STATISTICAL ANALYSIS PLAN - TABLES, FIGURES AND LISTINGS SHELL APPROVAL

Study name:	DPI-201: A Phase 2, Single-Dose, Randomized, Open-Label, Active-Controlled, Crossover, Pharmacodynamic, and Pharmacokinetic Comparative Study of a Novel Pramlintide-Insulin Co-Formulation in Adults with Type 1 Diabetes Mellitus
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The above SAP / TFL Shell has been reviewed and approved by Worldwide:

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STATISTICAL ANALYSIS PLAN - TABLES, FIGURES AND LISTINGS SHELL APPROVAL

The above SAP / TFL Shell has been reviewed and approved by the Sponsor:

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Date: 14-NOV-2019

STATISTICAL ANALYSIS PLAN - TABLES, FIGURES AND LISTINGS SHELL APPROVAL

The above SAP / TFL Shell has been reviewed and approved by the Sponsor:

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Date: 14 Nov 2019

Statistical Analysis Plan

Title: Phase 2, Single-Dose, Randomized, Open-Label, Active-Controlled, Crossover, Pharmacodynamic, and Pharmacokinetic Comparative Study of a Novel Pramlintide-Insulin Co-Formulation in Adults with Type 1 Diabetes Mellitus

Protocol Number: DPI-201

Protocol Version: 3.0 / 06SEP2019

SAP Version 1.0

SAP Issue Date: 14-NOV-2019

SAP Author: Tuomas Kemppainen, MSc

Previous SAP Versions

No previous versions

SAP Amendments Before Database Lock

Version	Issue Date	Section	Revision / Addition	Rationale
0.1	28-AUG-2019			First draft for internal review.
0.2	02-SEP-2019			First draft for Sponsor review.
0.3	19-SEP-2019			Second draft for Sponsor review. Including TFL shells.
0.4	08-OCT-2019			Pre-final version.
1.0	08-NOV-2019			Version 1.0

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
AE	adverse event
AESI	adverse event of special interest
ALT	alanine aminotransferase
ANOVA	analysis of variance
AOC	area over the curve
AST	aspartate aminotransferase
AUC	area under the concentration-time curve
AUC_{0-90}	area under the concentration-time curve from 0 to 90 minutes post-dosing
AUC_{0-180}	area under the concentration-time curve from 0 to 180 minutes post-dosing
AUC_{0-360}	area under the concentration-time curve from 0 to 360 minutes post-dosing
BGM	blood glucose measurement
BMI	body mass index
BP	blood pressure
CLIA	Clinical Laboratory Improvement Act
C_{max}	maximum plasma concentration
CRF	case report form
CRO	contract research organization
eCRF	electronic case report form
ECG	electrocardiogram
EDC	electronic data capture
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GLP-1	Glucagon-like peptide-1
HbA1c	glycated hemoglobin
HBV	hepatitis B virus
HCV	hepatitis C virus
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
HR	heart rate

Abbreviation	Definition
IB	Investigator's Brochure
I:C	insulin-to-carbohydrate
ICF	informed consent form
IEC	Independent Ethics Committee
ICH	International Conference on Harmonisation
IME	important medical event
IND	Investigational New Drug
IRB	institutional review board
IUD	intra-uterine device
IWRS	Interactive Web Response System
MedDRA	Medical Dictionary for Regulatory Activities
NRS	Numeric Rating Scale
PD	pharmacodynamics(s)
PE	physical examination
PK	pharmacokinetic(s)
PT	Preferred Term
PRAM9	Co-formulation of a fixed-ratio combination of 9 µg pramlintide per unit of regular insulin
RBC	red blood cells
SAE	serious adverse event
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	standard deviation
SE	standard error
SOC	System Organ Class
T1D	Type 1 diabetes mellitus
TEAE	treatment-emergent adverse event
T_{max}	time to maximum plasma concentration
ULN	upper limit of normal
WHO	World Health Organization

1 INTRODUCTION

This document details the planned statistical analyses for the Xeris Pharmaceuticals, Inc., protocol "DPI-201" study titled "A Phase 2, Single-Dose, Randomized, Open-Label, Active-Controlled, Crossover, Pharmacodynamic, and Pharmacokinetic Comparative Study of a Novel Pramlintide-Insulin Co-Formulation in Adults with Type 1 Diabetes Mellitus".

The proposed analyses are based on the contents of the final version 3.0 of the protocol (dated 06-SEP-2019).

Analyses for pharmacokinetic (PK) parameters will be covered in a separate Statistical Analysis Plan (SAP).

This is a randomized, open-label, active-controlled, single-dose, 3-treatment, 3-period, 3-way crossover, comparative PD, and PK inpatient study in adults with Type 1 Diabetes Mellitus (T1D).

Most people with diabetes are still unable to achieve glycemic targets with sole insulin therapy alone, particularly after mealtime. Physiologic restoration of the hormonal responses during meals, via pramlintide and insulin, has been demonstrated to reduce postprandial hyperglycemia and to improve blood glucose time in range.

The synergy between insulin and pramlintide provides improved glucose control while reducing meal-time insulin requirements. Reduced insulin utilization may also reduce the effects associated with long-term insulin use such as weight gain and higher risks of hypoglycemia.

A pramlintide-insulin co-formulation may help reduce the burden associated with co-administration (e.g., reduce the number of injections per day). Additionally, coformulations of pramlintide and insulin may also improve treatment compliance and persistency.

2 STUDY OBJECTIVES

2.1 Primary Objective

The primary objective of this study is to evaluate the PD properties of a single dose of PRAM9 (referred to as XP-3924 in tables, listings, figures) compared to single doses of regular insulin and regular insulin plus pramlintide (co-administered as separate injections) in adults with T1D.

2.2 Secondary Objectives

The secondary objectives of this study are to evaluate the safety and PK profiles of a single dose of PRAM9 compared to single doses of regular insulin and regular insulin plus pramlintide (co-administered as separate injections) in adults with T1D.

3 ENDPOINTS

3.1 Primary Endpoint

Analysis of the primary endpoint will be performed using the PD Analysis Set. The PD effects upon plasma glucose levels will be compared between the treatments as defined by the following primary endpoint:

- Area under the curve area from administration to 180 min ($AUC_{0\text{-}180}$) (mg/dL × minutes) for plasma glucose > 180 mg/dL.

3.2 Secondary Endpoints

3.2.1 Safety Endpoints

All safety analyses will be performed using the Safety Analysis Set.

The following safety variables will be compared between the treatments:

- Incidence of adverse events (AEs) and serious adverse events (SAEs)
- Change from baseline in laboratory safety variables
- Change from baseline in vital sign measurements
- Change from baseline in body weight
- Local tolerability assessments, including:
    - Incidence of erythema and or edema formation at site of injection assessed using the Draize scale (See Protocol Appendix 1)
    - Subjective injection site discomfort as reported by subjects using a 11-point Numeric Rating Scale (NRS) (See Protocol Appendix 2).
- Hypoglycemic events
    - Time to IV Dextrose administration from study drug administration
    - Time to hypoglycemic event from study drug administration
    - Time to resolution of hypoglycemic event from IV Dextrose administration
    - Proportion of subjects reaching euglycemia after IV Dextrose administration
    - Average amount of IV Dextrose

3.2.2 Pharmacodynamic Endpoints

All PD analyses will be performed using the PD Analysis Set. The following variables will be compared between the treatments:

- Mean proportional time with plasma glucose X mg/dL (during 0-t minutes post-injection of study drug), where X=(<54, <70, >180, >250) and t=(90, 180, 360) leading to 12 parameters. The primary PD endpoint will be X='>180' and t='180'.
- Mean proportional time after glucose challenge for plasma glucose levels between 126 to 180 mg/dL (during 40 to 180 minutes post-injection of study drug)
- $AUC_{0\text{-}t}$ (mg/dL × minutes) for plasma glucose X mg/dL, where X=(>180, >250) and t=(90, 180, 360) leading to 6 parameters.
- $AOC_{0\text{-}t}$ (mg/dL × minutes) for plasma glucose X mg/dL, where X=(<54, <70) and t=(90, 180, 360) leading to 6 parameters.
- Plasma glucose C_{max} and T_{max}.

4 SAMPLE SIZE

Up to 21 subjects will be qualified for the study and will complete the overnight stay as part of Visit 2 to ensure that 18 total subjects are randomized to a study treatment sequence. The target of 18 randomized subjects is considered sufficient to allow an initial evaluation of PK/PD response and safety of the novel pramlintide-insulin formulation. Formal sample size calculations were not conducted.

5 RANDOMIZATION

On the morning of Visit 2, subjects will be randomized into the appropriate treatment sequence order to receive each of the 3 study treatments (PRAM9, regular insulin, and co-administered regular insulin plus pramlintide). The study statistician will create the randomization sequence using random permuted block methodology. Study drug administration randomization sequences are as follows:

Cohort	Period 1	Period 2	Period 3
1	PRAM9	Regular insulin	Regular insulin + pramlintide
2	Regular insulin	Regular insulin + pramlintide	PRAM9
3	Regular insulin + pramlintide	PRAM9	Regular insulin
4	PRAM9	Regular insulin + pramlintide	Regular insulin
5	Regular insulin	PRAM9	Regular insulin + pramlintide
6	Regular insulin + pramlintide	Regular insulin	PRAM9

6 PLANNED ANALYSES

No statistical analysis plan (SAP) prepared in advance of the data can be absolutely definitive and the final Clinical Study Report (CSR) may contain additional tables or statistical tests if warranted by the data obtained. The justification for any such additional analyses, or deviations from this SAP, will be fully documented in the final clinical study report (CSR).

6.1 Analysis Sets

Subjects excluded from the analysis sets and the reason for their exclusion will be listed in Appendix 16.2 of the CSR.

Analyses performed on the Safety Analysis Set will use the actual treatment received. All other populations will use the randomized treatment.

6.1.1 Enrolled Set

The Enrolled Set includes all subjects who gave informed consent.

6.1.2 Randomized Set

The Randomized Set includes all subjects who were randomized to the treatment sequence.

6.1.3 Safety Analysis Set

The Safety Analysis Set includes all randomized subjects who received any study drug.

6.1.4 PD Analysis Set

The PD Analysis Set includes all subjects from Safety Analysis Set who had blood glucose measured at pre-dose and 180 minutes post-dose, and at least one time point between pre-dose and 180 minutes post-dose.

6.2 Derived Data

This section describes the derivations required for statistical analysis. Unless otherwise stated, variables derived in the source data will not be re-calculated.

6.2.1 Age

Age at screening will be collected in the CRF.

6.2.2 Race

Where more than one race category has been selected for a subject, these race categories will be combined into a single category labeled "Multiple Race" in the summary tables. The listings will reflect the original selected categories.

6.2.3 Baseline

The baseline is defined as the last non-missing value (either scheduled, unscheduled or repeat) that is collected before dosing of each treatment period.

6.2.4 Duration / Study Day / Time

Study day will be calculated as the number of days from first dose of the study drug on period 1 (Study Day 1).

- date of event – date of first dose of study drug on period 1 (+ 1), for events on or after first dose
- date of event – date of first dose of study drug on period 1, for events before first dose.

6.2.5 Conventions for Missing and Partial Dates

All rules explained below for partial / missing dates will be followed unless contradicted by any other data recorded on the electronic Case Report Form (eCRF).

All dates presented in the individual subject listings will be as recorded on the eCRF (i.e., not completed as per the below rules).

6.2.6 Missing / Partial Start / Stop Date of Adverse Events (AE) and Concomitant Medications

Missing and partial start and stop date will be imputed for analysis purposes as follows.

Partial or missing stop date will be imputed as follows:

If the stop date is completely missing and the event has resolved, or the subject has stopped taking the concomitant medication, the stop date will be imputed as the date of the subject's last clinic visit in the study.

- If only the year is known, the stop date will be imputed as "31-Dec" of that year or as the date of the subject's last clinic visit in the study if in the same year.

- If the month and year are known, the stop date will be imputed as the last day of that month unless the stop date corresponds to the same month as the subject's last clinic visit in which case the date of subject's last clinic visit in the study will be used instead.

Missing start date will be imputed as follows:

- If the stop date occurs on or after the start of study drug or the event / concomitant medication is ongoing, the start date will be imputed as the date of the first dose of study drug.
- If the stop date occurs before the start of study drug, the start date of the event / concomitant medication will be imputed as the subject's screening date or the stop date of the event / concomitant medication whichever is earlier.

Partial start date (year present, but month and day missing)

- If the stop date occurs on or after the start of study drug or the event / concomitant medication is ongoing, and the year is the same as the year of first dosing the start date will be imputed as "01-Jan" of the same year or the date of the first dose of study drug whichever is latest. If the year is different from the year of first dosing "01-Jan" will be used.
- If the stop date occurs before the start of study drug, the start date of the event / concomitant medication will be imputed as the "01-Jan" of the same year.

Partial start date (month and year present, but day missing)

- If the stop date occurs on or after the start of study drug or the event / concomitant medication is ongoing, the start date will be imputed as the first day of the same month and year unless this partial start date is in same month as the first dose of study drug in which case the date of first dose of study drug will be used.
- If the stop date occurs before the start of study drug, the start date will be imputed as the first day of the month and year of the partial stop date.

If the start time is missing it will be imputed only in the case where the start date of the concomitant medication / event corresponds to the date of the study drug dosing. The time will be imputed as the same time as the study drug dosing for each period. In all other cases the time will not be imputed.

6.2.7 Missing Last Dates of Study Drug Dosing

Study drug dosing dates and times will not be imputed. This is single dose cross-over study and the dosing information need to be collected in the CRF.

6.2.8 Missing Diagnosis Dates

If the month and year are present but the day is missing, the diagnosis date will be set to first day of the relevant month. If only the year is recorded the diagnosis date will be set as "01-Jan" for that year.

6.2.9 Exposure to Study Drug

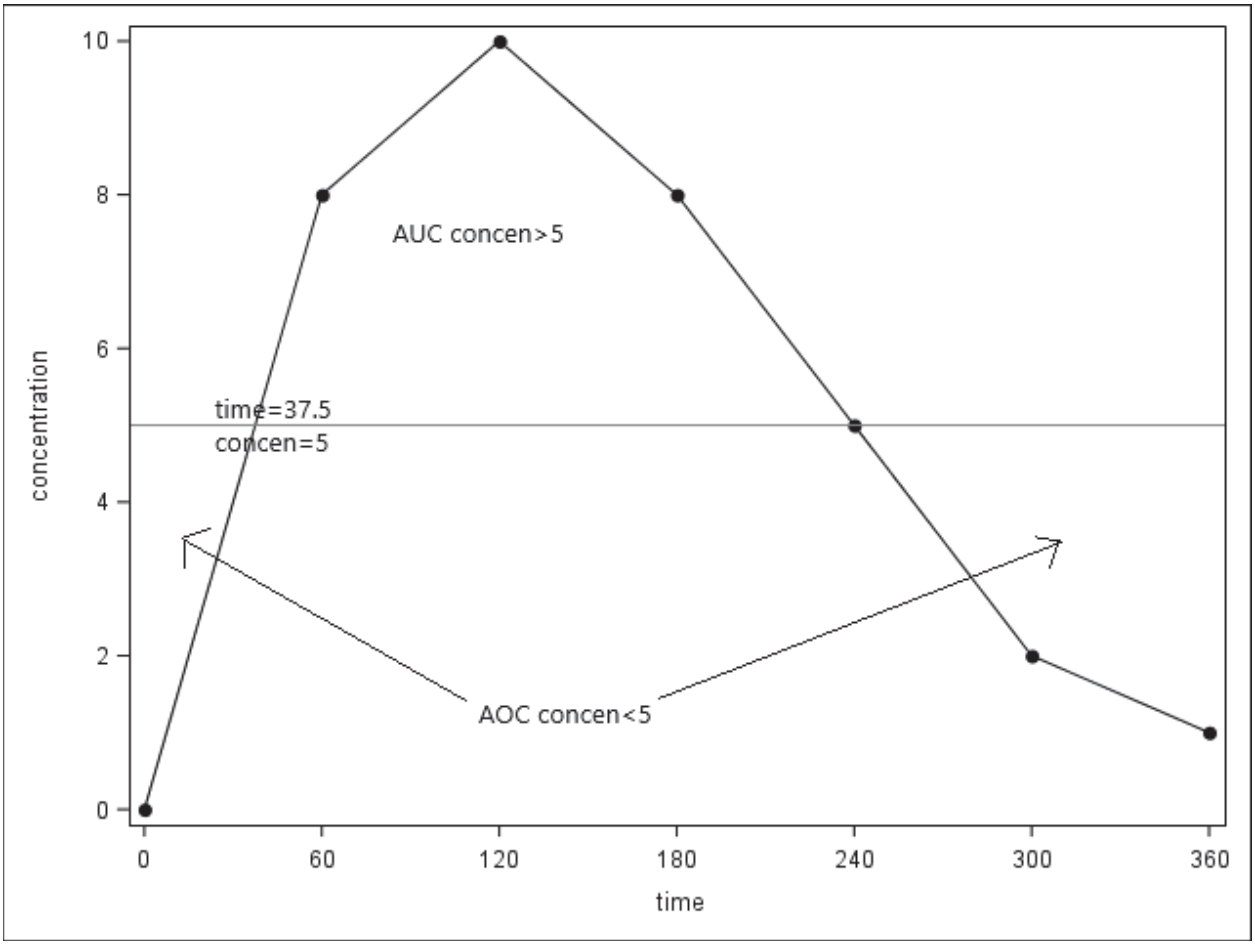
Exposure to study drug will not be calculated as this is a single dose study.

6.2.10 Inexact Values

In the case where a laboratory or PD variable is recorded as "> x", "≥ x", "< x" or "≤ x", a value of x will be taken for analysis purposes.

6.2.11 Primary Endpoint and PD Parameters

The figure below is presented only to show the idea of the calculation of PD parameters and the shape of the curve is based on dummy data. PD parameters will be calculated using linear trapezoidal rule.



AUC_{0-t} (mg/dL × minutes) for plasma glucose > XXX mg/dL

From the above example figure the area under the curve (AUC) for concentration > 5 is calculated as follows:

(60-37.5)(0+3)/2 + (120-60)(3+5)/2 + (180-120)(5+3)/2 + (240-180)(3+0)/2 = 33.75 + 240 + 240 + 90 = 603.75

Mean proportional time for plasma glucose < XXX mg/dL

From the above example figure the mean proportional time for concentration < 5 is calculated as follows:

(37.5 - 0 + 360 - 240) / (360-0) = 157.5 / 360 = 43.75%

AOC_{0-t} (mg/dL × minutes) for plasma glucose < XXX mg/dL

From the above example figure the area over the curve (AOC) for concentration < 5 is calculated as follows:

(37.5-0)(5+0)/2 + (300-240)(0+3)/2 + (360-300)(3+4) = 93.75 + 90 + 210 = 393.75

6.2.12 Unscheduled Visits

Only scheduled post-baseline values will be tabulated. Post-baseline repeat / unscheduled assessments will not be tabulated, although these post-baseline assessments will be listed in the relevant appendices to the CSR.

6.3 Conventions

All data listings, summaries, figures and statistical analyses will be generated using SAS version 9.4 or higher[1].

Summaries will be presented by treatment group or treatment sequence as appropriate. Treatment group labels will be displayed as follows:

- XP-3924
- Regular Insulin
- Regular Insulin + Pramlintide
- Overall

Treatment sequence labels will be displayed as follows:

- A-B-C
- B-C-A
- C-A-B
- A-C-B
- B-A-C
- C-B-A
- Overall

Where

A = XP-3924

B = Regular Insulin

C = Regular Insulin + Pramlintide.

Listings will be sorted in the following order treatment group / sequence, subject, parameter, and visit unless otherwise stated. All data will be listed, subjects who were not randomized will be displayed after the randomized treatment / sequence groups.

Continuous variables will be summarized by the number of non-missing observations, mean, median, standard deviation, and minimum and maximum. For all tabulations of changes from baseline data, the lower and upper 95% confidence limits for the mean for the individual treatments will be given. Summaries for PD parameters will also include 95% confidence interval, coefficient of variation (%CV) and quartiles (Q1 and Q3).

Categorical variables will be summarized by presenting the frequency and percent. Percentages will be based on the number of non-missing observations or the subject population unless otherwise specified. For each variable, all categories will be shown. Zero frequencies (but not the percent) within a category will be presented.

6.3.1 Decimal Places

Decimal places for derived data described in section 6.2 will be determined by the scale of measurement unless otherwise stated. No decimal places will be displayed if the smallest calculated value is ≥ 100; 1 decimal place will be displayed when the smallest value is within the interval (10, 100), with 10 being inclusive; 2 decimal places will be displayed when the smallest value is within (1, 10), with 1 being inclusive; and so on for even smaller scales of measurement.

Derived data where it is known in advance the result will be an integer for example day, month, year, number of days and total scores (for rating scales) will be presented with zero decimal places.

Means, medians and percentiles will be displayed to one more decimal place than the data**,** dispersion statistics (e.g. standard deviation) will have two more decimal places, and the minimum and maximum will be displayed to the same number of decimal places as reported in the raw data. Percentages will be displayed with one decimal place.

P-values will be quoted to 3 decimal places. P-values < 0.001 will be presented as p<0.001. Where this value is less than 0.05, 0.01 or 0.001, attention will be drawn to this fact using the conventional "*", "**" or "***" annotation, respectively.

6.4 Subject Disposition

Subject disposition will be summarized as follows:

- The number of subjects who failed screening and the reasons for failure will be tabulated for enrolled set.
- The number of subjects included in the analysis sets will be summarized by treatment sequence and overall for the enrolled set.
- The number of early withdrawals and the reasons for withdrawals will be tabulated by treatment sequence and overall for the enrolled set.

6.5 Protocol Deviations

Protocol Deviations will be summarized in frequency table by treatment sequence (including overall).

A listing of protocol deviations will be provided within Appendix 16.2 of the CSR.

6.6 Baseline Comparability

The comparability of treatment sequences with respect to subject demographics and baseline characteristics will be assessed in a descriptive manner, but no formal statistical testing will be performed.

Standard continuous or categorical variable summaries will be presented by randomized treatment sequence and overall for the following variables based on the Safety Analysis Set.

- Demographic data
  - Age
  - Sex (Male, Female)
  - Childbearing potential for Female (Yes, No)
  - Race (White, Black or African American, Asian, American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander)
  - Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
  - Height (cm)
  - Weight (kg)
  - BMI (kg/m^2).

6.7 Medical History

Medical history will be coded using the Medical Dictionary of Regulated Activities (MedDRA) (version 22.0). All medical history will be presented by treatment sequence and overall for the Safety Analysis Set by primary system organ class and preferred term.

6.8 Prior/Concomitant Medications

All prior/concomitant medications will be presented by treatment sequence and overall for the Safety Analysis Set. Prior medications are defined as all medications ending before the date of first dose of study drug. Concomitant medications are defined as medications taken on or after the date of first dose of study drug. Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary (version WHODrug Global B3 Mar 2019) and summarized using Anatomic Therapeutic Chemical (ATC) Level 4 and preferred term.

6.9 Exposure to Study Drug

Study drug administration will be summarized in frequency table by treatment sequence, treatment period and treatment group for the Safety Analysis Set.

6.10 Treatment Compliance

Not applicable.

6.11 Efficacy Analyses

All statistical tests will be performed using a two-tailed 5% overall significance level, unless otherwise stated. All comparisons between treatments will be reported with 95% confidence intervals for the difference.

6.11.1 Primary Endpoint

$AUC_{0\text{-}180}$ (mg/dL × minutes) for plasma glucose > 180 mg/dL will be summarized using descriptive statistics by period (including overall) and treatment group in PD Analysis Set.

Treatment groups will be compared using analysis of variance (ANOVA) model including sequence, period and treatment as fixed effects and subject within sequence as random effect. The hypothesis to be tested is as follows:

H_0: Means are equal between treatment groups.

H_a: Means are not equal across the treatment groups.

The SAS code for analysis is as follows:

```
proc mixed data=dataset order=internal;
class subject sequence period treatment;
model response=sequence period treatment / ddfm=kr;
random subject(sequence);
```

```
lsmeans treatment / diff cl e;
ods output tests3=test1 lsmeans=lsm1 diffs=dif1;
run;
```

6.11.2 Multiplicity

All secondary endpoints and the supportive analyses will be considered as descriptive evidence of efficacy and will be analyzed without any procedures to account for multiple comparisons.

6.12 Pharmacodynamic Analyses

The endpoints specified in section 3.2.2 (except plasma glucose T_{max}) will be analyzed similarly to the primary endpoint in PD Analysis Set.

Plasma glucose T_{max} will be compared between treatment groups using Wilcoxon Signed Rank test. Comparison will be done separately for each pairwise comparisons between the treatment groups (PRAM9 vs. Regular Insulin, PRAM9 vs. Regular Insulin + Pramlintide, Regular Insulin vs. Regular Insulin + Pramlintide). The SAS code for analysis is as follows:

```
proc univariate data=paired1 mu0=0;
var diff;
run;
```

Where diff is the difference between the two compared treatment groups for each subject.

6.13 Safety Analyses

The safety analyses will be presented by the treatment received for the Safety Analysis Set if not otherwise stated.

6.13.1 Adverse Events

A treatment emergent adverse event (TEAE) is defined as:

- Any AE that has an onset on or after the first dose of study drug
- Any pre-existing AE that has worsened in severity on or after the first dose of study drug.

The following rules will be used to assign a TEAE to a treatment group:

- A TEAE will be assigned to the treatment received immediately before onset.
- Any TEAE reported within the washout period between doses will be attributed to the previous treatment.
- If the severity of a TEAE increases in a later period, the TEAE at the increased severity will be assigned to the treatment received immediately before the increase in severity.

A treatment-related AE is defined as an AE as having suspected relationship to the study drug. If an AE has missing relationship it is assumed to be related to the study drug for analysis purposes.

Maximum severity (severe) will be assumed for an AE with missing severity.

Adverse Events will be coded using the Medical Dictionary of Regulated Activities (MedDRA) (version 22.0) primary system organ class and preferred term.

The following tables will be presented for AEs by treatment group and overall. Additionally, tables will be presented by treatment period and overall.

- Overall incidence and the number of:
  - Any AEs
  - TEAEs
  - Treatment-Related TEAEs
  - Severe or life-threatening TEAEs
  - Serious TEAEs
  - Treatment-Related Serious TEAEs
  - SAEs leading to death
  - TEAEs leading to early withdrawal.
  - Serious TEAEs leading to early withdrawal.
- For the above AE categories tables including incidence and number of events will be presented by system organ class and preferred term.

All AEs will be listed.

6.13.2 Laboratory Data

Descriptive statistics of the observed values and change from baseline (continuous data) will be presented overall by visit for each hematology and serum chemistry parameter. Each measurement (continuous data) will be classed as below, within, or above normal range, based on ranges supplied by the laboratory used (Altasciences for PK and Worldwide for routine safety labs). Shift tables in relation to the normal range from baseline to each follow-up visit will be presented.

6.13.3 C-Peptide and HbA1c

C-Peptide and HbA1c will be collected only at screening visit.

Descriptive statistics of the observed values will be presented overall.

6.13.4 Urine Drug Screen

Urine drug screen will be collected only at screening visit and will include the following analytes: cocaine, THC, opiates, amphetamines, methamphetamine and phencyclidine.

Urine drug screen data will be listed only.

6.13.5 Urine Pregnancy Test

Urine pregnancy test data will be listed only.

6.13.6 Vital Signs

Descriptive statistics for observed values and changes from baseline in the following vital signs will be presented by treatment group (including overall) and visit:

- Systolic blood pressure (mmHg)
- Diastolic blood pressure (mmHg)
- Heart rate (bpm)
- Respiration rate (breath / min)
- Body temperature (degrees Celsius)
- Body weight (kg).

6.13.7 Electrocardiogram Data

ECG will be collected only at screening visit.

Descriptive statistics for observed values in the following ECG variables will be tabulated overall at screening:

- PR Duration (ms)
- RR Interval (ms)
- QRS Duration (ms)
- QT Interval (ms)
- QTc Interval (ms)
- QTcF Interval (ms)
- QTcB Interval (ms)
- Ventricular Rate (bpm).

Overall interpretation (Normal, Abnormal NCS, and Abnormal CS) will be presented overall at screening in frequency table.

6.13.8 Physical Examination

The body systems within the physical examination data at the end of the study will be summarized overall for the shift from baseline to the end of the study (Normal, Abnormal (NCS), Abnormal (CS), Not Done).

All physical examination data will be listed.

6.13.9 Draize Scale

Draize scale will be presented by treatment group and overall by time point (30 min, 90 min and 360 min post-dose) in frequency table.

Data will be summarized for Erythema Formation:

- 0 - No erythema
- 1 - Very slight erythema
- 2 - Well defined erythema
- 3 - Moderate erythema
- 4 - Severe erythema

and Edema Formation:

- 0 - No edema
- 1 - Very slight edema
- 2 - Slight edema
- 3 - Moderate edema
- 4 - Severe edema

6.13.10 Injection Site Discomfort Assessment

Injection Site Discomfort Assessment includes:

- Numeric Rating Scale (NRS) for Injection Site Discomfort
  - 11-point scale from 0 to 10
- 1a. How would you describe any discomfort you felt from the study drug? (Check all that apply):

- None (Please ignore question 1b.)
- Pain (eg, throbbing, soreness, muscle ache)
- Itching
- Tingling, twitching, or numbness
- Irritation (eg, burning, stinging)
- Other

- 1b. About how long did the discomfort last after the injection? (Check one):
  - Less than 1 minute
  - 1-2 minutes
  - 3-5 minutes
  - 6-9 minutes
  - at least 10 minutes (Please complete question 1c before leaving the clinic.)
- 1c. In total, how long did the discomfort last after the injection? (Please enter a number below):
  - _____ Minutes

For NRS, descriptive statistics for observed values will be presented by treatment group (including overall) and time point (10 min, 30 min post-dose).

Questions 1a, 1b and 1c are answered only once after each dosing and will be presented in frequency tables (1a and 1b) and using descriptive statistics (1c) by treatment group (including overall).

6.13.11 Hypoglycemic Events

Time to event endpoints will be analyzed by comparing the survivor functions between treatment arms using Kaplan-Meier methodology. Estimates and 95% confidence intervals for the median time to event, and 25th and 75th percentiles will be reported. Log-rank test will be performed to test the homogeneity of survival curves between the treatment groups.

Kaplan-Meier plots by treatment group will be provided including the number of subjects remaining at risk at each time point.

The SAS code for analysis is as follows:

```
proc lifetest data=dataset method=km outsurv=surv
plots=survival(atrisk=(0 to 50 by 5) /*cb=hw test*/);
time time*cens(1);
strata treatment / order=internal;
run;
```

Where time is the time to the event and cens(1) is the censoring variable with censored records defined in brackets.

Time to IV Dextrose administration from study drug administration

Calculated as time in minutes from study drug administration to administration of IV Dextrose. If subject is not receiving IV Dextrose then subject will be censored at the start of glucose challenge or 4 hours after the study drug administration whichever is the earliest.

Time to hypoglycemic event from study drug administration

Calculated as time in minutes from study drug administration to the start of hypoglycemic event. If subject is not having hypoglycemic event then subject will be censored at the start of glucose challenge or the time of next study drug administration or the follow-up visit in case of last treatment period whichever is the earliest.

Time to resolution of hypoglycemic event from IV Dextrose administration

Will be calculated only for subjects who experience hypoglycemic event. Calculated as time in minutes from administration of IV Dextrose to the time of resolution of hypoglycemic event. Resolution is defined and blood glucose reading crossing the 70 mg/dL threshold. Resolution timepoint will be estimated using linear estimation. Censoring will not be done as hypoglycemic events should be resolved before subjects are discharged from the clinic.

Proportion of subjects reaching euglycemia after IV dextrose administration

Proportion of subjects reaching the euglycemia (blood glucose >=70 mg/dL) at 10, 20, 30 minutes post-IV-Dextrose-administration will be summarized in frequency table by treatment group.

Average Amount of IV Dextrose

Amount of IV Dextrose administered after hypoglycemic event will be summarized using descriptive statistics by treatment group.

Treatment groups will be compared using paired t-test. Comparison will be done separately for each pairwise comparisons between the treatment groups (PRAM9 vs. Regular Insulin, PRAM9 vs. Regular Insulin + Pramlintide, Regular Insulin vs. Regular Insulin + Pramlintide). The SAS code for analysis is as follows:

```
proc ttest data=paired1;
paired result1*result2;
run;
```

Where result1 and result2 are the doses for treatment groups.

7 INTERIM ANALYSIS

No interim analyses are planned.

8 DATA SAFETY MONITORING BOARD ANALYSIS

No data safety monitoring board (DSMB) analyses are planned.

9 CHANGES TO PLANNED PROTOCOL ANALYSIS

Several PD parameters were added for mean proportional time with different cutoffs for plasma glucose levels and timepoints leading to total of 12 parameters. Similar update was done for AUC0-t parameters also leading to total of 12 different parameters.

Analysis for hypoglycemic events (time to IV Dextrose administration, time to hypoglycemic event, time to resolution of hypoglycemic event, proportion of subjects reaching euglycemia and average amount of IV Dextrose) were added.

10 REFERENCES

1. SAS Institute Inc., Cary, NC, 27513, USA

11 LIST OF TABLES, FIGURES AND LISTINGS

The following table includes details of the tables, figures and listings to be included within each section of the eCTD. The eCTD section is shown in bold. The following validation methods maybe used:

- Independent programming of numbers and manual review of format (IP)
- Independent programming by statistician of numbers and manual review of format (Stat IP)
- Manual review (MR)
- Code review (CR)

Table Number	Table Title	Validation Method	Shell Number (if repeat)
Items in bold are not table titles but references to the section headings within eCTD.			
14.1	**Demographics Data**		
14.1.1	**Disposition**		
14.1.1.1	Subject Enrollment and Screen Failures– Enrolled Set	IP	
14.1.1.2	Analysis Sets – Enrolled Set	IP	
14.1.1.3	Subject Disposition – Randomized Set	IP	
14.1.2	**Demographics**		
14.1.2.1	Demographics – Safety Analysis Set	IP	
14.1.3	**Baseline Characteristics**		
14.1.3.1	Medical History – Safety Analysis Set	IP	
14.1.4.1	Prior Medications – Safety Analysis Set	IP	
14.1.4.2	Concomitant Medications – Safety Analysis Set	IP	14.1.4.1
14.2	**Efficacy Data**		
14.2.1	**Primary Efficacy Endpoint**		
	Not Applicable		
14.2.2	**Secondary Efficacy Endpoints**		
	Not Applicable		
14.3	**Safety Data**		
14.3.1	**Displays of Adverse Events**		
14.3.1.1.1	Overall Summary Adverse Events (TEAEs) by Treatment Group – Safety Analysis Set	IP	
14.3.1.1.2	Overall Summary Adverse Events (TEAEs) by Treatment Period – Safety Analysis Set	IP	14.3.1.1.1

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.3.1.2.1	Any AEs by Primary System Organ Class and Preferred Term by Treatment Group – Safety Analysis Set	IP	
14.3.1.2.2	Any AEs by Primary System Organ Class and Preferred Term by Treatment Period – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.3.1	TEAEs by Primary System Organ Class and Preferred Term by Treatment Group – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.3.2	TEAEs by Primary System Organ Class and Preferred Term by Treatment Period – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.4.1	Treatment-Related TEAEs by Primary System Organ Class and Preferred Term by Treatment Group – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.4.2	Treatment-Related TEAEs by Primary System Organ Class and Preferred Term by Treatment Period – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.5.1	Severe or Life-Threatening TEAEs by Primary System Organ Class and Preferred Term by Treatment Group – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.5.2	Severe or Life-Threatening TEAEs by Primary System Organ Class and Preferred Term by Treatment Period – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.6.1	Serious TEAEs by Primary System Organ Class and Preferred Term by Treatment Group – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.6.2	Serious TEAEs by Primary System Organ Class and Preferred Term by Treatment Period – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.7.1	Treatment-Related Serious TEAEs by Primary System Organ Class and Preferred Term by Treatment Group – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.7.2	Treatment-Related Serious TEAEs by Primary System Organ Class and Preferred Term by Treatment Period – Safety Analysis Set	IP	14.3.1.2.1

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.3.1.8.1	SAEs Leading to Death by Primary System Organ Class and Preferred Term by Treatment Group – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.8.2	SAEs Leading to Death by Primary System Organ Class and Preferred Term by Treatment Period – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.9.1	TEAEs Leading to Early Withdrawal by Primary System Organ Class and Preferred Term by Treatment Group – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.9.2	TEAEs Leading to Early Withdrawal by Primary System Organ Class and Preferred Term by Treatment Period – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.10.1	Serious TEAEs Leading to Early Withdrawal by Primary System Organ Class and Preferred Term by Treatment Group – Safety Analysis Set	IP	14.3.1.2.1
14.3.1.10.2	Serious TEAEs Leading to Early Withdrawal by Primary System Organ Class and Preferred Term by Treatment Period – Safety Analysis Set	IP	14.3.1.2.1
14.3.2	**Listings of Deaths, Other Serious and Significant Adverse Events**		
14.3.3	**Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events**		
	Not Applicable	IP	
14.3.4	**Abnormal Laboratory Values**		
14.3.5	**Extent of Exposure, Dosage Information, And Compliance**		
14.3.5.1	Exposure by Treatment Sequence – Safety Analysis Set	IP	
14.3.5.2	Exposure by Treatment Group	IP	
14.3.6	**Vital Signs and Physical Examination**		
14.3.6.1.1	Vital Signs, Descriptive Statistics and Changes from Baseline to Post-Dose Assessments – Safety Analysis Set	IP	
14.3.6.2.1	Physical Examination Data, Shift Table – Safety Analysis Set	IP	
14.3.7	**Other Safety**		

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.3.7.1.1	Hematology Data, Descriptive Statistics – Safety Analysis Set	IP	14.3.6.1.1
14.3.7.1.2	Hematology Data, Normal Range Shifts – Safety Analysis Set	IP	14.3.6.2.1
14.3.7.2.1	Serum Chemistry Data, Descriptive Statistics – Safety Analysis Set	IP	14.3.6.1.1
14.3.7.2.2	Serum Chemistry Data, Normal Range Shifts – Safety Analysis Set	IP	14.3.6.2.1
14.3.7.3.1	C-Peptide and HbA1c Data, Descriptive Statistics – Safety Analysis Set	IP	14.3.6.1.1
14.3.7.4.1	ECG Data, Descriptive Statistics – Safety Analysis Set	IP	14.3.6.1.1
14.3.7.4.2	ECG Data, Overall Interpretation Summary – Safety Analysis Set	IP	
14.3.7.5.1	Draize Scale, Descriptive Statistics – Safety Analysis Set	IP	
14.3.7.6.1	Injection Site Discomfort Assessment – Numeric Rating Scale (NRS), Descriptive Statistics – Safety Analysis Set	IP	14.3.6.1.1
14.3.7.6.2	Injection Site Discomfort Assessment – Injection Site Discomfort Description and Duration Questionnaire, Descriptive Statistics – Safety Analysis Set	IP	
14.3.8.1	Time to IV Dextrose Administration from Study Drug Administration by Treatment Group – Safety Analysis Set	IP	
14.3.8.2	Time to Hypoglycemic Event from Study Drug Administration by Treatment Group – Safety Analysis Set	IP	14.3.8.1
14.3.8.3	Time to Resolution of Hypoglycemic Event from IV Dextrose Administration by Treatment Group – Safety Analysis Set	IP	14.3.8.1
14.3.8.4	Proportion of Subjects Reaching Euglycemia after IV Dextrose Administration by Treatment Group – Safety Analysis Set	IP	
14.3.8.5	Average Amount of IV Dextrose by Treatment Group – Safety Analysis Set	IP	

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.4	**PK Tables**		
	Separate SAP for PK analyses		
14.5	**PD Tables**		
14.5.1	Plasma Glucose Concentration Data, Descriptive Statistics – PD Analysis Set	IP	14.4.1.1
14.5.2	Plasma Glucose PD Parameter Data, Descriptive Statistics and Analysis – PD Analysis Set	Stat IP	14.4.1.2

Figure Number	Figure Title	Validation Method	Shell Number (if repeat)
14.3.1.1	Time to IV Dextrose Administration from Study Drug Administration by Treatment Group – Safety Analysis Set	IP	
14.3.1.2	Time to Hypoglycemic Event from Study Drug Administration by Treatment Group– Safety Analysis Set	IP	14.3.1.1
14.3.1.3	Time to Resolution of Hypoglycemic Event from IV Dextrose Administration by Treatment Group– Safety Analysis Set	IP	14.3.1.1
14.5.1.1	Plasma Glucose Concentration Data, Mean Profiles on Linear Scale – PD Analysis Set	IP	
14.5.1.2	Plasma Glucose Concentration Data, Individual Profiles on Linear Scale – PD Analysis Set	IP	

Listing Number	Listing Title	Validation Method	Shell Number (if repeat)
16.2	**Subject Data Listings**		
16.2.1	**Discontinued Subjects**		
16.2.1.1	Screen Failures – Enrolled Set	IP	
16.2.1.2	Inclusion/Exclusion Criteria – Enrolled Set	IP	
16.2.1.3	Study Completion – Safety Analysis Set	IP	
16.2.2	**Protocol Deviations**		
16.2.2.1	Protocol Deviations – Enrolled Set	IP	
16.2.3	**Subjects Excluded from the Efficacy Analyses**		
16.2.3.1	Analysis Sets – Enrolled Set	IP	
16.2.4	**Demographic Data**		
16.2.4.1	Demographic Data – Safety Analysis Set	IP	
16.2.4.2	Medical History – Safety Analysis Set	IP	
16.2.4.2	Prior/Concomitant Medications – Safety Analysis Set	IP	
16.2.5	**Compliance and / or Drug Concentration Data**		
16.2.5.1.1	Exposure – Safety Analysis Set	IP	
16.2.6	**Individual Efficacy Response Data**		
	Not Applicable		
16.2.7	**Adverse Event Listings**		
16.2.7.1	Adverse Events – Safety Analysis Set	IP	
16.2.8	**Individual Laboratory Measurements and Other Safety**		
16.2.8.1.1	Vital Sign Data – Safety Analysis Set	IP	
16.2.8.2.1	Physical Examination Data – Safety Analysis Set	IP	
16.2.8.3.1	Hematology Data – Safety Analysis Set	IP	
16.2.8.3.2	Serum Chemistry Data – Safety Analysis Set	IP	
16.2.8.3.3	C-Peptide and HbA1c Data – Safety Analysis Set	IP	
16.2.8.3.4	Urine Drug Screen Data – Safety Analysis Set	IP	
16.2.8.3.5	Urine Pregnancy Test Data – Safety Analysis Set	IP	
16.2.8.4.1	ECG Data – Safety Analysis Set	IP	
16.2.8.5.1	Draize Scale Data – Safety Analysis Set	IP	
16.2.8.6.1	Injection Site Discomfort Assessment Data – Safety Analysis Set	IP	
16.2.8.7.1	Plasma Glucose Concentration Data, Descriptive Statistics – Safety Analysis Set	IP	

Listing Number	Listing Title	Validation Method	Shell Number (if repeat)
16.2.8.7.2	Plasma Glucose PD Parameter Data – Safety Analysis Set	IP	
16.2.8.7.3	Glucose Challenge – Safety Analysis Set	IP	
16.2.8.8.1	Hypoglycemic Events – Safety Analysis Set	IP	

Table 14.1.1.1
Subject Enrollment and Screen Failures
Enrolled Set

	Overall (N=xxx) n (%)
Number of Subjects Enrolled	xx (xx.x)
Site	
Site 1	xx (xx.x)
Site 2	xx (xx.x)
Site 3	xx (xx.x)
...	xx (xx.x)
Number of Screen Failures	xx (xx.x)
Reason for Screen Failure (a)	
Reason 1	xx (xx.x)
Reason 2	xx (xx.x)
Reason 3	xx (xx.x)
...	xx (xx.x)

PROGRAMMING NOTE: Reasons: 'Withdrawal of Consent', 'Did Not Meet Inclusion/Exclusion Criteria', 'Adverse Event', 'Lost to Follow-Up', 'Pregnancy', 'Other'.

(a) Percentages are based on the number of screen failures.

Table 14.1.1.2
Analysis Sets
Enrolled Set

Analysis Set	A-B-C (N=xxx) n (%)	B-C-A (N=xxx) n (%)	C-A-B (N=xxx) n (%)	A-C-B (N=xxx) n (%)	B-A-C (N=xxx) n (%)	C-B-A (N=xxx) n (%)	Overall (N=xxx) n (%)
Analysis Set 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Analysis Set 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Analysis Set 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)

PROGRAMMING NOTE: Use analysis sets: 'Enrolled Set', 'Randomized Set', 'Safety Analysis Set', 'PD Analysis Set'.

PROGRAMMING NOTE: Do not display treatment sequence frequencies for 'Enrolled Set' where only overall should be displayed.

Percentages are based on number of subjects in Randomized Set.
Enrolled Set: All subjects who gave informed consent.
Randomized Set: All subjects who were randomized to the treatment sequence.
Safety Analysis Set: All randomized subjects who received any study drug.
PD Analysis Set: Subset of the Safety Analysis Set, which includes subjects who had blood glucose measured at pre-dose and 180 minutes post-dose, and at least one time point between pre-dose and 180 minutes post-dose.

Table 14.1.1.3
Subject Disposition
Randomized Set

Disposition	A-B-C (N=xxx) n (%)	B-C-A (N=xxx) n (%)	C-A-B (N=xxx) n (%)	A-C-B (N=xxx) n (%)	B-A-C (N=xxx) n (%)	C-B-A (N=xxx) n (%)	Overall (N=xxx) n (%)
Completed Study (a)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Early Withdrawal (a)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Primary Reason for Early Withdrawal (b)							
Reason 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason 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)
Time to Early Withdrawal (days)							
n	xx	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

PROGRAMMING NOTE: Reasons: 'Withdrawal of Consent', 'Did Not Meet Inclusion/Exclusion Criteria', 'Adverse Event', 'Lost to Follow-Up', 'Pregnancy', 'Other'.

(a) Percentages are based on the number of subjects in Full Analysis Set.
(b) Percentages are based on the number of early withdrawals.

Table 14.1.2.1
Demographics
Safety Analysis Set

Parameter	A-B-C (N=xxx)	B-C-A (N=xxx)	C-A-B (N=xxx)	A-C-B (N=xxx)	B-A-C (N=xxx)	C-B-A (N=xxx)	Overall (N=xxx)
Categorical Variable 1, n (%)							
Category 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Category 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Category 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)
Continuous Variable 1 (unit)							
n	xx	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

PROGRAMMING NOTE: Age (years), Gender ('Male', 'Female'), Childbearing Potential ('Yes', 'No'), Ethnicity ('Hispanic or Latino', 'Not Hispanic or Latino'), Race ('White', 'Black or African American', 'Asian', 'American Indian or Alaska Native', 'Native Hawaiian or Other Pacific Islander', 'Multiple'), Weight (kg), Height (cm) and Body Mass Index (kg/m2).

Table 14.1.3.1
Medical History
Safety Analysis Set

System Organ Class Preferred Term	A-B-C (N=xxx) n (%) / Events	B-C-A (N=xxx) n (%) / Events	C-A-B (N=xxx) n (%) / Events	A-C-B (N=xxx) n (%) / Events	B-A-C (N=xxx) n (%) / Events	C-B-A (N=xxx) n (%) / Events	Overall (N=xxx) n (%) / Events
Any	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
System Organ Class 1	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 1	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 2	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 3	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
...	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
System Organ Class 2	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 1	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 2	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 3	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
...	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx

PROGRAMMING NOTE:

n = Number of subjects with event, Events = Total number of events.
Medical Histories are coded using MedDRA version 22.0.

Table 14.1.4.1
Prior Medications
Safety Analysis Set

ATC Level 4 Preferred Term	A-B-C (N=xxx) n (%)	B-C-A (N=xxx) n (%)	C-A-B (N=xxx) n (%)	A-C-B (N=xxx) n (%)	B-A-C (N=xxx) n (%)	C-B-A (N=xxx) n (%)	Overall (N=xxx) n (%)
Any	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
ATC Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 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)
ATC Class 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 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)

PROGRAMMING NOTE:

Medications are coded using WHO Drug Dictionary version WHODrug Global B3 Mar 2019.

Table 14.1.4.2
Concomitant Medications
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.1.4.1.

Table 14.3.1.1.1
Overall Summary of Adverse Events by Treatment Group
Safety Analysis Set

AE Category	XP-39249 (N=xxx) n (%) / Events	Regular Insulin (N=xxx) n (%) / Events	Regular Insulin + Pramlintide (N=xxx) n (%) / Events	Overall (N=xxx) n (%) / Events
Category 1	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Category 2	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Category 3	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
...	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx

PROGRAMMING NOTE: Include AE Categories: 'Any AEs', 'TEAEs', 'Treatment-Related TEAEs', 'Severe or Life-Threatening TEAEs', 'Serious TEAEs', 'Treatment-Related Serious TEAEs', 'SAEs Leading to Death', 'TEAEs Leading to Early Withdrawal', 'Serious TEAEs Leading to Early Withdrawal'.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.1.2
Overall Summary of Adverse Events by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.1.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.2.1
Any AEs by Primary System Organ Class and Preferred Term by Treatment Group
Safety Analysis Set

System Organ Class Preferred Term	XP-3924 (N=xxx) n (%) / Events	Regular Insulin (N=xxx) n (%) / Events	Regular Insulin + Pramlintide (N=xxx) n (%) / Events	Overall (N=xxx) n (%) / Events
Any	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
System Organ Class 1	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 1	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 2	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 3	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
...	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
System Organ Class 2	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 1	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 2	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
Preferred Term 3	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx
...	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx	xx (xx.x) / xx

PROGRAMMING NOTE:

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.
Program: XXX.SAS

Table 14.3.1.2.2
Any AEs by Primary System Organ Class and Preferred Term by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.2.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.3.1
TEAEs by System Organ Class and Preferred Term by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.1.2.1.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.3.2
TEAEs by System Organ Class and Preferred Term by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.3.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.4.1
Treatment-Related TEAEs by Primary System Organ Class and Preferred Term by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.1.2.1.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.4.2
Treatment-Related TEAEs by Primary System Organ Class and Preferred Term by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.4.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.5.1
Severe or Life-Threatening TEAEs by Primary System Organ Class and Preferred Term by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.1.2.1.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.5.2
Severe or Life-Threatening TEAEs by Primary System Organ Class and Preferred Term by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.5.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.6.1
Serious TEAEs by Primary System Organ Class and Preferred Term by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.1.2.1.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.6.2
Serious TEAEs by Primary System Organ Class and Preferred Term by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.6.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.7.1
Treatment-Related Serious TEAEs by Primary System Organ Class and Preferred Term by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.1.2.1.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.7.2
Treatment-Related Serious TEAEs by Primary System Organ Class and Preferred Term by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.7.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.8.1
SAEs Leading to Death by Primary System Organ Class and Preferred Term by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.1.2.1.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.8.2
SAEs Leading to Death by Primary System Organ Class and Preferred Term by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.8.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.9.1
TEAEs Leading to Early Withdrawal by Primary System Organ Class and Preferred Term by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.1.2.1.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.9.2
TEAEs Leading to Early Withdrawal by Primary System Organ Class and Preferred Term by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.9.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.10.1
Serious TEAEs Leading to Early Withdrawal by Primary System Organ Class and Preferred Term by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.1.2.1.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.1.10.2
Serious TEAEs Leading to Early Withdrawal by Primary System Organ Class and Preferred Term by Treatment Period
Safety Analysis Set

PROGRAMMING NOTE: Repeat Table 14.3.1.10.1 using Treatment Period instead of Treatment Group.

n = Number of subjects with event, Events = Total number of events.
Adverse events are coded using MedDRA version 22.0.
TEAE = Treatment-Emergent Adverse Event.

Table 14.3.5.1
Exposure by Treatment Sequence
Safety Analysis Set

Exposure	A-B-C (N=xxx) n (%)	B-C-A (N=xxx) n (%)	C-A-B (N=xxx) n (%)	A-C-B (N=xxx) n (%)	B-A-C (N=xxx) n (%)	C-B-A (N=xxx) n (%)	Overall (N=xxx) n (%)
Subjects with 3 treatments	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects with 2 treatments	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects with 1 treatments	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects with 0 treatments	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects with Period 1 treatment	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects with Period 2 treatment	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects with Period 3 treatment	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

PROGRAMMING NOTE:

Table 14.3.5.2
Exposure by Treatment Group
Safety Analysis Set

Exposure	XP-3924 (N=xxx) n (%)	Regular Insulin (N=xxx) n (%)	Regular Insulin + Pramlintide (N=xxx) n (%)	Overall (N=xxx) n (%)
Number of subjects treated	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

PROGRAMMING NOTE:

Table 14.3.6.1.1
Vital Signs, Descriptive Statistics and Changes from Baseline to Post-Dose Assessments
Safety Analysis Set

Parameter: XXX (Unit)

Treatment	Visit	Timepoint	n	Mean	SD	Median	Min	Max
XP-3924 (N=xxx)	Visit 1	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 2	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 2	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 3	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 3	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
	...	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	...	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
Regular Insulin (N=xxx)	Visit 1	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 2	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 2	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 3	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 3	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
	...	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	...	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
Regular Insulin + Pramlintide (N=xxx)	Visit 1	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 2	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 2	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 3	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 3	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
	...	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx

Table 14.3.6.1.1
Vital Signs, Descriptive Statistics and Changes from Baseline to Post-Dose Assessments
Safety Analysis Set

Parameter: XXX (Unit)

Treatment	Visit	Timepoint	n	Mean	SD	Median	Min	Max
	...	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
Overall (N=xxx)	Visit 1	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 2	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 2	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 3	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	Visit 3	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx
	...	Observed value	xx	xx.x	xx.xx	xx.x	xx	xx
	...	Change from BL	xx	xx.x	xx.xx	xx.x	xx	xx

PROGRAMMING NOTE: For each treatment group include following visits: 'Pre-Dose', '30 min Post-Dose', '180 min Post-Dose', '360 min Post-Dose'.

PROGRAMMING NOTE: For overall treatment group include following visits: 'Screening', 'Follow-Up'.

Table 14.3.6.2.1
Physical Examination Data, Shift Table
Safety Analysis Set

Parameter: XXX (Unit)

Treatment	Screening	Follow-Up Normal n (%)	Follow-Up Abnormal (NCS) n (%)	Follow-Up Abnormal (CS) n (%)	Follow-Up Not Done n (%)	Overall n (%)
Overall (N=xxx)	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Overall (N=xxx)	Abnormal (NCS)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Overall (N=xxx)	Abnormal (CS)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Overall (N=xxx)	Not Done	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Overall (N=xxx)	Overall	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

PROGRAMMING NOTE: Percentages are based on number of subjects who had both Screening and Follow-up records.

Table 14.3.7.1.1
Hematology Data, Descriptive Statistics
Safety Analysis Set

Parameter: XXX (Unit)

PROGRAMMING NOTE: Same shell as Table 14.3.6.1.1 including only overall treatment and visits 'Screening', 'Follow-Up'.

PROGRAMMING NOTE: Include parameters as listed in the Protocol.

Table 14.3.7.1.2
Hematology Data, Normal Range Shifts
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.6.2.1 using categories 'Low', 'Normal', 'High', 'Overall'.

PROGRAMMING NOTE: Include parameters as listed in the Protocol.

PROGRAMMING NOTE: Percentages are based on number of subjects who had both Screening and Follow-up records.

Table 14.3.7.2.1
Serum Chemistry Data, Descriptive Statistics
Safety Analysis Set

Parameter: XXX (Unit)

PROGRAMMING NOTE: Same shell as Table 14.3.6.1.1 including only overall treatment and visits 'Screening', 'Follow-Up'.

PROGRAMMING NOTE: Include parameters as listed in the Protocol.

Table 14.3.7.2.2
Serum Chemistry Data, Normal Range Shifts
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.6.2.1 using categories 'Low', 'Normal', 'High', 'Overall'.

PROGRAMMING NOTE: Include parameters as listed in the Protocol.

PROGRAMMING NOTE: Percentages are based on number of subjects who had both Screening and Follow-up records.

Table 14.3.7.3.1
C-Peptide and HbA1c Data, Descriptive Statistics
Safety Analysis Set

Parameter: XXX (Unit)

PROGRAMMING NOTE: Same shell as Table 14.3.6.1.1 including only overall treatment and visit 'Screening'.

Table 14.3.7.4.1
ECG Data, Descriptive Statistics
Safety Analysis Set

Parameter: XXX (Unit)

PROGRAMMING NOTE: Same shell as Table 14.3.6.1.1 including only overall treatment and visit 'Screening'.

Table 14.3.7.4.2
ECG Data, Overall Interpretation Summary
Safety Analysis Set

Parameter	Result	Overall (N=xxx) n (%)
XXX (Unit)	Normal	xx (xx.x)
XXX (Unit)	Abnormal NCS	xx (xx.x)
XXX (Unit)	Abnormal CS	xx (xx.x)

PROGRAMMING NOTE: Including only visit 'Screening'.

PROGRAMMING NOTE: Percentages are based on number of subjects who had record at the visit.

NCS = Not Clinically Significant, CS = Clinically Significant.

Table 14.3.7.5.1
Draize Scale, Descriptive Statistics
Safety Analysis Set

Parameter: XXX (Unit)

Timepoint	Result	XP-3924 (N=xxx) n (%)	Regular Insulin (N=xxx) n (%)	Regular Insulin + Pramlintide (N=xxx) n (%)	Overall (N=xxx) n (%)
XXX	Result 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
XXX	Result 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
XXX	Result 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

PROGRAMMING NOTE: Erythema Formation: '0 - No erythema', '1 - Very slight erythema', '2 - Well defined erythema', '3 - Moderate erythema', '4 - Severe erythema'.

PROGRAMMING NOTE: Edema Formation: '0 - No edema', '1 - Very slight edema', '2 - Well defined edema', '3 - Moderate edema'.

PROGRAMMING NOTE: Including timepoints '30 min Post-Dose', '90 min Post-Dose', '360 min Post-Dose'.

PROGRAMMING NOTE: Percentages are based on number of subjects who had record at the timepoint.

Table 14.3.7.6.1
Injection Site Discomfort Assessment - Numeric Rating Scale (NRS), Descriptive Statistics
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.6.1.1 not having change from BL. Use 'Timepoint' Instead of 'Visit'.

PROGRAMMING NOTE: Including timepoints '10 min Post-Dose', '30 min Post-Dose'.

PROGRAMMING NOTE: Percentages are based on number of subjects who had record at the timepoint.

Table 14.3.7.6.2
Injection Site Discomfort Assessment - Injection Site Discomfort Description and Duration Questionnaire, Descriptive Statistics
Safety Analysis Set

Result	XP-3924 (N=xxx)	Regular Insulin (N=xxx)	Regular Insulin + Pramlintide (N=xxx)	Overall (N=xxx)
How would you describe any discomfort you felt from the study drug? n (%)				
None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pain	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Itching	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Tingling, twitching, or numbness	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Irritation	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
About how long did the discomfort last after the injection? n (%)				
Less than 1 minute	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1-2 minutes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3-5 minutes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
6-9 minutes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At least 10 minutes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
In total, how long did the discomfort last after the injection? (minutes)				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx

PROGRAMMING NOTE: Percentages are based on number of subjects who had study treatment. Add missing categories if needed.

Table 14.3.8.1
Time (minutes) to IV Dextrose Administration from Study Drug Administration by Treatment Group
Safety Analysis Set

	XP-3924 (N=xxx)	Regular Insulin (N=xxx)	Regular Insulin + Pramlintide (N=xxx)
Number (%) of Subjects with Event	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number (%) of Subjects Censored	xx (xx.x)	xx (xx.x)	xx (xx.x)
Kaplan-Meier estimates (95% CI)			
25th percentile	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Median	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
75th percentile	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Log-Rank			
Chi-Square (DF)	xx.xx (x)	xx.xx (x)	xx.xx (x)
p-value	x.xxx	x.xxx	x.xxx
Mean Time (min) (SE)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)

PROGRAMMING NOTE:

If hypo event occurs after glucose challenge then it will not be included as event and will be censored at the time of glucose challenge. Only events occurring after treatment and prior to glucose challenge are included as events.

Table 14.3.8.2
Time (minutes) to Hypoglycemic Event from Study Drug Administration by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.8.1.

If hypo event occurs after glucose challenge then it will not be included as event and will be censored at the time of glucose challenge. Only events occurring after treatment and prior to glucose challenge are included as events.

Table 14.3.8.3
Time (minutes) to Resolution of Hypoglycemic Event from IV Dextrose Administration by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Table 14.3.8.1.

PROGRAMMING NOTE:

Censoring will not be done as hypoglycemic events should be resolved before subjects are discharged from the clinic.

Table 14.3.8.4
Proportion of Subjects Reaching Euglycemia after IV Dextrose Administration by Treatment Group
Safety Analysis Set

Timepoint	XP-3924 (N=xxx) n / f (%)	Regular Insulin (N=xxx) n / f (%)	Regular Insulin + Pramlintide (N=xxx) n / f (%)
XXX	xx / xx (xx.x)	xx / xx (xx.x)	xx / xx (xx.x)
XXX	xx / xx (xx.x)	xx / xx (xx.x)	xx / xx (xx.x)
XXX	xx / xx (xx.x)	xx / xx (xx.x)	xx / xx (xx.x)

PROGRAMMING NOTE: Including timepoints '10 min', '20 min', '30 min'.

PROGRAMMING NOTE:

Table 14.3.8.5
Average Amount of IV Dextrose (g) by Treatment Group
Safety Analysis Set

Treatment	n	Mean	SD	Median	Min	Max	Q1	Q3	95% CI	%CV
XP-3924 (N=xxx)	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin (N=xxx)	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin + Pramlintide (N=xxx)	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x

Treatment Comparison	Mean	SE	95% CI	p-value
XP-3924 vs. Regular Insulin	xx.xx	xx.xxx	(xx.xx, xx.xx)	x.xxx
XP-3924 vs. Regular Insulin + Pramlintide	xx.xx	xx.xxx	(xx.xx, xx.xx)	x.xxx
Regular Insulin vs. Regular Insulin + Pramlintide	xx.xx	xx.xxx	(xx.xx, xx.xx)	x.xxx

PROGRAMMING NOTE:

Table 14.5.1
Plasma Glucose Concentration Data, Descriptive Statistics
PD Analysis Set

Parameter: XXX (Unit)

Treatment	Timepoint	n	Mean	SD	Median	Min	Max	Q1	Q3	95% CI	%CV
XP-3924 (N=xxx)	Timepoint 1	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
XP-3924 (N=xxx)	Timepoint 2	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
XP-3924 (N=xxx)	Timepoint 3	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
XP-3924 (N=xxx)	...	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin (N=xxx)	Timepoint 1	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin (N=xxx)	Timepoint 2	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin (N=xxx)	Timepoint 3	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin (N=xxx)	...	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin + Pramlintide (N=xxx)	Timepoint 1	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin + Pramlintide (N=xxx)	Timepoint 2	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin + Pramlintide (N=xxx)	Timepoint 3	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin + Pramlintide (N=xxx)	...	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Overall (N=xxx)	Timepoint 1	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Overall (N=xxx)	Timepoint 2	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Overall (N=xxx)	Timepoint 3	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Overall (N=xxx)	...	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x

PROGRAMMING NOTE: Timepoints: 'Pre-Dose', '10 min', '20 min', '30 min', '40 min', '50 min', '60 min', '90 min', '120 min', '180 min'.

Table 14.5.2
Plasma Glucose PD Parameter Data, Descriptive Statistics and Analysis
PD Analysis Set

Parameter: XXX (Unit)

Treatment	n	Mean	SD	Median	Min	Max	Q1	Q3	95% CI	%CV
XP-3924 (N=xxx)	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin (N=xxx)	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x
Regular Insulin + Pramlintide (N=xxx)	xx	xx.x	xx.xx	xx.x	xx	xx	xx.x	xx.x	(xx.x, xx.x)	xx.x

Effect	Degrees of Freedom	Error Degrees of Freedom	F-Statistic	p-value
Sequence	xx.x	xx.x	xx.xx	x.xxx
Period	xx.x	xx.x	xx.xx	x.xxx
Treatment	xx.x	xx.x	xx.xx	x.xxx

Table 14.5.2
Plasma Glucose PD Parameter Data, Descriptive Statistics and Analysis
PD Analysis Set
Parameter: XXX (Unit)

Treatment	LS Mean	SE	95% CI	p-value
XP-3924	xx.xx	xx.xxx	(xx.xx, xx.xx)	x.xxx
Regular Insulin	xx.xx	xx.xxx	(xx.xx, xx.xx)	x.xxx
Regular Insulin + Pramlintide	xx.xx	xx.xxx	(xx.xx, xx.xx)	x.xxx

Treatment Comparison	LS Mean	SE	95% CI	p-value
XP-3924 vs. Regular Insulin	xx.xx	xx.xxx	(xx.xx, xx.xx)	x.xxx
XP-3924 vs. Regular Insulin + Pramlintide	xx.xx	xx.xxx	(xx.xx, xx.xx)	x.xxx
Regular Insulin vs. Regular Insulin + Pramlintide	xx.xx	xx.xxx	(xx.xx, xx.xx)	x.xxx

PROGRAMMING NOTE: Include parameters as specified in the Statistical Analysis Plan.

PROGRAMMING NOTE: Parameter 'Plasma glucose Tmax' is analysed using Wilcoxon Signed Rank Test so output will not have ANOVA type 3 tests or LS means. Only p-values for pairwise comparisons are displayed.

PROGRAMMING NOTE: Parameter 'Tmax' is analysed using Wilcoxon Signed Rank Test so output will not have ANOVA type 3 tests or LS means. Only p-values for pairwise comparisons are displayed.

Listing 16.2.1.1
Screen Failures
Enrolled Set

Subject Number	Date	Reason /	Other Reason
12345	DDMMMYYYY	Reason Text	Other Reason Specification Text
23456	DDMMMYYYY	Reason Text	Other Reason Specification Text
34567	DDMMMYYYY	Reason Text	Other Reason Specification Text
...			

PROGRAMMING NOTE:

Listing 16.2.1.2
Inclusion/Exclusion Criteria
Enrolled Set

Subject Number	Date	Inclusion/ Exclusion	Criteria Not Met
12345	DDMMMYYYY	Inclusion	Inclusion Criteria not met text
12345	DDMMMYYYY	Exclusion	Exclusion Criteria met text
23456	DDMMMYYYY	Inclusion	Inclusion Criteria not met text
23456	DDMMMYYYY	Exclusion	Exclusion Criteria met text
34567	DDMMMYYYY	Inclusion	Inclusion Criteria not met text
34567	DDMMMYYYY	Exclusion	Exclusion Criteria met text
...			

PROGRAMMING NOTE:

Listing 16.2.1.3
Study Completion
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Completed Study	Date of Final Contact (Study Day)	Date of Completion/ Termination (Study Day)	Primary Reason for Termination (AE number)	Other Reason
12345	Yes/No	DDMMMYYYY (NN)	DDMMMYYYY (NN)	Reason Text (AENUM)	Other Reason Specification Text
23456	Yes/No	DDMMMYYYY (NN)	DDMMMYYYY (NN)	Reason Text (AENUM)	Other Reason Specification Text
34567	Yes/No	DDMMMYYYY (NN)	DDMMMYYYY (NN)	Reason Text (AENUM)	Other Reason Specification Text
...					

PROGRAMMING NOTE: Exposure unit: days.

Listing 16.2.2.1
Protocol Deviations
Enrolled Set

Treatment Sequence: XXX

Subject Number	Date of Deviation (Study Day)	Classification	Deviation	Deviation Specification
12345	DDMMMYYYY (NN)	Major/Minor	Deviation text	Deviation specification text
23456	DDMMMYYYY (NN)	Major/Minor	Deviation text	Deviation specification text
34567	DDMMMYYYY (NN)	Major/Minor	Deviation text	Deviation specification text
...				

PROGRAMMING NOTE:

Listing 16.2.3.1
Analysis Sets
Enrolled Set

Treatment Sequence: XXX

Subject Number	Enrolled Set	Randomized Set	Safety Analysis Set	PK/PD Analysis Set
12345	Yes/No	Yes/No	Yes/No	Yes/No
23456	Yes/No	Yes/No	Yes/No	Yes/No
34567	Yes/No	Yes/No	Yes/No	Yes/No
...				

PROGRAMMING NOTE:

Listing 16.2.4.1
Demographic Data
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	ICF Version	Date/Time of Informed Consent (Study Day)	Age (years)/ Date of Birth	Gender	Ethnicity	Race	Height (cm)	Weight (kg)	BMI (kg/m2)
12345	DDMMMYYYY	DDMMMYYYY/ HH:MM (NN)	NN/ DDMMMYYYY	M/F	Ethnicity	Race	NN.N	NN.N	NN.N
23456	DDMMMYYYY	DDMMMYYYY/ HH:MM (NN)	NN/ DDMMMYYYY	M/F	Ethnicity	Race	NN.N	NN.N	NN.N
34567	DDMMMYYYY	DDMMMYYYY/ HH:MM (NN)	NN/ DDMMMYYYY	M/F	Ethnicity	Race	NN.N	NN.N	NN.N
...									

PROGRAMMING NOTE:

Listing 16.2.4.2
Medical History
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Start Date (Study Day)	End Date (Study Day) / Ongoing?	Body System	System Organ Class / Preferred Term / Verbatim Term
12345	DDMMMYYYY (NN)	DDMMMYYYY (NN)/ Ongoing	Body System	System Organ Class /Preferred Term
12345	DDMMMYYYY (NN)	DDMMMYYYY (NN) / Ongoing	Body System	System Organ Class /Preferred Term
23456	DDMMMYYYY (NN)	DDMMMYYYY (NN) / Ongoing	Body System	System Organ Class /Preferred Term
23456	DDMMMYYYY (NN)	DDMMMYYYY (NN) / Ongoing	Body System	System Organ Class /Preferred Term
34567	DDMMMYYYY (NN)	DDMMMYYYY (NN) / Ongoing	Body System	System Organ Class /Preferred Term
34567	DDMMMYYYY (NN)	DDMMMYYYY (NN) / Ongoing	Body System	System Organ Class /Preferred Term
...				

PROGRAMMING NOTE:

Listing 16.2.4.3
Prior/Concomitant Medications
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Prior/ Concomitant (Treatment Group)	Start Date/ Time (Study Day)	End Date/ Time (Study Day) / Ongoing?	Medication / Preferred Term / ATC Level 2 / ATC Level 4	Indication/ Reason / Specify	Dose / Unit / Frequency / Route
12345	Prior/ Concomitant (XXX)	DDMMMYYYY/ HH:MM (NN)	DDMMMYYYY/ HH:MM (NN) / Ongoing	Medication Text /Preferred Term Text /ATC Level 2 Text /ATC Level 4 Text	Reason / Specification Text	Dose /Unit /Frequency /Route
12345	Prior/ Concomitant (XXX)	DDMMMYYYY/ HH:MM (NN)	DDMMMYYYY/ HH:MM (NN) / Ongoing	Medication Text /Preferred Term Text /ATC Level 2 Text /ATC Level 4 Text	Reason / Specification Text	Dose /Unit /Frequency /Route
23456	Prior/ Concomitant (XXX)	DDMMMYYYY/ HH:MM (NN)	DDMMMYYYY/ HH:MM (NN) / Ongoing	Medication Text /Preferred Term Text /ATC Level 2 Text /ATC Level 4 Text	Reason / Specification Text	Dose /Unit /Frequency /Route
23456	Prior/ Concomitant (XXX)	DDMMMYYYY/ HH:MM (NN)	DDMMMYYYY/ HH:MM (NN) / Ongoing	Medication Text /Preferred Term Text /ATC Level 2 Text /ATC Level 4 Text	Reason / Specification Text	Dose /Unit /Frequency /Route
34567	Prior/ Concomitant (XXX)	DDMMMYYYY/ HH:MM (NN)	DDMMMYYYY/ HH:MM (NN) / Ongoing	Medication Text /Preferred Term Text /ATC Level 2 Text /ATC Level 4 Text	Reason / Specification Text	Dose /Unit /Frequency /Route
34567	Prior/ Concomitant (XXX)	DDMMMYYYY/ HH:MM (NN)	DDMMMYYYY/ HH:MM (NN) / Ongoing	Medication Text /Preferred Term Text /ATC Level 2 Text /ATC Level 4 Text	Reason / Specification Text	Dose /Unit /Frequency /Route
...						

PROGRAMMING NOTE: For 'Other' unit, frequency and route also include text specification.

Listing 16.2.5.1.1
Exposure
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Visit / Date / Time / (Study Day)	Treatment Administered	Full Dose Administered?	Dose	Reason Dose Adjusted	Dosing Comments
12345	Visit 1 DDMMMYYYY/ HH:MM (NN)	XXX	Y/N	NN	Reason Text	Comment text
12345	Visit 2 DDMMMYYYY/ HH:MM (NN)	XXX	Y/N	NN	Reason Text	Comment text
23456	Visit 1 DDMMMYYYY/ HH:MM (NN)	XXX	Y/N	NN	Reason Text	Comment text
23456	Visit 2 DDMMMYYYY/ HH:MM (NN)	XXX	Y/N	NN	Reason Text	Comment text
34567	Visit 1 DDMMMYYYY/ HH:MM (NN)	XXX	Y/N	NN	Reason Text	Comment text
34567	Visit 2 DDMMMYYYY/ HH:MM (NN)	XXX	Y/N	NN	Reason Text	Comment text
...						

PROGRAMMING NOTE:

Listing 16.2.7.1
Adverse Events
Safety Analysis Set

Treatment Group: XXX

Subject Number	System Organ Class / Preferred Term / AE Term	TEAE	SAE	Start Date/Time (Study Day)	End Date/Time (Study Day) / Ongoing	Severity	Relation to Study Treatment	Action Taken	Other Action Taken	Outcome
12345	System Organ Class /Preferred Term /Verbatim	Y/N	Y/N	DDMMMYYYY/ HH:MM (N)	DDMMMYYYY/ HH:MM (N) / Ongoing	Severity	Relation	Action	Y / Specify	Outcome
23456	System Organ Class /Preferred Term /Verbatim	Y/N	Y/N	DDMMMYYYY/ HH:MM (N)	DDMMMYYYY/ HH:MM (N) / Ongoing	Severity	Relation	Action	Y / Specify	Outcome
34567	System Organ Class /Preferred Term /Verbatim	Y/N	Y/N	DDMMMYYYY/ HH:MM (N)	DDMMMYYYY/ HH:MM (N) / Ongoing	Severity	Relation	Action	Y / Specify	Outcome
...										

PROGRAMMING NOTE:

Listing 16.2.8.1.1
Vital Sign Data
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Parameter (Unit)	Visit / Timepoint	Treatment Group	Date/Time (Study Day)	Position	Result	Change from Pre-Dose	Clinically Significant	Not Done / Reason
12345	Parameter 1 (Unit)	Visit 1 / Timepoint X	XXX	DDMMMYYYY/ HH:MM (NN)	Position	NN.N	NN.N	No/Yes	
12345	Parameter 1 (Unit)	Visit 2 / Timepoint X	XXX	DDMMMYYYY/ HH:MM (NN)	Position	NN.N	NN.N	No/Yes	
	Parameter 2 (Unit)	Visit 1 / Timepoint X	XXX	DDMMMYYYY/ HH:MM (NN)	Position	NN.N	NN.N	No/Yes	
	Parameter 2 (Unit)	Visit 2 / Timepoint X	XXX	DDMMMYYYY/ HH:MM (NN)	Position	NN.N	NN.N	No/Yes	
	Parameter 3 (Unit)	Visit 1 / Timepoint X	XXX	DDMMMYYYY/ HH:MM (NN)	Position	NN.N	NN.N	No/Yes	
	Parameter 3 (Unit)	Visit 2 / Timepoint X	XXX	DDMMMYYYY/ HH:MM (NN)	Position	NN.N	NN.N	No/Yes	
	Parameter 4 (Unit)	Visit 1 / Timepoint X	XXX	DDMMMYYYY/ HH:MM (NN)	Position	NN.N	NN.N	No/Yes	
	Parameter 4 (Unit)	Visit 2 / Timepoint X	XXX	DDMMMYYYY/ HH:MM (NN)	Position	NN.N	NN.N	No/Yes	

...

PROGRAMMING NOTE:

Listing 16.2.8.2.1
Physical Examination Data
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Parameter (Unit)	Visit	Treatment Group	Date/Time (Study Day)	Result	Reason
12345	Parameter 1	Visit 1	XXX	DDMMMYYYY/ HH:MM (NN)	Normal / Abnormal NCS / Abnormal CS / Not Done	
	Parameter 2	Visit 1	XXX	DDMMMYYYY/ HH:MM (NN)	Normal / Abnormal NCS / Abnormal CS / Not Done	
	Parameter 3	Visit 1	XXX	DDMMMYYYY/ HH:MM (NN)	Normal / Abnormal NCS / Abnormal CS / Not Done	
	Parameter 4	Visit 1	XXX	DDMMMYYYY/ HH:MM (NN)	Normal / Abnormal NCS / Abnormal CS / Not Done	
...						

PROGRAMMING NOTE:

Listing 16.2.8.3.1
Hematology Data
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Parameter (Unit)	Visit	Date/Time (Study Day)	Result	Normal Range	Reference Range Indicator	Change from Baseline	Not Done / Reason
12345	Parameter 1 (Unit)	Visit 1	DDMMMYYYY HH:MM (NN)	NN.N	LL.L - HH.H	Low/Normal/High	NN.N	
12345	Parameter 1 (Unit)	Visit 2	DDMMMYYYY HH:MM (NN)	NN.N	LL.L - HH.H	Low/Normal/High	NN.N	
	Parameter 2 (Unit)	Visit 1	DDMMMYYYY HH:MM (NN)	NN.N	LL.L - HH.H	Low/Normal/High	NN.N	
	Parameter 2 (Unit)	Visit 2	DDMMMYYYY HH:MM (NN)	NN.N	LL.L - HH.H	Low/Normal/High	NN.N	
	Parameter 3 (Unit)	Visit 1	DDMMMYYYY HH:MM (NN)	NN.N	LL.L - HH.H	Low/Normal/High	NN.N	
	Parameter 3 (Unit)	Visit 2	DDMMMYYYY HH:MM (NN)	NN.N	LL.L - HH.H	Low/Normal/High	NN.N	
	Parameter 4 (Unit)	Visit 1	DDMMMYYYY HH:MM (NN)	NN.N	LL.L - HH.H	Low/Normal/High	NN.N	
	Parameter 4 (Unit)	Visit 2	DDMMMYYYY HH:MM (NN)	NN.N	LL.L - HH.H	Low/Normal/High	NN.N	

...

PROGRAMMING NOTE:

Listing 16.2.8.3.2
Serum Chemistry Data
Safety Analysis Set

Treatment Sequence: XXX

PROGRAMMING NOTE: Same shell as Listing 16.2.8.3.1.

Listing 16.2.8.3.3
C-Peptide and HbA1c Data
Safety Analysis Set

Treatment Sequence: XXX

PROGRAMMING NOTE: Same shell as Listing 16.2.8.3.1.

Listing 16.2.8.3.4
Urine Drug Screen Data
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Parameter (Unit)	Visit	Date (Study Day)	Result	Not Done / Reason
12345	Parameter 1 (Unit)	Visit 1	DDMMMYYYY HH:MM (NN)	XXX	
12345	Parameter 1 (Unit)	Visit 2	DDMMMYYYY HH:MM (NN)	XXX	
	Parameter 2 (Unit)	Visit 1	DDMMMYYYY HH:MM (NN)	XXX	
	Parameter 2 (Unit)	Visit 2	DDMMMYYYY HH:MM (NN)	XXX	
	Parameter 3 (Unit)	Visit 1	DDMMMYYYY HH:MM (NN)	XXX	
	Parameter 3 (Unit)	Visit 2	DDMMMYYYY HH:MM (NN)	XXX	
	Parameter 4 (Unit)	Visit 1	DDMMMYYYY HH:MM (NN)	XXX	
	Parameter 4 (Unit)	Visit 2	DDMMMYYYY HH:MM (NN)	XXX	
...					

PROGRAMMING NOTE:

Listing 16.2.8.3.5
Urine Pregnancy Test Data
Safety Analysis Set

Treatment Sequence: XXX

PROGRAMMING NOTE: Same shell as Listing 16.2.8.3.4.

Listing 16.2.8.4.1
ECG Data
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Parameter (Unit)	Visit	Date/Time (Study Day)	Position	Result	Not Done / Reason
12345	Parameter 1 (Unit)	Visit 1	DDMMMYYYY/ HH:MM (NN)	Position	NN.N / Normal / Abnormal (NCS) / Abnormal (CS)	
12345	Parameter 1 (Unit)	Visit 2	DDMMMYYYY/ HH:MM (NN)	Position	NN.N / Normal / Abnormal (NCS) / Abnormal (CS)	
	Parameter 2 (Unit)	Visit 1	DDMMMYYYY/ HH:MM (NN)	Position	NN.N / Normal / Abnormal (NCS) / Abnormal (CS)	
	Parameter 2 (Unit)	Visit 2	DDMMMYYYY/ HH:MM (NN)	Position	NN.N / Normal / Abnormal (NCS) / Abnormal (CS)	
	Parameter 3 (Unit)	Visit 1	DDMMMYYYY/ HH:MM (NN)	Position	NN.N / Normal / Abnormal (NCS) / Abnormal (CS)	
	Parameter 3 (Unit)	Visit 2	DDMMMYYYY/ HH:MM (NN)	Position	NN.N / Normal / Abnormal (NCS) / Abnormal (CS)	
...						

PROGRAMMING NOTE: For overall interpretation add also ECG Interpretation Text together with the result.

Listing 16.2.8.5.1
Draize Scale Data
Safety Analysis Set

Treatment Sequence: XXX

PROGRAMMING NOTE: Same shell as Listing 16.2.8.2.1 but without 'Clinically Significant' and 'Not Done' columns.

PROGRAMMING NOTE: Results are as follows for Erythema Formation:

0 - No erythema
1 - Very slight erythema
2 - Well defined erythema
3 - Moderate erythema
4 - Severe erythema

and for Edema Formation:

0 - No edema
1 - Very slight edema
2 - Slight edema
3 - Moderate edema
4 - Severe edema.

Listing 16.2.8.6.1
Injection Site Discomfort Assessment Data
Safety Analysis Set

Treatment Sequence: XXX

PROGRAMMING NOTE: Same shell as Listing 16.2.8.2.1 but without 'Clinically Significant' column.

PROGRAMMING NOTE: Add possible comment together with result.

PROGRAMMING NOTE: Results include:

11 point numeric rating scale.

1a. How would you describe any discomfort you felt from the study drug? (Check all that apply):

- None (Please ignore question 1b.)
- Pain (eg, throbbing, soreness, muscle ache)
- Itching
- Tingling, twitching, or numbness
- Irritation (eg, burning, stinging)
- Other

1b. About how long did the discomfort last after the injection? (Check one):

- Less than 1 minute
- 1-2 minutes
- 3-5 minutes
- 6-9 minutes
- at least 10 minutes (Please complete question 1c before leaving the clinic.)

1c. In total, how long did the discomfort last after the injection? (Please enter a number below):

_____ Minutes

Listing 16.2.8.7.1
Plasma Glucose Concentration Data
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Visit	Treatment Group	Date (Study Day)	Time	Result (<Unit>)	Not Done / Reason
12345	Visit 1	XXX	DDMMMYYYY (NN)	HH:MM	NN.N	
				HH:MM	NN.N	
				HH:MM	NN.N	
				HH:MM	NN.N	
				HH:MM	NN.N	
...						

PROGRAMMING NOTE: Visits: 'Visit 2', 'Visit 3', 'Visit 4'.

Listing 16.2.8.7.2
Plasma Glucose PD Parameter Data
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Visit	Treatment Group	Parameter	Result	Not Done / Reason
12345	Visit 1	XXX	Parameter 1 (Unit)	NN.N	
12345	Visit 1	XXX	Parameter 2 (Unit)	NN.N	
12345	Visit 1	XXX	Parameter 3 (Unit)	NN.N	
12345	Visit 1	XXX	Parameter 4 (Unit)	NN.N	
12345	Visit 1	XXX	Parameter 5 (Unit)	NN.N	
12345	Visit 1	XXX	Parameter 6 (Unit)	NN.N	
12345	Visit 1	XXX	Parameter 7 (Unit)	NN.N	
12345	Visit 1	XXX	Parameter 8 (Unit)	NN.N	
...					

PROGRAMMING NOTE: Include parameters as specified in the Statistical Analysis Plan.

Listing 16.2.8.7.3
Glucose Challenge
Safety Analysis Set

Treatment Sequence: XXX

Subject Number	Visit	Treatment Group	Date/Time (Study Day) of Challenge Start	Date/Time (Study Day) of Challenge End	Did subject complete 100% of Glucose Challenge	Amount of Glucose Challenge Complete (%)
12345	Visit 1	XXX	DDMMMYYYY/ HH:MM (NN)	DDMMMYYYY/ HH:MM (NN)	No/Yes	NN
12345	Visit 2	XXX	DDMMMYYYY/ HH:MM (NN)	DDMMMYYYY/ HH:MM (NN)	No/Yes	NN
12345	Visit 3	XXX	DDMMMYYYY/ HH:MM (NN)	DDMMMYYYY/ HH:MM (NN)	No/Yes	NN
...						

PROGRAMMING NOTE:

Listing 16.2.8.8.1
Hypoglycemic Events
Safety Analysis Set

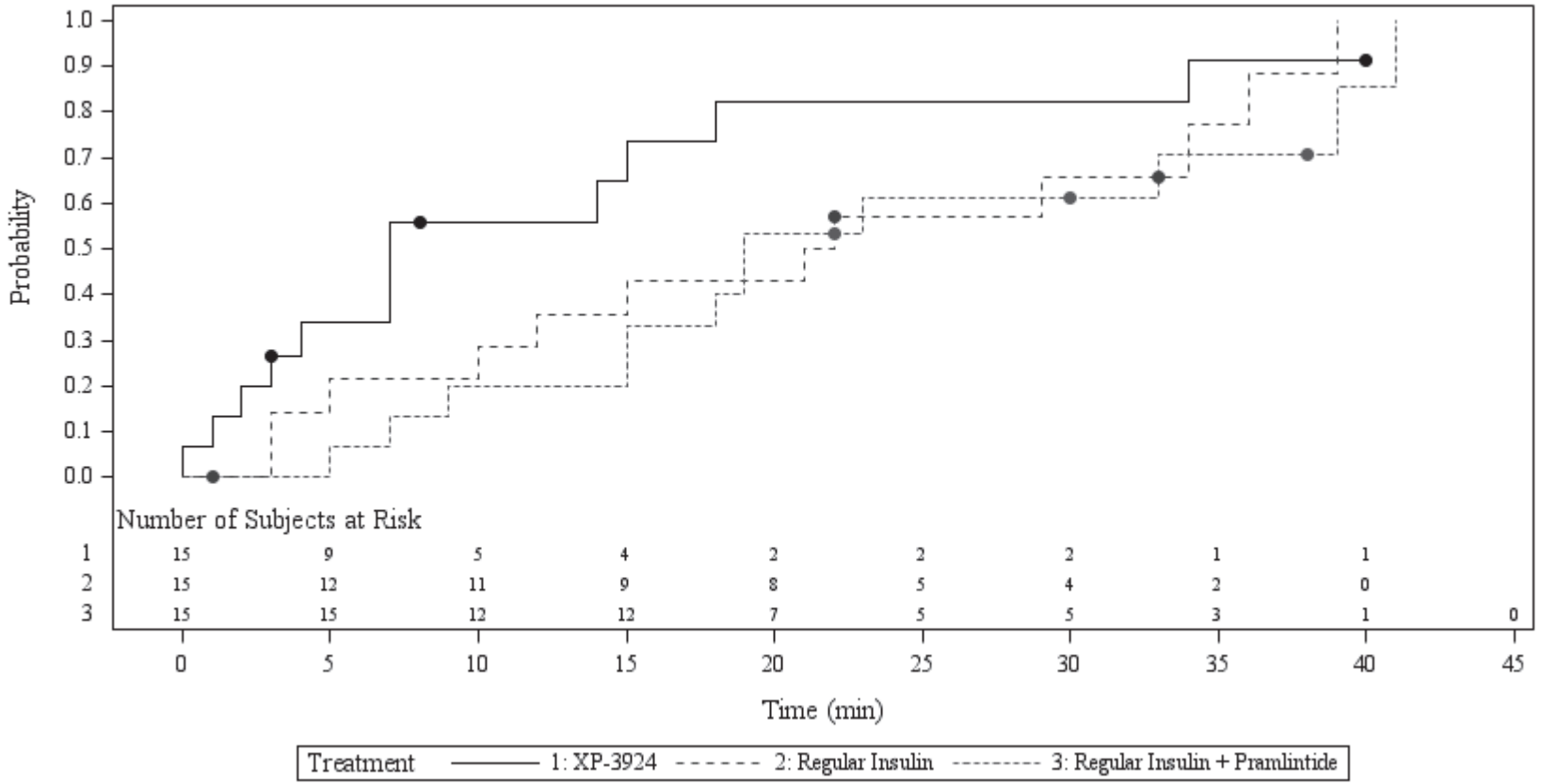
Treatment Sequence: XXX

Subject Number	Visit	Treatment Group	Experienced Hypo Event	Time to Hypo Event (minutes)	Time to IV Dextrose Administration (minutes) (Amount of IV Dextrose (g) needed for BG>70 mg/dL)	Time to Resolution of Hypo Event after IV Dextrose Administration (minutes)
12345	Visit 1	XXX	No/Yes	NN*	NN* (NN)	NN
12345	Visit 2	XXX	No/Yes	NN*	NN* (NN)	NN
12345	Visit 3	XXX	No/Yes	NN*	NN* (NN)	NN
...						

PROGRAMMING NOTE:

If hypo event occurs after glucose challenge then it will not be included as event and will be censored at the time of glucose challenge. Only events occurring after treatment and prior to glucose challenge are included as events.
* = Censored.

Figure 14.3.1.1
Time (minutes) to IV Dextrose Administration from Study Drug Administration by Treatment Group
Safety Analysis Set



PROGRAMMING NOTE:

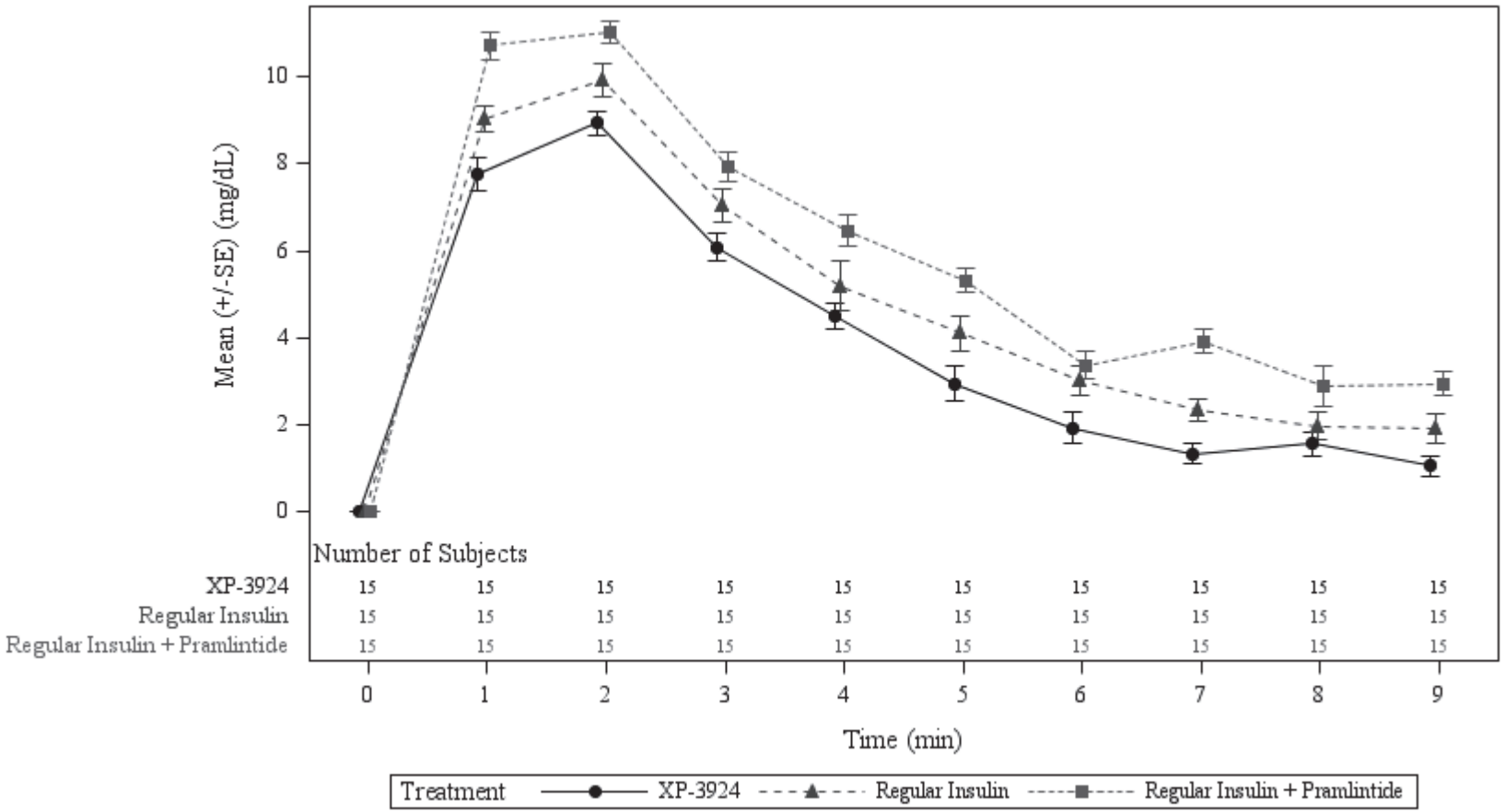
Figure 14.3.1.2
Time (minutes) to Hypoglycemic Event from Study Drug Administration by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Figure 14.3.1.1.

Figure 14.3.1.3
Time (minutes) to Resolution of Hypoglycemic Event from IV Dextrose Administration by Treatment Group
Safety Analysis Set

PROGRAMMING NOTE: Same shell as Figure 14.3.1.1.

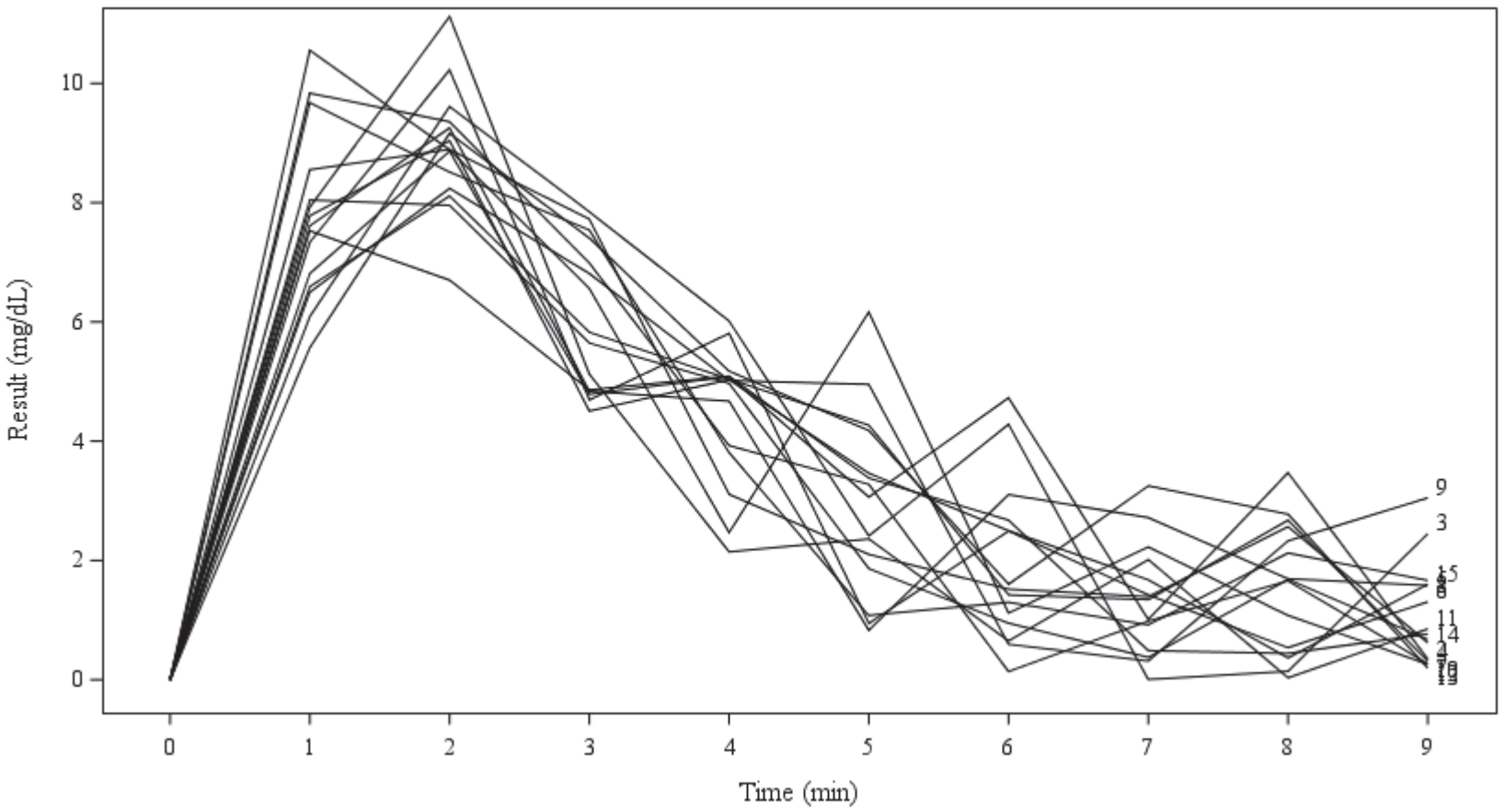
Figure 14.5.1.1
Plasma Glucose Concentration Data, Mean Profiles on Linear Scale
PD Analysis Set



PROGRAMMING NOTE:

Figure 14.5.1.2
Plasma Glucose Concentration Data, Individual Profiles on Linear Scale
PD Analysis Set

Treatment: XXX



PROGRAMMING NOTE: Repeat for treatments 'XP-3924', 'Regular Insulin', 'Regular Insulin + Pramlintide'.

Certificate Of Completion

Envelope Id: BC295336D9504C59B86A748098257AEB
Status: Completed
Subject: Please DocuSign: DPI-201_SAP_v1.0_2019-11-14_sponsor_signed.pdf
Source Envelope:
Document Pages: 116
Signatures: 2
Certificate Pages: 2
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Disabled
Time Zone: (UTC) Dublin, Edinburgh, Lisbon, London

Envelope Originator:
Tuomas Kemppainen
3800 Paramount Parkway
Suite 400
Morrisville, NC 27560
tuomas.kemppainen@worldwide.com
IP Address: 91.152.17.218

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In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp
Witness Events	**Signature**	**Timestamp**
Notary Events	**Signature**	**Timestamp**
Envelope Summary Events	**Status**	**Timestamps**
Envelope Sent	Hashed/Encrypted	15-Nov-2019 | 08:58
Certified Delivered	Security Checked	15-Nov-2019 | 09:30
Signing Complete	Security Checked	15-Nov-2019 | 13:58
Completed	Security Checked	15-Nov-2019 | 13:58
Payment Events	**Status**	**Timestamps**