					

Medications are coded using World Health Organization Drug Dictionary Enhanced (WHO-DD) September 2016.
Sorted by descending total incidence by ATC and preferred name within ATC.
Prior medications are those stopped before end of surgery.
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: *Only present overall sites. Use this template for the following tables:*

Table 14.3-6.2: Tabulation of Incidence of Concomitant Medications – Safety Analysis Set.

On these tables change the footnote 'Prior medications are those stopped before end of surgery' to read 'Concomitant medications are those taken between the end of surgery and discharge from study' on Table 14.3-6.2.

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Table 14.3-7: Tabulation of Incidence of Reoperations Due to Hematoma or Wound Dehiscence – Safety Analysis Set

Site: Overall

	DepoTXA 400 [N=XX] n (%)	DepoTXA 800 [N=XX] n (%)	DepoTXA 1200 [N=XX] n (%)	IV TXA [N=XX] n (%)	Total [N=XX] n (%)
Did the Subject have a Reoperation due to a Hematoma or Wound Dehiscence?					
Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Number of subjects treated with the respective treatment is used as denominator for the respective percentages.

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

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Table 14.4-1a: Summary of Pharmacokinetic Parameters (for Subjects Enrolled Prior to Prorocol Amendment 2) - PK Analysis Set

Site: Overall

PK Parameter	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
AUC(0-infinity) (hr*ng/mL)	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
AUC(0-last) (hr*ng/mL)	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

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

Note to programmer: *Pharmacokinetic parameters to appear on this table are, in order of appearance, AUC(0-infinity) (hr*ng/mL), AUC(0-last) (hr*ng/mL), Global Cmax (ng/mL), Global Tmax (hr), Early Cmax (ng/mL), Early Tmax (hr), Late Cmax (ng/mL), Late Tmax (ng/mL), half-life (hr), Lambda_z (/hr).*

Table 14.4-1b: Summary of Pharmacokinetic Parameters (for Subjects Enrolled After Protocol Amendment 2) - PK Analysis Set

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Table 14.4-2a: Summary of DepoTXA (ng/mL) Over Time (for Subjects Enrolled Prior to Protocol Amendment 2) - PK Analysis Set

Site: Overall

Time	Statistic	DepoTXA 400 [N=XX]	DepoTXA 800 [N=XX]	DepoTXA 1200 [N=XX]	IV TXA [N=XX]
5 min	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
15 min	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
Ect.	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

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 of appearance, For all subjects: at 5, 15, and 30 minutes; and at 1, 2, 4, 6, 8, 12, 16, and 24 hours after study drug administration for all treatment groups and for DepoTXA-treated subjects only: additional timepoints at 36, 48, 60, 72, and 96 hours after study drug administration.*

Table 14.4-2a: Summary of DepoTXA (ng/mL) Over Time (for Subjects Enrolled After Protocol Amendment 2) - PK Analysis Set

14. TABLE OF CONTENTS FOR LISTINGS

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-1: Subject Disposition – All Subjects

Treatment: TTTTTTT

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

Source: *list SAS datasets used to create listing* *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. Screen Failures should be indicated under treatment at the top of the table and the reason for screen failure should be provided.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-2: Randomization and Analysis Sets – Randomized Subjects

Treatment: TTTTTTT

				Analysis Sets		
Site	Subject	Date and Time	Randomization Number	Safety	PK	Efficacy
XXX	XXX-YYYY	DDMONYYYYTHH:MM	XXXXX	XXX	XXX	XXX

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-3: Demographics – All Subjects
Treatment: TTTTTTT

Site	Subject	Birth Date	Age (yrs)	ASA Class	Sex	Race	Ethnicity
XXX	XXX-YYYY	DDMONYYYY	XX		XXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXXXX

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-4.1: Surgery Characteristics – Randomized Subjects

Treatment: TTTTTTT

			Surgery Time						
Site	Subject	Date	Start	Stop	Duration (hr)	Procedure Name	Incision Length (cm)	Anesthesia Type	Primary Surgeon
XXX	XXX-YYYY	DDMONYYYY	HH:MM	HH:MM	XX.X	Right TKA	xx.x	xxxxxxx	xxx
XXX	XXX-YYYY	DDMONYYYY	HH:MM	HH:MM	XX.X	Left TKA	xx.x	xxxxxxx	xxx
XXX	XXX-YYYY	DDMONYYYY	HH:MM	HH:MM	XX.X	Right TKA	xx.x	xxxxxxx	xxx
XXX	XXX-YYYY	DDMONYYYY	HH:MM	HH:MM	XX.X	Left TKA	xx.x	xxxxxxx	xxx
XXX	XXX-YYYY	DDMONYYYY	HH:MM	HH:MM	XX.X	Right TKA	xx.x	xxxxxxx	xxx
XXX	XXX-YYYY	DDMONYYYY	HH:MM	HH:MM	XX.X	Right TKA	xx.x	xxxxxxx	xxx

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-4.2: Tourniquet Characteristics – Randomized Subjects

Treatment: TTTTTTT

				Tourniquet Time			
Site	Subject	Date	Tourniquet Used?	Start	Stop	Duration (hr)	Maximum Pressure (mmHg)
XXX	XXX-YYYY	DDMONYYYY	xxx	HH:MM	HH:MM	XX.X	xxx
XXX	XXX-YYYY	DDMONYYYY	xxx	HH:MM	HH:MM	XX.X	xxx
XXX	XXX-YYYY	DDMONYYYY	xxx	HH:MM	HH:MM	XX.X	xxx
XXX	XXX-YYYY	DDMONYYYY	xxx	HH:MM	HH:MM	XX.X	xxx
XXX	XXX-YYYY	DDMONYYYY	xxx	HH:MM	HH:MM	XX.X	xxx
XXX	XXX-YYYY	DDMONYYYY	xxx	HH:MM	HH:MM	XX.X	xxx

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

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Listing 16.2-5: Study Drug Administration – Randomized Subjects

		Study Treatment			Start	Stop	Total Volume
Site	Subject	Randomized	Actual	Date	Time	Time	(mL)
XXX	XXX-YYYY	XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	DDMONYYYY	HH:MM	HH:MM	X
XXX	XXX-YYYY	XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	DDMONYYYY	HH:MM	HH:MM	X
XXX	XXX-YYYY	XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	DDMONYYYY	HH:MM	HH:MM	X
XXX	XXX-YYYY	XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	DDMONYYYY	HH:MM	HH:MM	X
XXX	XXX-YYYY	XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	DDMONYYYY	HH:MM	HH:MM	X
XXX	XXX-YYYY	XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	DDMONYYYY	HH:MM	HH:MM	X

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-6.1.1: Calculated Blood Loss - Method 1 – Randomized Subjects

Randomized Treatment: TTTTTTT

Site	Subject	Date and Time	Timepoint	Blood Volume Transfused (mL)	Hematocrit (%)	Calculated Blood Volume (mL)	Calculated Blood Loss (mL)
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Baseline	xxx.x	xxx.x	xxxx.x	N/A
		DDMONYYYYTHH:MM	PACU	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	6 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	12 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	24 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	48 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	72 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	120 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	Day 7	xxx.x	xxx.x	xxxx.x	xxx.x
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Baseline	xxx.x	xxx.x	xxxx.x	N/A
		DDMONYYYYTHH:MM	PACU	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	6 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	12 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	24 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	48 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	72 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	120 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	Day 7	xxx.x	xxx.x	xxxx.x	xxx.x

Note: Blood volume transfused is since the last Timepoint. Blood Volume is calculated according to section 9.8.1 of the Statistical Analysis Plan for study 404-C-201: For method 1, blood loss is in mL calculated by: $RBC_{lost} = BV_{baseline} * \left(Hct_{baseline} - Hct_{post-op\ hour}\right) + \mathrm{BV}_{transfused}$

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

Note to programmer: *Sort by collection date and time. Timepoints outside of the schedule windows should be listed under "Scheduled Timepoint" as "Unscheduled". Do not split a subject's data across pages.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-6.1.2: Calculated Blood Loss - Method 2 – Randomized Subjects

Randomized Treatment: TTTTTTT

Site	Subject	Date and Time	Timepoint	Blood Volume Transfused (g)	Hemaglobin (g/dL)	Calculated Blood Volume (mL)	Calculated Blood Loss (mL)
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Baseline	xxx.x	xxx.x	xxxx.x	N/A
		DDMONYYYYTHH:MM	PACU	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	6 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	12 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	24 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	48 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	72 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	120 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	Day 7	xxx.x	xxx.x	xxxx.x	xxx.x
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Baseline	xxx.x	xxx.x	xxxx.x	N/A
		DDMONYYYYTHH:MM	PACU	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	6 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	12 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	24 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	48 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	72 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	120 hrs	xxx.x	xxx.x	xxxx.x	xxx.x
		DDMONYYYYTHH:MM	Day 7	xxx.x	xxx.x	xxxx.x	xxx.x

Blood volume transfused is since the last Timepoint. Blood Volume is calculated according to section 9.8.1 of the Statistical Analysis Plan for study 404-C-201: For method 2, blood loss is in mL calculated by:

$$RBC_{lost} = \frac{1000*(BV_{baseline}*(Hb_{baseline}-Hb_{post-op\ hour})*0.001+52*\mathrm{BV}_{transfused})}{Hb_{baseline}}$$

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

Note to programmer: *Sort by collection date and time. Timepoints outside of the schedule windows should be listed under "Scheduled Timepoint" as "Unscheduled". Do not split a subject's data across pages.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201

Listing 16.2-6.2: Blood Transfusion - Randomized Subjects

Treatment: TTTTTTT

Site	Subject	Start Date and Time	End Date and Time	# of Units	Associated Adverse Event
XXX	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
XXX	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*
	XXX-YYYY	DDMONYYYYTHH:MM	DDMONYYYYTHH:MM	x	*Preferred Term*

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-6.3: Passive and Active Knee Flexion - Randomized Subjects
Treatment: TTTTTTT

Site	Subject	Timepoint [1]	Time of Assesment[2]	Date and Time	Passive Knee Flexion (Degrees)	Active Knee Flexion (Degrees)
XXX	XXX-YYYY	Baseline	N/A	DDMONYYYYTHH:MM	XXX	XXX
		Day 1	N/A	DDMONYYYYTHH:MM	XXX	XXX
		Day 2	N/A	DDMONYYYYTHH:MM	XXX	XXX
		Day 3	N/A	DDMONYYYYTHH:MM	XXX	XXX
XXX	XXX-YYYY	Baseline	AM	DDMONYYYYTHH:MM	XXX	XXX
		Day 1	AM	DDMONYYYYTHH:MM	XXX	XXX
		Day 1	PM	DDMONYYYYTHH:MM	XXX	XXX
		Day 2	AM	DDMONYYYYTHH:MM	XXX	XXX
		Day 2	PM	DDMONYYYYTHH:MM	XXX	XXX
		Day 3	AM	DDMONYYYYTHH:MM	XXX	XXX
		. . .				

[1] Timepoints are Day 1 through Day 3 prior to Protocol Amendment 2 and Day 1 through Day 5 after Protocol Amendment 2.
[2] AM/PM is collected only after Amendment 2.

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-6.4: TUG Test - Randomized Subjects

Treatment: TTTTTTT

Site	Subject	Timepoint[1]	Date and Time	Done?	Reason not done	Duration of Test (seconds)	Aid Used?	Physical Assistance
XXX	XXX-YYYY	Baseline	DDMONYYYYTHH:MM	Y		XXX	XXX	X
		Day 1	DDMONYYYYTHH:MM	N	XXXXXXXXXXXXXXX			
		Day 2-AM	DDMONYYYYTHH:MM	Y		XXX	XXX	X
		Day 2-PM	DDMONYYYYTHH:MM	Y		XXX	XXX	X
		Unscheduled	DDMONYYYYTHH:MM	Y		XXX	XXX	X
		Unscheduled	DDMONYYYYTHH:MM	Y		XXX	XXX	X
		Day 7	DDMONYYYYTHH:MM	Y		XXX	XXX	X

Physical Assistance: 1=Total Assistance 2=Maximal Assistance 3=Moderate Assistance
4=Minimal Assistance 5=Supervision 6=Modified Independence 7=Complete Independence
[1] Hospital Discharge only applies to the subjects enrolled after Protocol Amendment 2.

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-6.5: Numeric Rating Scale (NRS) - Randomized Subjects

TREATMENT: *treatment-name*

				Time From Dose				
Site	Subject	Timepoint	Date Time	Scheduled (hr)	Actual (hr)	Deviation (hrs)	NRS Score	NRS-R Performed?
XXX	XXX-YYYY	D1 Preop	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		PACU	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		2h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		4h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		6h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		8h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		12h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		16h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		24h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		36h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		48h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		72h	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y
		Day 7	DDMONYYYYTHH:MM	XX.XX	XX.XX	XXXX	XX.X	Y

NRS: 0=No pain to 10=Worst Pain Imaginable ND=Not Done NA=Not Applicable
* = out of window

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-6.6: Knee and Thigh Circumfrence Measurements - Randomized Subjects

TREATMENT: *treatment-name*

				Thigh (cm)		Knee (cm)		
Site	Subject	Timepoint	Date Time	Right	Left	Right	Left	Procedure Name
XXX	XXX-YYYY	D1 Preop	DDMONYYYYTHH:MM	XX.X	XX.X	XX.X	XX.X	Right TKA
		48h	DDMONYYYYTHH:MM	XX.X	XX.X	XX.X	XX.X	Right TKA
		Day7	DDMONYYYYTHH:MM	XX.X	XX.X	XX.X	XX.X	Right TKA
XXX	XXX-YYYY	D1 Preop	DDMONYYYYTHH:MM	XX.X	XX.X	XX.X	XX.X	Left TKA
		48h	DDMONYYYYTHH:MM	XX.X	XX.X	XX.X	XX.X	Left TKA
		Day7	DDMONYYYYTHH:MM	XX.X	XX.X	XX.X	XX.X	Left TKA
XXX	XXX-YYYY	D1 Preop	DDMONYYYYTHH:MM	XX.X	XX.X	XX.X	XX.X	Right TKA
		48h	DDMONYYYYTHH:MM	XX.X	XX.X	XX.X	XX.X	Right TKA
		Day7	DDMONYYYYTHH:MM	XX.X	XX.X	XX.X	XX.X	Right TKA

ND=Not Done, NA=Not Applicable
* = out of window

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

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Listing 16.2-6.7: Surgical Wound Aspect Score (SWAS) - Randomized Subjects

TREATMENT: *treatment-name*

				Numerical Score			
Site	Subject	Timepoint	Date Time	Wound Oozing	Erythema	Ecchymosis	Blisters
XXX	XXX-YYYY	D1 Preop	DDMONYYYYTHH:MM	x	x	x	x
		48h	DDMONYYYYTHH:MM	x	x	x	x
		Day7	DDMONYYYYTHH:MM	x	x	x	x
XXX	XXX-YYYY	D1 Preop	DDMONYYYYTHH:MM	x	x	x	x
		48h	DDMONYYYYTHH:MM	x	x	x	x
		Day7	DDMONYYYYTHH:MM	x	x	x	x
XXX	XXX-YYYY	D1 Preop	DDMONYYYYTHH:MM	x	x	x	x
		48h	DDMONYYYYTHH:MM	x	x	x	x
		Day7	DDMONYYYYTHH:MM	x	x	x	x

ND=Not Done, NA=Not Applicable,
* = out of window

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

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Listing 16.2-7: Phone Calls – Randomized Subjects

Treatment: TTTTTTT

Site	Subject	Date of Phone Contact	Scheduled Timepoint	Was the Call Made?	Was there a reoperation?	Number of Reoperations	Independent Ambulation?	Date of Ind. Amb.
XXX	XXX-YYYY	DDMONYYYY	Day 14	Y	N	NA	N	NA
	XXX-YYYY	DDMONYYYY	Day 30	Y	N	NA	Y	DDMONYYYY
	XXX-YYYY	DDMONYYYY	Day 60	Y	N	NA	Y	DDMONYYYY
XXX	XXX-YYYY	DDMONYYYY	Day 14	N	ND	NA	ND	NA
	XXX-YYYY	DDMONYYYY	Day 30	Y	N	NA	N	NA
	XXX-YYYY	DDMONYYYY	Day 60	Y	N	NA	Y	DDMONYYYY
XXX	XXX-YYYY	DDMONYYYY	Day 14	Y	N	NA	N	NA
	XXX-YYYY	DDMONYYYY	Day 30	Y	N	NA	N	NA
	XXX-YYYY	DDMONYYYY	Day 60	Y	Y	x	N	NA

ND=Not Done, NA=Not Applicable

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-8: Neurological Assessment – Randomized Subjects

Treatment: TTTTTTTT

Site	Subject	Date and Time Of Assessment	Time From Dose: Scheduled (hr)	Time From Dose: Actual (hr)	Time From Dose: Deviation (mins)	Questions: 1	2	3	4	5	6
XXX	XXX-YYYY	DDMONYYYYTHH:MM	Screening	NA	NA	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	D1 PREOP	NA	NA	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	12	0.XX	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	24	X	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	36	ND							
		DDMONYYYYTHH:MM	48	X	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	60	X	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	72	XX	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	96	XX	X	XXX	XXX	XXX	XXX	XXX	XXX
	XXX-YYYY	DDMONYYYYTHH:MM	Screening	NA	NA	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	D1 PREOP	NA	NA	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	12	XX	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	24	XX	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	36	XX	-X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	48	XX	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	60	XX	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	72	XX	X	XXX	XXX	XXX	XXX	XXX	XXX
		DDMONYYYYTHH:MM	96	XX	X	XXX	XXX	XXX	XXX	XXX	XXX

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 no related to the use of eye glasses?
6) Are your muscles twitching?

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-9: Electrocardiogram Findings – Investigator Assessment – All Subjects
Treatment: DepoTXA 400

			Time From Dose				
Site	Subject	Date and Time of Sample	Scheduled Timepoint	Actual (hr)	Deviation (mins)	Finding	If "Abnormal", specify
XXX	XXX-YYYY	DDMONYYYYTHH:MM	D1PreOp	NA	NA	Normal	
		DDMONYYYYTHH:MM	1h	XX.X	X	Normal	
		DDMONYYYYTHH:MM	12h	XX.X	X	Normal	
	XXX-YYYY	DDMONYYYYTHH:MM	D1PreOp	NA	NA	Normal	
		DDMONYYYYTHH:MM	1h	XX.X	X	Normal	
		DDMONYYYYTHH:MM	12h	XX.X	X	Normal	
	XXX-YYYY	DDMONYYYYTHH:MM	D1PreOp	NA	NA	Normal	
		DDMONYYYYTHH:MM	1h	XX.X	X	Normal	
		DDMONYYYYTHH:MM	12h	XX.X	X	Normal	

NA=Not applicable ND=Not done
Source: *list SAS datasets used to create listing* *DDMONYYYYTHH:MM*
SAS *X.Y* *program_name*

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-10: Vital Signs – All Subjects

Treatment: TTTTTTTT

SITE: XXX

			Time from Dose				Blood Pressure				
Subject	Visit	Date and Time	Sched (hr)	Actual (hr)	Devi-ation (mins)	Heart Rate (bpm)	Sys. (mmHg)	Dia. (mmHg)	Height (cm)	Weight (kg)	Body Mass Index (m/kg^2)
XXX-YYYY	Screening	DDMONYYYYTHH:MM	NA	NA	NA	XX	XXX	XXX	XXX	XXX	XXX
	D1 Preop	DDMONYYYYTHH:MM	0	X	X	XX	XXX	XXX			
	5 min	DDMONYYYYTHH:MM	0.08	X	X	XX	XXX	XXX			
	15 min	DDMONYYYYTHH:MM	0.25	X	X	XX	XXX	XXX			
	30 min	DDMONYYYYTHH:MM	0.50	X	-X	XX	XXX	XXX			
	1h	DDMONYYYYTHH:MM	1	X	X	XX	XXX	XXX			
	2h	DDMONYYYYTHH:MM	2	X	X	XX	XXX	XXX			
	4h	DDMONYYYYTHH:MM	4	X	X	XX	XXX	XXX			
	6h	DDMONYYYYTHH:MM	6	X	X	XX	XXX	XXX			
	8h	DDMONYYYYTHH:MM	8	X	X	XX	XXX	XXX			
	12h	DDMONYYYYTHH:MM	12	X	X	XX	XXX	XXX			
	16h	DDMONYYYYTHH:MM	16	X	X	XX	XXX	XXX			
	24h	DDMONYYYYTHH:MM	24	X	X	XX	XXX	XXX			
	36h	DDMONYYYYTHH:MM	36	X	X	XX	XXX	XXX			
	48h	DDMONYYYYTHH:MM	48	X	X	XX	XXX	XXX			
	60h	DDMONYYYYTHH:MM	60	X	X	XX	XXX	XXX			
	72h	DDMONYYYYTHH:MM	72	X	X	XX	XXX	XXX			
	96h	DDMONYYYYTHH:MM	96	X	X	XX	XXX	XXX			

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-11.1: All Adverse Events – All Subjects

Treatment: TTTTTTT

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	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. This this template for the following listings:*
Listing 16.2-11.2.1: Treatment-Emergent Adverse Events – Randomized Subjects
Listing 16.2-11.2.2: Treatment-Emergent Study Drug Related Adverse Events – Randomized Subjects
Listing 16.2-11.3: All Serious Adverse Events – All Subjects
Listing 16.2-11.3.CT: All Non-Serious Adverse Events – All Subjects
Listing 16.2-11.4.1: Treatment-Emergent Serious Adverse Events – Randomized Subjects
Listing 16.2-11.4.1.CT: Treatment-Emergent Non-Serious Adverse Events – Randomized Subjects
Listing 16.2-11.4.2: Treatment-Emergent Study Drug Related Serious Adverse Events – Randomized Subjects

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Listing 16.2-12.1: All Prior Medications – Randomized Subjects
Treatment: TTTTTTT

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	XXXXXXXXXXXXXXXXXXXX
			ATC Level 3	XXXXXXXXXXXXXXXXXXXXXX
			ATC Level 4	XXXXXXXXXXXXXXXXXXXX
			Preferred Name	XXXXXXXXXXXXXXXXXXXX
			Verbatim	XXXXXXXXXXXXXXXXXXXX
			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 an 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 16.2-12.2: Concomitant Medications – Randomized Subjects

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-13: Medical/Surgical History – Randomized Subjects
Treatment: TTTTTTT

Site	Subject	Date Start	Stop	Number	Classification	Term
XXX	XXX-YYYY	DDMONYYYY	DDMONYYYY	X	System Organ Class: Preferred Term: Verbatim:	

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

Note to programmer: *If ongoing put ONGOING in stop date column.*

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-14: Informed Consent – All Subjects
Treatment: TTTTTTT

			Date			Met Criteria	
Site	Subject	Subject Initials	Screening Visit	Signed Consent	Protocol Version	Inclusion	Exclusion
XXX	XXX-YYYY	ABC	DDMONYYYY	DDMONYYYY	AMENDMENT 2	YES	YES

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-15.1: Subject Eligibility – All Subjects

Treatment: TTTTTTTTTTTTT

Site	Subject	Date of Informed Consent	Date of Eligibility Assessment	Criteria Failed
XXX	XXX-YYYY	DDMONYYYY	DDMONYYYY	
XXX	XXX-YYYY	DDMONYYYY	DDMONYYYY	
XXX	XXX-YYYY	DDMONYYYY	DDMONYYYY	
XXX	XXX-YYYY	DDMONYYYY	DDMONYYYY	Inclusion: 1, 4 Exclusion: 8, 10, 12

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

Note to programmer: *If subject was not randomized treatment should be 'NOT RANDOMIZED'. Criteria Failed may take any or all of the following values: Inclusion 1, 2, 3, 4 or 5 and Exclusion 1 through 12. Insert a page break after each treatment group.*

Pacira Pharmaceuticals (Page 1 of 2) Protocol: 404-C-201
Listing 16.2-15.2: Subject Eligibility – Inclusion/Exclusion Criteria

Inclusion/Exclusion Criteria	
Inclusion 1	Male or female, ≥18 years of age at screening.
Inclusion 2	Scheduled to undergo elective unilateral open TKA under general, spinal, or regional anesthesia.
Inclusion 3	American Society of Anesthesiology (ASA) physical status 1, 2, or 3.
Inclusion 4	Female patient must be surgically sterile; or at least 2 years postmenopausal; or have a monogamous partner who is surgically sterile; or practicing double-barrier contraception; or practicing abstinence (must agree to use double-barrier contraception in the event of sexual activity); or using an insertable, injectable, or transdermal, contraceptive approved by the FDA for greater than 2 months prior to screening. All women of childbearing potential (ie, premenopausal without permanent sterilization) must commit to the use of an acceptable form of birth control for the duration of the study and for 30 days after completion of the study.
Inclusion 5	Able to provide informed consent, adhere to the study visit schedule, and complete all study assessments.

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

Pacira Pharmaceuticals (Page 2 of 2) Protocol: 404-C-201
Listing 16.2-15.2: Subject Eligibility – Inclusion/Exclusion Criteria

Inclusion/Exclusion Criteria	
Exclusion 1	Currently pregnant, nursing, or planning to become pregnant during the study or within 30 days after study drug administration.
Exclusion 2	Planned concurrent surgical procedure (eg, bilateral TKA).
Exclusion 3	Prior open knee surgery on ipsilateral knee. Prior arthroscopy is permitted.
Exclusion 4	Patients taking a medication with a known procoagulant effect (eg, combination hormonal contraceptives, Factor IX complex concentrates or anti-inhibitor coagulant concentrates, or all-trans retinoic acid).
Exclusion 5	Contraindication or hypersensitivity to TXA.
Exclusion 6	History of thrombosis or prior VTE.
Exclusion 7	Known coagulopathy or active intravascular clotting.
Exclusion 8	Prior myocardial infarction.
Exclusion 9	Prior cardiovascular accident (stroke) or subarachnoid hemorrhage.
Exclusion 10	History of epilepsy.
Exclusion 11	Presence of an intravascular stent.
Exclusion 12	History of impaired kidney function, chronic respiratory disease, rheumatoid arthritis, coagulopathy, or loss of sensation in extremities.
Exclusion 13	Renal insufficiency as indicated by serum creatinine >upper limit of normal (by central laboratory assessment).
Exclusion 14	Anemia (Hb level <10 g/dL).
Exclusion 15	Uncontrolled anxiety, psychiatric, or neurological disorder that might interfere with study assessments.
Exclusion 16	Acquired defective color vision.
Exclusion 17	Malignancy in the last 2 years, with the exception of non-metastatic basal cell or squamous cell carcinoma of the skin or localized carcinoma in situ of the cervix.
Exclusion 18	Suspected or known history of drug or alcohol abuse within the previous year.
Exclusion 19	Body weight <50 kg (110 pounds) or a body mass index >44 kg/m^2.
Exclusion 20	Administration of an investigational drug within 30 days or 5 elimination half-lives of such investigational drug, whichever is longer, prior to study drug administration, or planned administration of another investigational product or procedure during the patient's participation in this study.

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-16: Pregnancy Test – All Subjects

Treatment: TTTTTTTTT

Site	Subject	Visit	Date	Sex	Childbearing Potential	Pregnancy Test Result
XXX	XXX-YYYY	Screening	DDMONYYYY	Female	YES	NEGATIVE
		D1 Preop	DDMONYYYY			NEGATIVE
	XXX-YYYY	Screening	DDMONYYYY	Female	NO	NOT APPLICABLE
		D1 Preop	DDMONYYYY			NOT APPLICABLE
	XXX-YYYY	Screening	DDMONYYYY	Male		NOT APPLICABLE
		D1 Preop	DDMONYYYY			NOT APPLICABLE

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

Note to programmer: *Possible results for screening tests are: POSITIVE, NEGATIVE, NOT DONE, or NOT APPLICABLE (if Childbearing Potential = 'NO' or Sex = 'Male').*

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-17: Protocol Deviations – All Subjects

Treatment: TTTTTTT

Site	Subject	Start Date and Time	Protocol Deviation Coded Term	Description	Action Taken
XXX	XXX-YYYY	DDMONYYYYTHH:MM	XXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXX

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

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-18.1: Pharmacokinetic Concentrations – All Subjects
Treatment: DepoTXA 400 (Enrolled After Protocol Amendment 2)

		Date and Time of				Time From Dose			
Site	Subject	Dose Infusion Date	Start Time	End Time	PK Sample	Scheduled (hr)	Actual (hr)	Deviation (mins)	Concentration (ng/mL)
XXX	XXX-YYYY	DDMONYYYY	HH:MM	HH:MM	DDMONYYYYTHH:MM	0	XX	X	BLOQ
					DDMONYYYYTHH:MM	0.08	0.XX	X	XXX.X
					DDMONYYYYTHH:MM	0.25	0.XX	X	XXX.X
					DDMONYYYYTHH:MM	0.50	X	X	XXX.X
					DDMONYYYYTHH:MM	1	ND		
					DDMONYYYYTHH:MM	2	X	-X	XXX.X
					DDMONYYYYTHH:MM	4	X	X	XXX.X
					DDMONYYYYTHH:MM	6	X	X	XXX.X
					DDMONYYYYTHH:MM	8	XX	-X	XXX.X
					DDMONYYYYTHH:MM	12	XX	X	XXX.X
					DDMONYYYYTHH:MM	16	XX	X	XXX.X
					DDMONYYYYTHH:MM	24	XX	X	XXX.X
					DDMONYYYYTHH:MM	36	XX	X	XXX.X
					DDMONYYYYTHH:MM	48	XX	-X	XXX.X
					DDMONYYYYTHH:MM	60	XX	X	XXX.X
					DDMONYYYYTHH:MM	72	XX	X	XXX.X
					DDMONYYYYTHH:MM	96	XX	X	XXX.X

BLOQ=below limit of quantitation ND=Not Done
Note: Actual time (hr) is calculated from Infusion End Time.

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

Note to programmer: *Insert a page break after each subject. If a sample was not collected – put ND in actual column under time from dose. Sort listing within subject by sample date and time.*
Sort by Treatment, Enrolled Prior to Protocol Amendment 2, then Enrolled After Protocol Amendment 2, Subject, PK date/time

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-18.2: Pharmacokinetic Parameters – All Subjects
Treatment: DepoTXA 400 (Enrolled Prior to Protocol Amendment 2)

				Early		Late			
Site	Subject	AUC(0-inf) (ng*hr/mL)	AUC(0-last) (ng*hr/mL)	Cmax ng/mL	Tmax (hr)	Cmax ng/mL	Tmax (hr)	Half-life (hr)	Lamba_z (hr)
XXX	XXX-YYYY	XXXX.XX	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	X.XXX	X.XXX
	XXX-YYYY	NC	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	NC	NC
	XXX-YYYY	XXXX.XX	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	X.XXX	X.XXX
	XXX-YYYY	XXXX.XX	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	X.XXX	X.XXX
	XXX-YYYY	XXXX.XX	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	X.XXX	X.XXX
YYY	XXX-YYYY	XXXX.XX	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	X.XXX	X.XXX
	XXX-YYYY	XXXX.XX	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	X.XXX	X.XXX
	XXX-YYYY	XXXX.XX	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	X.XXX	X.XXX
	XXX-YYYY	XXXX.XX	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	X.XXX	X.XXX
	XXX-YYYY	XXXX.XX	XXXX.XX	XXX.X	XX.X	XX.X	XX.X	X.XXX	X.XXX

NC=Not Calculated
Source: *list SAS datasets used to create listing* *DDMONYYYYTHH:MM*
SAS *X.Y* *program_name*

Note to programmer: *If a parameter was not calculated – put NC in column.*
Sort by Treatment, Enrolled Prior to Protocol Amendment 2, then Enrolled After Protocol Amendment 2, Subject

Pacira Pharmaceuticals (Page X of Y) Protocol: 404-C-201
Listing 16.2-19: Unique Adverse Events Terms and Associated Coded Terms

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

Coded using MedDRA version 19.1 or higher.
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: 404-C-201
Listing 16.2-20: 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 World Health Organization Drug Dictionary Enhanced (WHO-DD) September 2016
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*

15. TABLE OF CONTENTS FOR FIGURES

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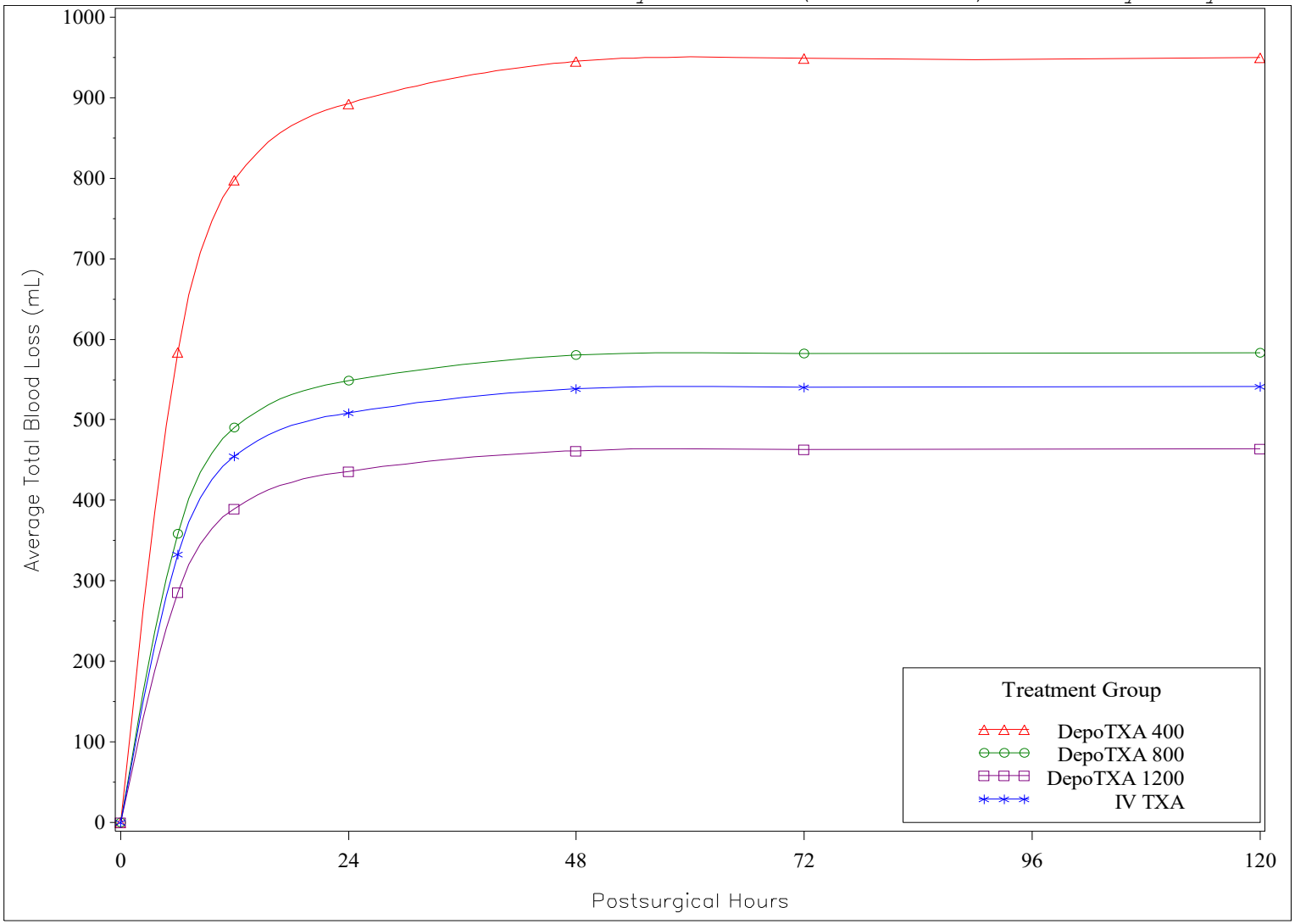
Figure 14.2-9.1: Plot of Total Blood Loss over Time by Treatment (Method 1 Hct) - Efficacy Analysis Set



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

Note to programmer: *Margins on the y-axis should be adjusted, but consistent for figures 14.2-9.1, 14.2-9.2, and 14.2-9.3. Use template Figure 14.2-9.1 for the following Figure:*

Figure 14.2-9.2: Plot of Total Blood Loss over Time by Treatment (Method 2 Hb) – Efficacy Analysis Set

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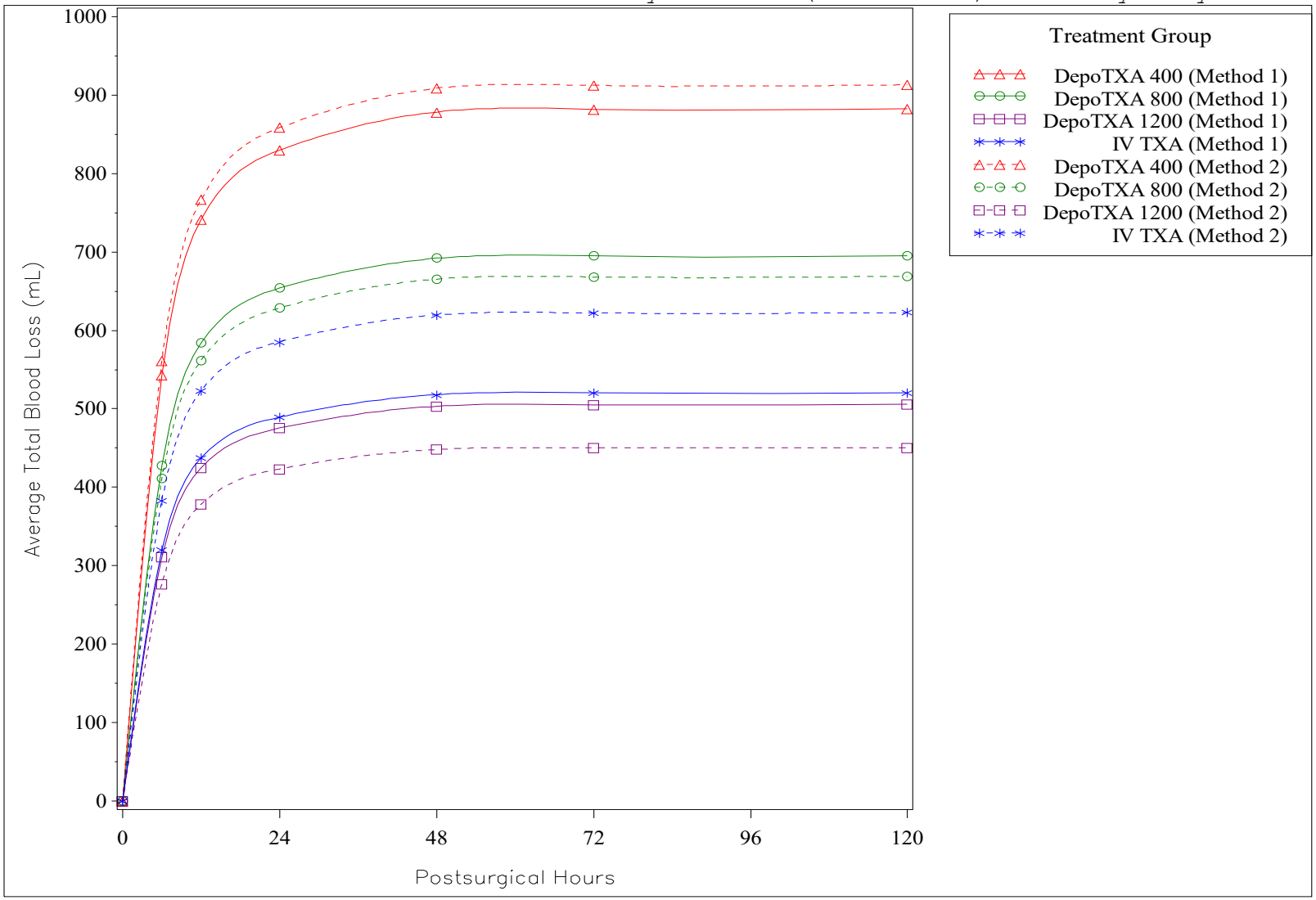
Figure 14.2-9.3: Plot of Total Blood Loss over Time by Treatment (Both Methods) – Efficacy Analysis Set



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

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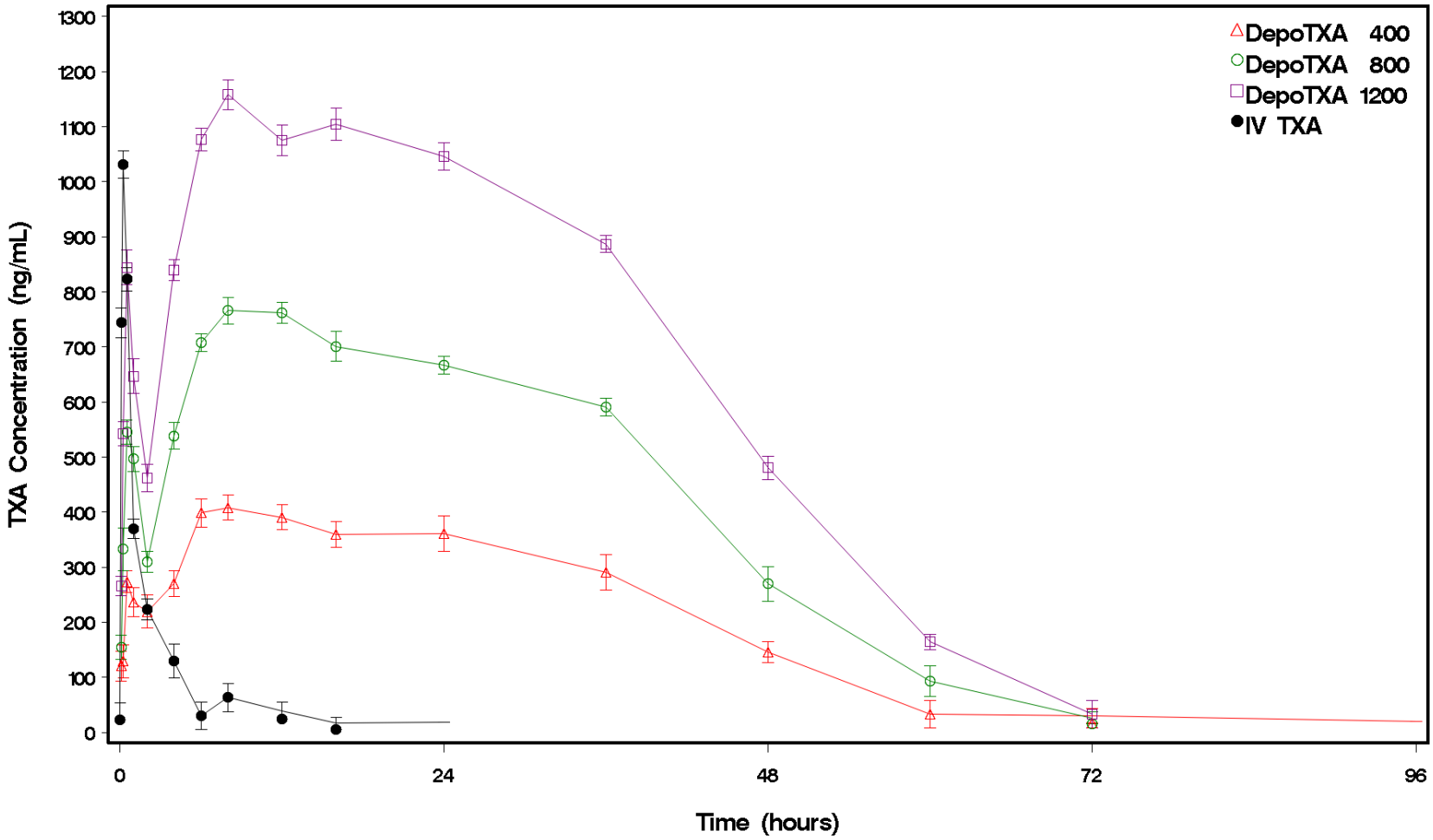
Figure 14.4-3.1: Plot of Mean (± SE) TXA Concentration (ng/mL) over Time by Treatment – PK Analysis Set



Source: *list SAS datasets used to create listing*
SAS X.Y

DDMONYYYYTHH:MM
program_name

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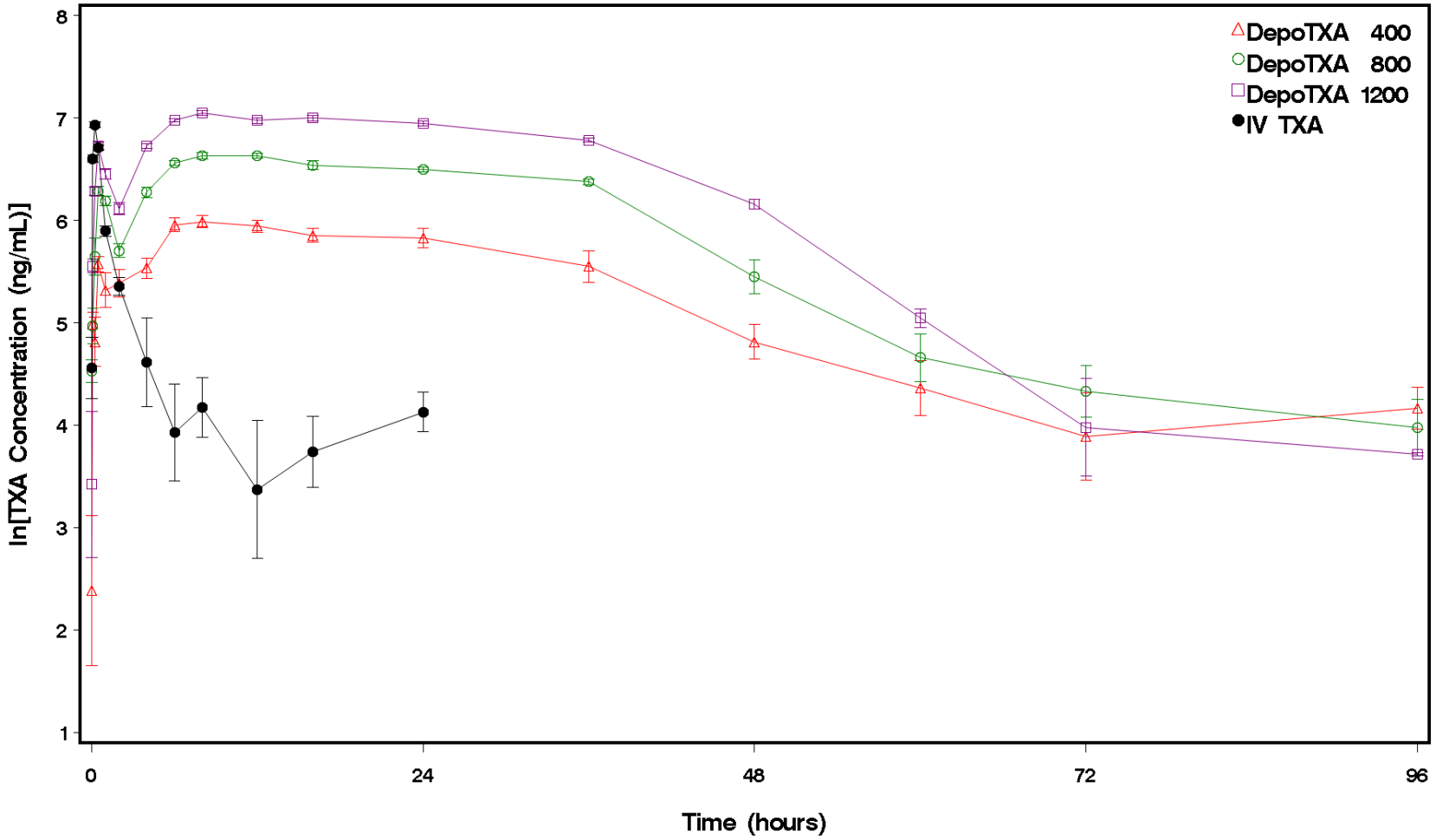
Figure 14.4-3.2: Plot of ln Mean (± SE) TXA Concentration (ng/mL) over Time by Treatment (for Subjects Enrolled After Protocol Amendment 2) – PK Analysis Set



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

SAS X.Y *program_name*
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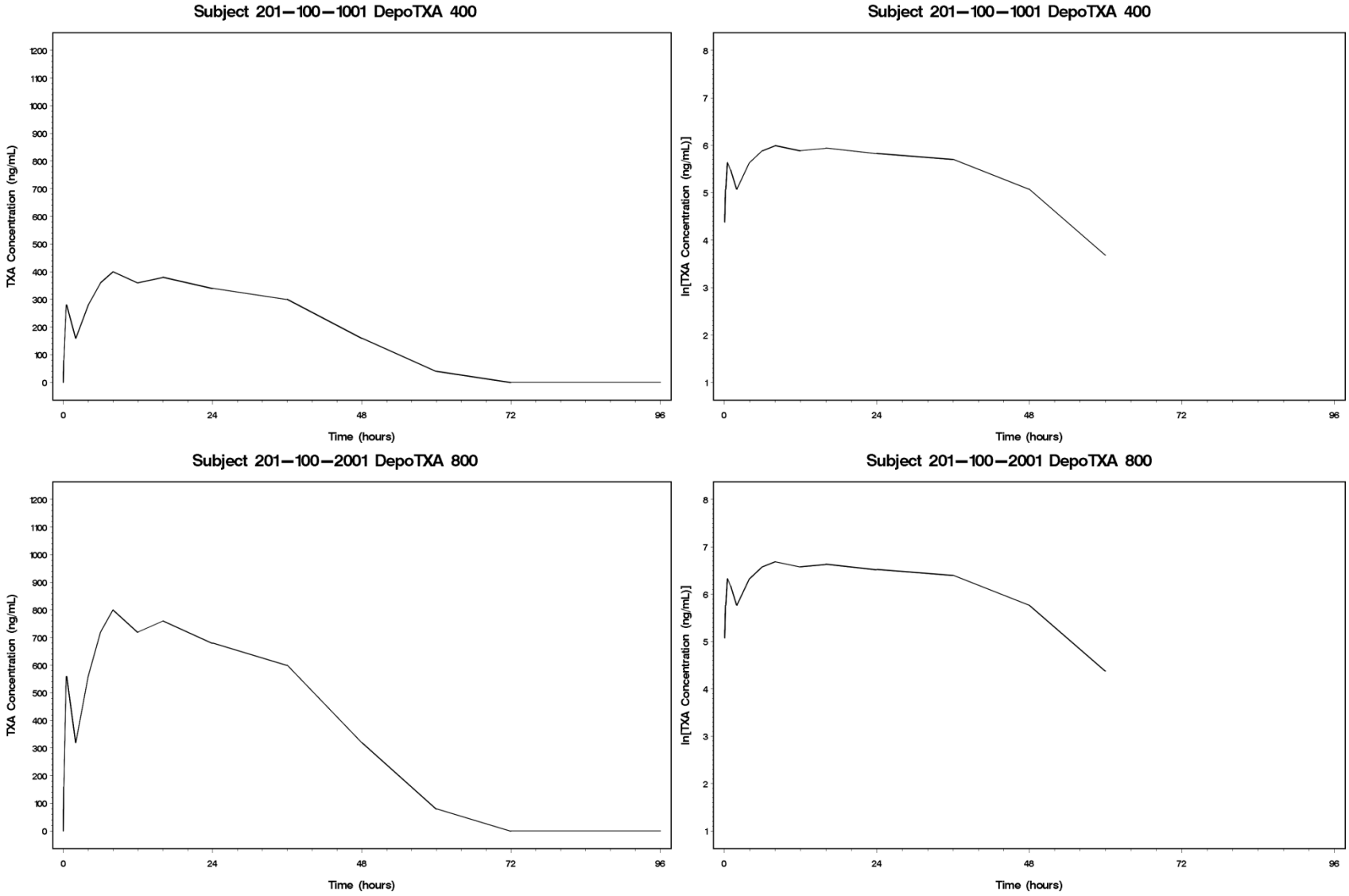
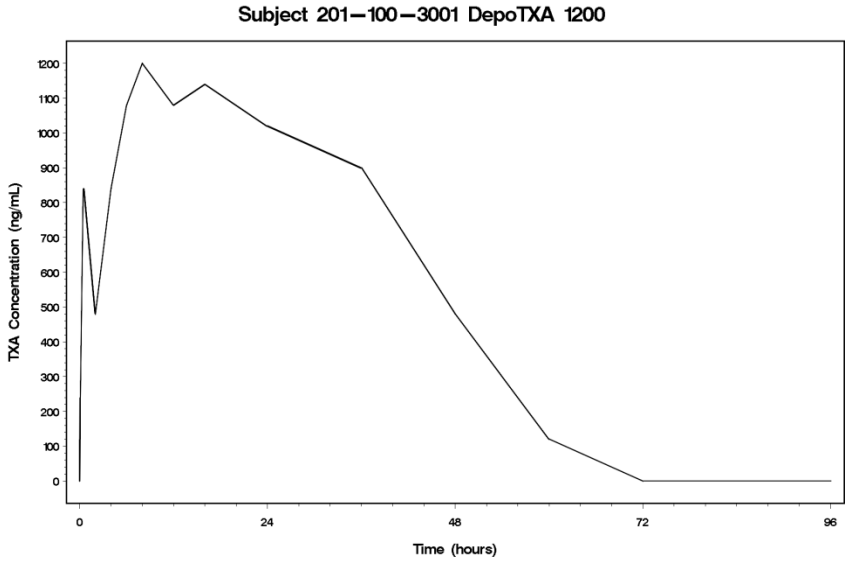
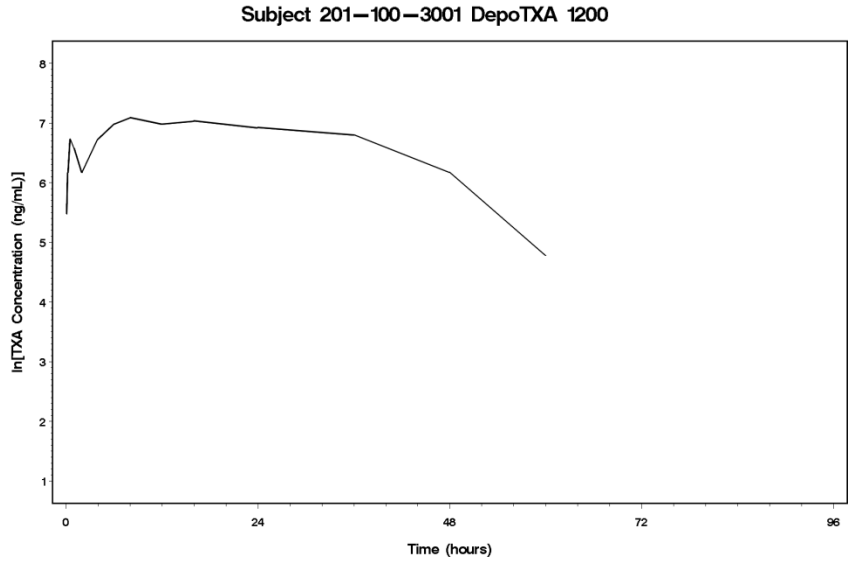
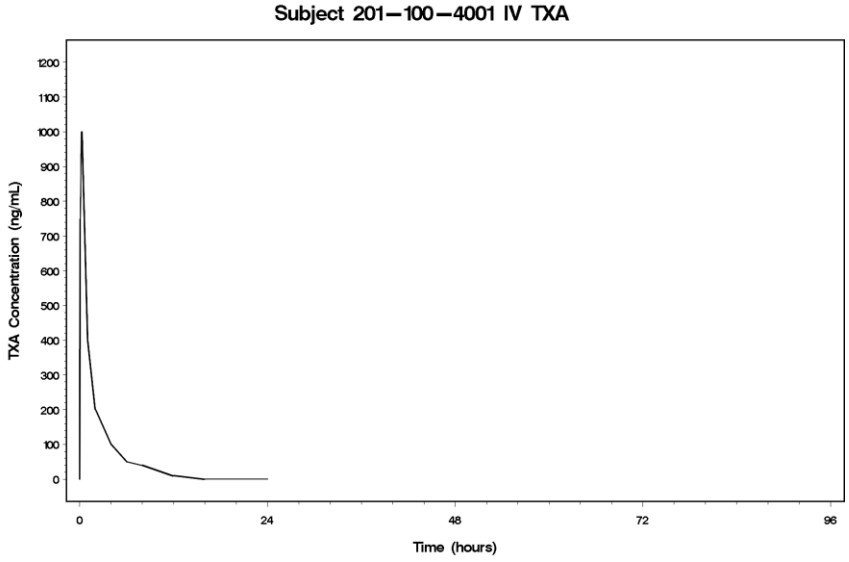
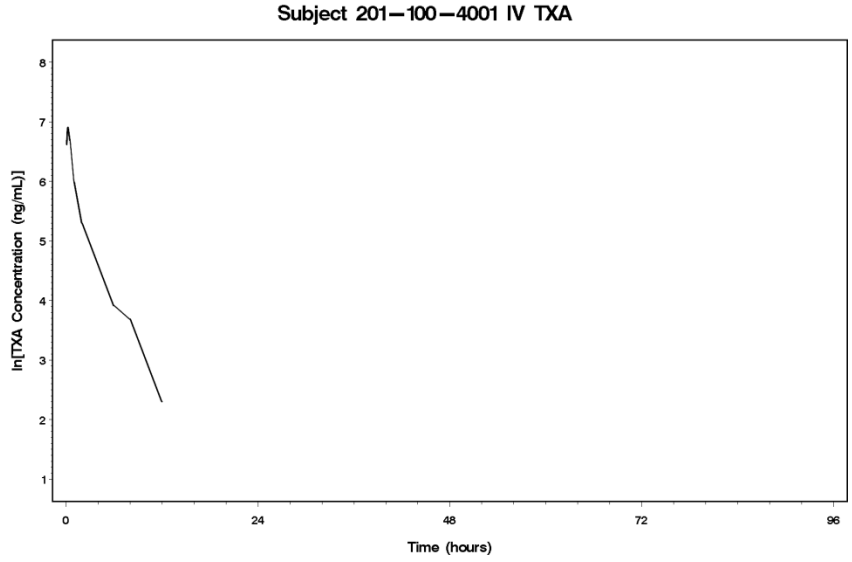
Figure 14.4-3.3: Plot of Individual Subject TXA Concentrations (ng/mL) over Time – PK Analysis Set




Subject 201−100−3001 DepoTXA 1200
TXA Concentration (ng/mL)
Time (hours)


Subject 201−100−3001 DepoTXA 1200
ln[TXA Concentration (ng/mL)]
Time (hours)


Subject 201−100−4001 IV TXA
TXA Concentration (ng/mL)
Time (hours)


Subject 201−100−4001 IV TXA
ln[TXA Concentration (ng/mL)]
Time (hours)

Note to programmer: *Margins on the y-axis should be adjusted, but consistent for figures 14.4-3.1, 14.4-3.2, and 14.4-3.3*

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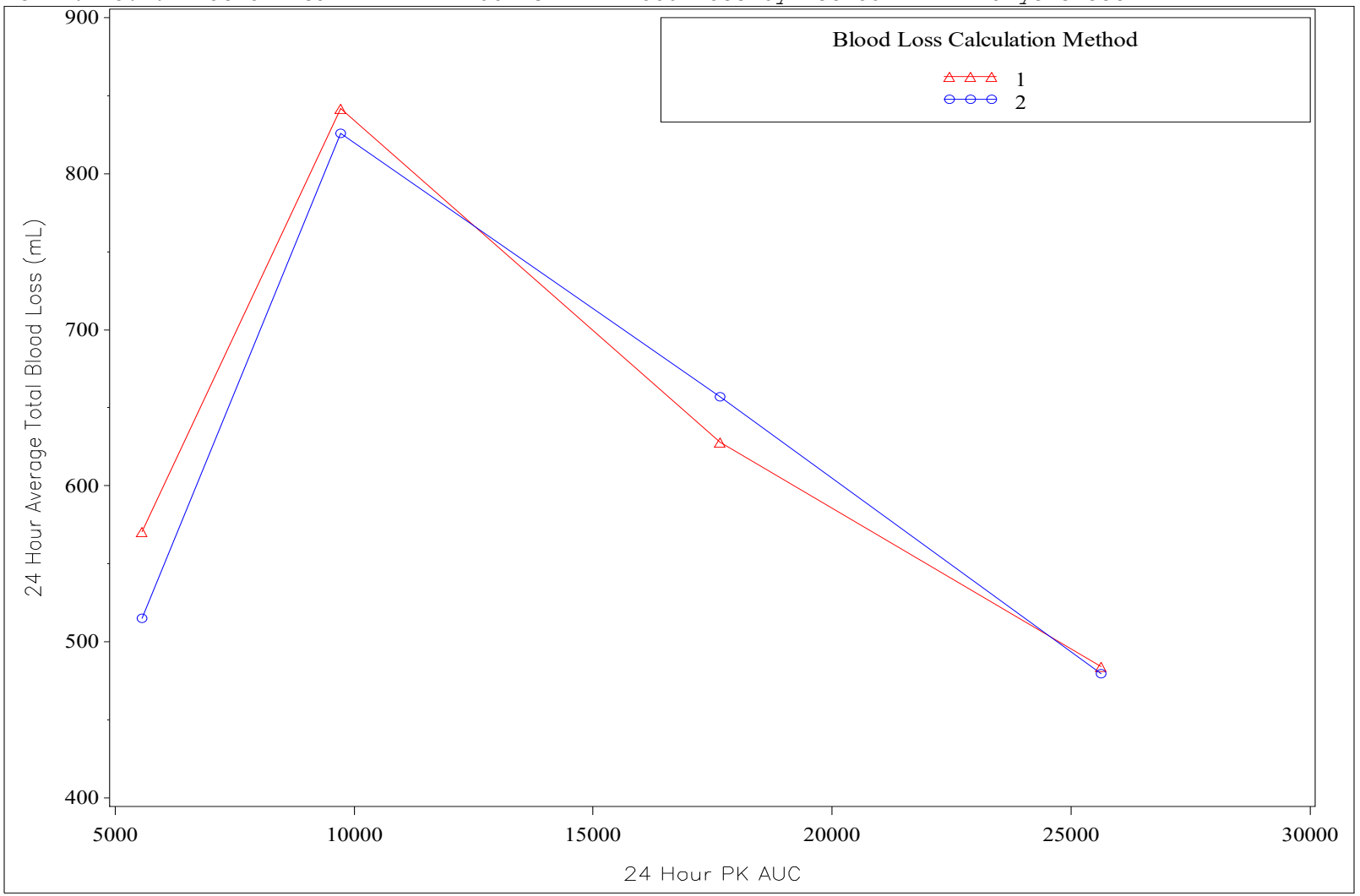
Figure 14.4-3.4: Plot of Mean TXA 24h AUC vs 24h Blood Loss by Method – PK Analysis Set



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

Note to programmer: *Set margins on the x-axis and y-axis as appropriate.*