STATISTICAL ANALYSIS PLAN
Protocol 1VIT13036

A Multi-center, Open-Label, Single Arm Study to Characterize the Pharmacokinetics and Pharmacodynamics Profile of Intravenous Ferric Carboxymaltose in Pediatric Subjects 1-17 years old with Iron Deficiency Anemia (IDA)

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Document Version History:

Version	Date	Author	Comments
1.0	6/8/15	Michelle Secic	Original
2.0	7/14/15	Michelle Secic	Revisions based on initial review from Luitpold
2.1	2/4/17	Michelle Secic	Excluded summary of potentially clinically significant (PCS) Vital Signs

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LIST OF ABBREVIATIONS

AE	Adverse event
AUC	Area Under the Curve
BMI	Body Mass Index
DSMB	Data and Safety Monitoring Board
EDC	Electronic Data Capture
ESA	Erythropoiesis stimulating agent
FCM	Ferric Carboxymaltose
HBsAg	Hepatitis B antigen
HCV	Hepatitis C viral antibody
HIV	Human Immunodeficiency Virus
ID	Iron deficiency
IDA	Iron deficiency anemia
IV	Intravenous
IWR	Interactive Web Response
MedDRA	Medical Dictionary for Regulatory Activities
PCS	Potentially Clinically Significant
PD	Pharmacodynamics
PK	Pharmacokinetics
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical analysis plan
SOC	System Organ Class
TEAE	Treatment emergent adverse event
TSAT	Transferrin Saturation

1. INTRODUCTION

Rapid growth, insufficient dietary intake, and limited absorption of dietary iron combine to place children at increased risk for iron deficiency. In addition, iron deficiency may contribute significantly to anemia due to malabsorption, gastrointestinal blood loss, or iatrogenically due to repeated blood samplings. As a result, iron deficiency anemia (IDA) remains the most common nutritional deficiency in children in the United States.

2. STUDY OBJECTIVES

The main objectives of this study are to characterize the pharmacokinetics and determine appropriate dosing and safety of Ferric Carboxymaltose for the pediatric population suffering from iron deficiency (ID) with anemia.

The pharmacokinetics component has its own separate statistical analysis plan (SAP). This SAP is intended to provide details on the dosing and safety components of the study, including the statistical methodology and associated tables and listings.

3. STUDY DESIGN

This is a phase II, open-label, non-randomized, multi-center, single arm study with two cohorts:

Cohort 1: 16 subjects will be treated with Ferric Carboxymaltose at 7.5 mg/kg with a maximum single dose of 750 mg, whichever is smaller.

Cohort 2 will initiate enrollment only after all subjects in Cohort 1 have completed 4 weeks of therapy and a Data and Safety Monitoring Board (DSMB) approves continuation.

Cohort 2: 16 subjects will be treated with Ferric Carboxymaltose at 15 mg/kg with a maximum single dose of 750 mg, whichever is smaller.

3.1. Inclusion/Exclusion Criteria

As per section 4.2.1 in the protocol, the following are the study inclusion and exclusion criteria.

Inclusion Criteria:

1. Male or female subjects 1 to 17 years of age (6 to 17 years of age in Russia only) with assent to participation and his/her parent or guardian is willing and able to sign the informed consent approved by the Independent Review Board / Ethics Committee.
2. Screening TSAT < 20%
3. Screening Hemoglobin < 11 g/dL
4. For subjects who are receiving an erythropoietin stimulating agent (ESA): stable ESA therapy (+/- 20% of current dose) for > 8 weeks prior to the qualifying screening visit and no ESA dosing or product changes anticipated for the length of the trial

Exclusion Criteria:

1. Known hypersensitivity reaction to any component of Ferric Carboxymaltose.
2. Subject previously randomized and treated in this study or any other clinical study of Ferric Carboxymaltose (FCM or VIT-45).
3. Body mass index (BMI) $\leq 5^{th}$ percentile for age
4. Male or Female subject 1 year of age weighing < 12kg.
5. History of acquired iron overload, hemochromatosis or other iron accumulation disorders.
6. Chronic kidney disease subjects on hemodialysis.
7. Screening Ferritin level > 300ng/mL
8. Subjects with significant severe diseases of the liver, hemopoietic system, cardiovascular system, psychiatric disorder or other conditions which on the opinion of the investigator may place a subject at added risk.
9. Any active infection.
10. Known positive hepatitis B antigen (HBsAg) or hepatitis C viral antibody (HCV) with evidence of active hepatitis.
11. Known positive HIV-1/HIV-2 antibodies (anti-HIV).
12. Anemia due to reasons other than iron deficiency (i.e. hemoglobinopathy). Subjects treated with vitamin B12 or folic acid deficiency are permitted.
13. Intravenous iron and /or blood transfusion in the 4 weeks prior to screening.
14. Immunosuppressive therapy that may lead to anemia (i.e. cyclophosphamide, azathioprine, mycophenolate mofetil). Note steroid therapy is permitted.
15. Administration and / or use of an investigational product (drug or device) within 30 days of screening.
16. Alcohol or drug abuse within the past six months.
17. Female subjects who are pregnant or lactating, or sexually active female who are of childbearing potential not willing to use an acceptable form of contraceptive precautions during the study.
18. Subject is unable to comply with study assessments.

3.2. Schedule of Visits

Subjects will have a screening period, baseline visit, 24, 48 and 72 hours post dosing visits, and visits at day 14, 28 and 35. The schedule of visits is summarized below:

Visit Day	Screening Period (Up to 14 Days)	Day -1	Day 0	24 and 48 hours post dosing	72 hours post dosing	Day 14 (week 2)	Day 28 (week 4)	Day 35 (week 5)
Informed Consent	X							
Assess entry criteria	X		X					
EDC	X		X					X
Medical History	X		X					
Physical Exam[1]			X					X
Vital Signs[6]	X		X		X	X	X	X
Height / Weight			X					
PK/PD Samples		X[2]	X[3]	X[4]	X[4]			
Hematology, Chemistry and Iron Indices	X				X	X	X	X
Serum pregnancy test	X							
Concomitant Medications	X		X		X	X	X	X
ESA Stability	X		X		X	X	X	X
Adverse Event Assessments[5]			X	X	X	X	X	X
Ferric Carboxymaltose			X					

[1] Includes clinical assessment of skin, cardiovascular, pulmonary, abdominal, and central nervous system
[2] Blood samples drawn at 8am, 12pm and 8pm for subject iron profile
[3] Blood samples PK/PD should be taken prior to Ferric Carboxymaltose dosing and additional samples for PK/PD should be taken at 1, 2, 6 and 12 hours post dosing.
[4] Blood samples should be taken approximately the same time of day as the Day 0 samples were drawn
[5] Adverse event assessments starting at the time of Ferric Carboxymaltose dosing
[6] Sitting vital signs including blood pressure and heart rate should be collected immediately pre-dosing, immediately and 30 minutes post dosing. Body temperature will also be collected pre-dose only. Vital signs on non-dosing days include sitting heart rate and blood pressure only.

4. PLANNED ANALYSES

4.1. Interim Analyses

An interim analysis of the safety data is planned after the first cohort of 16 patients have completed through week 4 of the study. The purpose of the interim analysis is for the DSMB to review the interim data and to make recommendations to Luitpold Pharmaceuticals concerning the merits of continuing the study and the safety of continuing enrollment into cohort 2.

Refer to the DSMB Charter to details on the planned review of the interim data.

4.2. Final Analysis

The final planned data analyses will be performed after all subjects have completed the study and after the database is locked.

4.3. Populations

There will be two analysis populations:

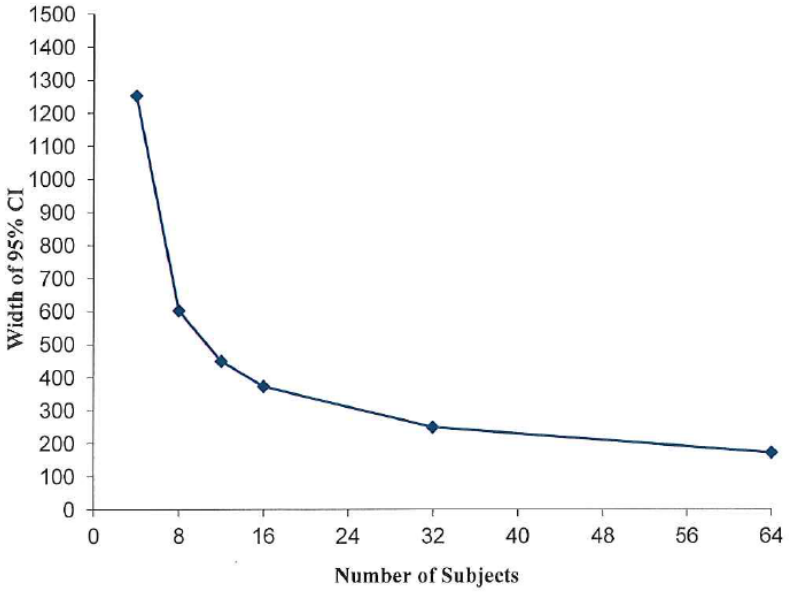
- The Safety Population: The safety population includes all subjects who receive Ferric Carboxymaltose.
- The Pharmacokinetics and Pharmacodynamics (PK/PD) Population: The PK/PD population includes all subjects in the safety population who have evaluable iron profiles and no protocol violation that could affect the PK/PD of Ferric Carboxymaltose.

All summaries will be presented for the safety population. Only demographic characteristics will be summarized for the PK/PD population.

5. SAMPLE SIZE CONSIDERATIONS

Determination of sample size for this study was a compromise between obtaining sufficiently precise estimates of pharmacokinetic parameters and the ethics of including a large number of pediatric patients in an experiment. The precision of estimation can be quantified as the width of the 95% confidence interval for area under the curve (AUC) from 0 to 72 (AUC_{0-72}) from this single-arm study (i.e., smaller width indicates better precision). Based on Study VIT-IV-CL-002 in adults, the standard deviation for total serum iron AUC_{0-72} following a 500 mg intravenous dose is approximately 300 mg-hour/mL. The width of a 95% confidence interval, using a standard deviation of 300 mg-hour/mL, is presented below for selected sample sizes.

As seen in the figure below, 16 patients appears to be a reasonable compromise between precision and number of exposed pediatric patients. Therefore, 32 subjects will be enrolled, with 16 subjects in each cohort. Within each cohort of 16 subjects there will be 8 subjects 1 to 6 years of age and 8 subjects >6 to 17 years of age. Subject enrollment and ages will be tracked and monitored via interactive web response (IWR) system.



6. REPORTING CONVENTIONS

Unless otherwise specified, standard descriptive statistics will be computed for measurements presented in summary tables. The standard descriptive statistics for continuous variables include: number of observations analyzed, mean, standard deviation, median, and range (minimum, and maximum). The standard descriptive statistics for categorical variables include: frequency distribution with the number and percent of subjects included in each category.

Calculation of percentage will use the denominator of the total number of subjects with non-missing data in the particular group of analysis population used in the data display unless otherwise specified.

All data listings, summaries, and statistical analyses will be generated using SAS® Version 9.1 or higher (SAS is registered trademarks of the SAS Institute Inc., Cary, NC, USA.)

7. STATISTICAL ANALYSES AND SUMMARIES

7.1. General Statistical Considerations

No formal hypothesis testing is planned for this study. Only descriptive, summary statistics are planned for assessment of dosing and safety.

7.2. Baseline Definitions

Baseline for this study is defined as Day 0. If the data is not captured at Day 0, or if the data at Day 0 is missing, the screening value will be used.

7.3. Subject Disposition

Subject disposition will be summarized as: enrolled/registered, treated, completed or discontinued. For those discontinued, the reason for discontinuation will be summarized.

7.4. Demographic Characteristics

Demographic characteristics will be summarized separately for the treatment groups, and separately for the two study populations (safety and PK/PD). Demographic characteristics will include: age, gender, ethnicity and race.

7.5. Medical/Surgical History

Medical/surgical histories will be summarized separately for the treatment groups. System organ class and condition/surgery will be coded with the Medical Dictionary for Regulatory Activities (MedDRA) Terminology.

7.6. Efficacy

Hemoglobin, ferritin and TSAT will be summarized at each visit, and for each treatment group. In addition, the change from baseline to each visit will be summarized for each treatment group.

7.7. Adverse Events

Adverse events (AEs) will be summarized for treatment emergent adverse events (TEAEs). TEAEs are defined as AEs that occur on or after the day of the first dose. MedDRA terminology will be used to classify all AEs with respect to system organ class (SOC) and preferred term (PT).

A summary of subjects with TEAEs will be presented for each treatment group. The summary will include counts and percentages for subjects who experience at least one AE, overall and by SOC and PT. This will be repeated for severe TEAEs, related TEAEs and serious TEAEs. Severity will be captured as Grade 1 through Grade 5 with Grades 3-5 categorized as severe. Related will be captured as: none, unlikely, possibly or probably, with related = possibly or probably. Serious will be captured with the standard serious adverse event (SAE) criteria.

Subjects who report the same PT on multiple occasions will be counted once for the preferred term under the highest severity when summarizing by severity, under the closest relationship to the drug when summarizing by relationship, under most serious when summarizing by seriousness.

7.8. Laboratory Values

Laboratory values will be summarized at each visit, and for each treatment group. In addition, the change from baseline to each visit, and the incidence of treatment-emergent potentially clinically significant (PCS) laboratory values will be summarized for each treatment group.

7.9. Vital Signs

Vital signs will be summarized at each visit, and for each treatment group and by age groups (1 - < 6 years, and 6-17 years). Height and weight will be summarized at Day 0 only. Blood pressure and heart rate will be summarized at all visits and as the change from pre to immediately post treatment and the change from pre to 30 minutes post-treatment. .

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2.0	7/14/15	Michelle Secic	Revisions based on initial review from Luitpold
2.1	6/17/16	Michelle Secic	Revised to exclude PCS vitals and stratify by age instead
2.2	6/21/16	Michelle Secic	Revised section 7.9 as per Luitpold comments
2.3	6/23/16	Michelle Secic	Revised sections 7.5 and 7.8 as per Luitpold
2.4	6/23/16	Michelle Secic	Revised vital signs table to include additional changes over time
2.5	6/24/16	Michelle Secic	Split vital signs table
FINAL	7/7/16	Michelle Secic	Finalized date and version

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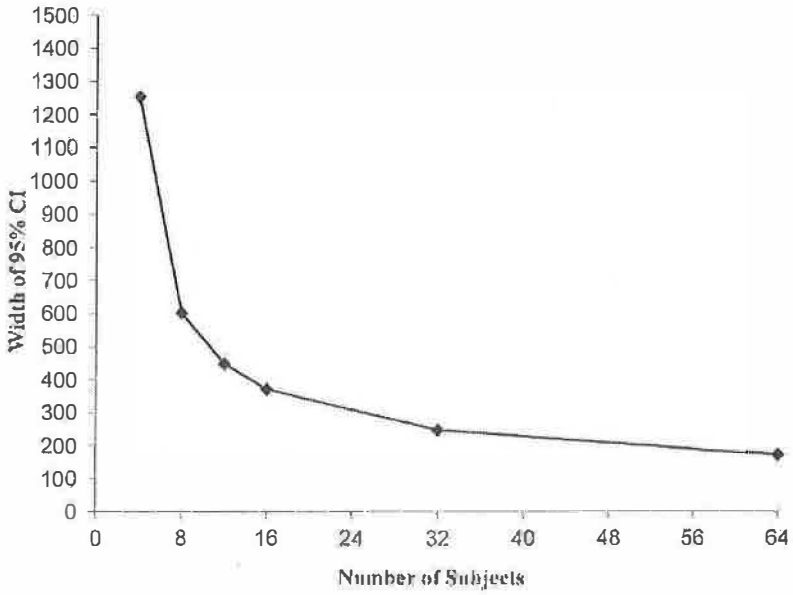

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Subjects who report the same PT on multiple occasions will be counted once for the preferred term under the highest severity when summarizing by severity, under the closest relationship to the drug when summarizing by relationship, under most serious when summarizing by seriousness.

7.8. Laboratory Values

Laboratory values will be summarized at each visit, and for each treatment group. In addition, the change from baseline to each visit, and the incidence of treatment-emergent potentially clinically significant (PCS) laboratory values will be summarized for each treatment group. The denominator is all subjects with normal baseline (< Grade III value) and at least one post baseline assessment in the safety population and the numerator is the number of subjects with

PCS (i.e., meets Grade III or Grade IV toxicity criteria from the National Cancer Institute Common Terminology Criteria) at post-baseline.

7.9. Vital Signs

Vital signs will be summarized for dosing day (Day 0), at each visit and for each treatment group. The change from baseline to each visit, will be summarized for each treatment group. In addition, summary statistics for vital signs will be stratified by age groups: 1 - <6years, and 6 to 17 years.

APPENDIX A – TABLE SHELLS

Table 14.1.1 Site and Population Summaries
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Appendix A - Shells for Study Tables

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Table 14.1.1 Site and Population Summaries

	Cohort 1	Cohort 2
Site	X	X
Site #1	X	X
Site #2	X	X
Etc.	X	X
In Safety Population	X	X
In PK Population	X	X

Table 14.1.1 Subject Disposition – Safety Population

Disposition	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
Registered/Enrolled	X (XX.X)	X (XX.X)
Completed Study	X (XX.X)	X (XX.X)
Discontinued due to:	X (XX.X)	X (XX.X)
Adverse Event	X (XX.X)	X (XX.X)
Intervention	X (XX.X)	X (XX.X)
Lost to Follow-up	X (XX.X)	X (XX.X)
Physician Decision	X (XX.X)	X (XX.X)
Withdrawal by Subject	X (XX.X)	X (XX.X)
Death	X (XX.X)	X (XX.X)
Study Terminated by Sponsor	X (XX.X)	X (XX.X)
Other	X (XX.X)	X (XX.X)

Table 14.1.2.1 Demographic Characteristics – Safety Population

Baseline Characteristic	Statistic	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
Age	N	XX	XX
	Mean (SD)	XX (XX.X)	XX (XX.X)
	Median	XX	XX
	Range	XX, XX	XX, XX
Gender	Male	X (XX.X)	X (XX.X)
	Female	X (XX.X)	X (XX.X)
Ethnicity	Hispanic or Latino	X (XX.X)	X (XX.X)
	Not Hispanic or Latino	X (XX.X)	X (XX.X)
Race [1]	American Indian/Alaska Native	X (XX.X)	X (XX.X)
	Asian	X (XX.X)	X (XX.X)
	Black/African American	X (XX.X)	X (XX.X)
	Native Hawaiian/Other Pacific Islander	X (XX.X)	X (XX.X)
	White	X (XX.X)	X (XX.X)

[1] Total may be more than 100% as this category is "check all that apply."

Table 14.1.2.2 Demographic Characteristics – PK/PD Population

Baseline Characteristic	Statistic	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
Age	N	XX	XX
	Mean (SD)	XX (XX.X)	XX (XX.X)
	Median	XX	XX
	Range	XX, XX	XX, XX
Gender	Male	X (XX.X)	X (XX.X)
	Female	X (XX.X)	X (XX.X)
Ethnicity	Hispanic or Latino	X (XX.X)	X (XX.X)
	Not Hispanic or Latino	X (XX.X)	X (XX.X)
Race [1]	American Indian/Alaska Native	X (XX.X)	X (XX.X)
	Asian	X (XX.X)	X (XX.X)
	Black/African American	X (XX.X)	X (XX.X)
	Native Hawaiian/Other Pacific Islander	X (XX.X)	X (XX.X)
	White	X (XX.X)	X (XX.X)

[1] Total may be more than 100% as this category is "check all that apply."

Table 14.1.3 Medical/Surgical History – Safety Population

System Organ Class	Condition/Surgery	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
System Organ Class #1	Condition/Surgery #1	X (XX.X)	X (XX.X)
	Condition/Surgery #2	X (XX.X)	X (XX.X)
	Etc.		
System Organ Class #2	Condition/Surgery #1	X (XX.X)	X (XX.X)
	Condition/Surgery #2	X (XX.X)	X (XX.X)
	Etc.		
Etc.	Condition/Surgery #1	X (XX.X)	X (XX.X)
	Condition/Surgery #2	X (XX.X)	X (XX.X)
	Etc.		

Table 14.2.1 Efficacy – Safety Population

Parameter	Visit	Statistic[1]	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
Hemoglobin	Screening	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to 72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
Ferritin	Screening	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to 72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX

Table 14.2.1 Efficacy – Safety Population

Parameter	Visit	Statistic[1]	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
	Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
TSAT	Screening	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to 72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX

Table 14.2.1 Efficacy – Safety Population

Parameter	Visit	Statistic[1]	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
	Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX

Table 14.2.2 Summary of Intolerance and ESA – Safety Population

	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
Drug Allergy Intolerance	X (XX.X)	X (XX.X)
IV Iron Intolerance	X (XX.X)	X (XX.X)
ESA	X (XX.X)	X (XX.X)

Table 14.3.1.1 Summary of Subjects with TEAEs – Safety Population

	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
Any Treatment-Emergent Adverse Event [1]	X (XX.X)	X (XX.X)
Serious	X (XX.X)	X (XX.X)
Severe [2]	X (XX.X)	X (XX.X)
Related to Study Drug [3]	X (XX.X)	X (XX.X)

[1] If a subject experiences the same event more than once, the first occurrence is tabulated
[2] Refers to CTCAE grade 3, 4, or 5.
[3] Related includes Possibly or Probably related to study drug.

Table 14.3.1.2 Occurrence of TEAEs – Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
SOC #1	Any	X (XX.X)	X (XX.X)
	PT #1	X (XX.X)	X (XX.X)
	PT #2	X (XX.X)	X (XX.X)
	PT #3	X (XX.X)	X (XX.X)
	Etc.		
SOC #2	Any	X (XX.X)	X (XX.X)
	PT #1	X (XX.X)	X (XX.X)
	PT #2	X (XX.X)	X (XX.X)
	PT #3	X (XX.X)	X (XX.X)
	Etc.		
Etc.			

All AEs in this table are treatment-emergent. The denominator for the calculation of the percentage is the number of subjects in the group and the numerator is the number of subjects in the group with at least one TEAE in the given system organ class or with the given preferred term. If a subject experiences the same event more than once, the first occurrence is tabulated.

Table 14.3.1.3 Occurrence of Severe TEAEs – Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
SOC #1	Any	X (XX.X)	X (XX.X)
	PT #1	X (XX.X)	X (XX.X)
	PT #2	X (XX.X)	X (XX.X)
	PT #3	X (XX.X)	X (XX.X)
	Etc.		
SOC #2	Any	X (XX.X)	X (XX.X)
	PT #1	X (XX.X)	X (XX.X)
	PT #2	X (XX.X)	X (XX.X)
	PT #3	X (XX.X)	X (XX.X)
	Etc.		
Etc.			

All AEs in this table are severe (Grade 3, 4 or 5) and treatment-emergent. The denominator for the calculation of the percentage is the number of subjects in the group and the numerator is the number of subjects in the group with at least one TEAE in the given system organ class or with the given preferred term. If a subject experiences the same event more than once, the first occurrence is tabulated.

Table 14.3.1.4 Occurrence of Related TEAEs – Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
SOC #1	Any	X (XX.X)	X (XX.X)
	PT #1	X (XX.X)	X (XX.X)
	PT #2	X (XX.X)	X (XX.X)
	PT #3	X (XX.X)	X (XX.X)
	Etc.		
SOC #2	Any	X (XX.X)	X (XX.X)
	PT #1	X (XX.X)	X (XX.X)
	PT #2	X (XX.X)	X (XX.X)
	PT #3	X (XX.X)	X (XX.X)
	Etc.		
Etc.			

All AEs in this table are related (possibly or probably) to study drug and treatment-emergent. The denominator for the calculation of the percentage is the number of subjects in the group and the numerator is the number of subjects in the group with at least one TEAE in the given system organ class or with the given preferred term. If a subject experiences the same event more than once, the first occurrence is tabulated.

Table 14.3.1.5 Occurrence of Serious TEAEs – Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
SOC #1	Any	X (XX.X)	X (XX.X)
	PT #1	X (XX.X)	X (XX.X)
	PT #2	X (XX.X)	X (XX.X)
	PT #3	X (XX.X)	X (XX.X)
	Etc.		
SOC #2	Any	X (XX.X)	X (XX.X)
	PT #1	X (XX.X)	X (XX.X)
	PT #2	X (XX.X)	X (XX.X)
	PT #3	X (XX.X)	X (XX.X)
	Etc.		
Etc.			

All AEs in this table are serious and treatment-emergent. The denominator for the calculation of the percentage is the number of subjects in the group and the numerator is the number of subjects in the group with at least one TEAE in the given system organ class or with the given preferred term. If a subject experiences the same event more than once, the first occurrence is tabulated.

Table 14.3.2.1 Laboratory Values – Safety Population

Parameter	Visit	Statistic[1]	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
Lab #1	Screening	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to 72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
Lab #2	Screening	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to 72 hours post-dose	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX

Table 14.3.2.1 Laboratory Values – Safety Population

Parameter	Visit	Statistic[1]	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
	Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 14	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 28	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
	Change from Screening to Day 35	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX
Etc.	Etc.	N	XX	XX
		Mean (SD)	XX (XX.X)	XX (XX.X)
		Median	XX	XX
		Range	XX, XX	XX, XX

Table 14.3.2.2 Incidence of Potentially Clinically Significant (PCS) Laboratory Values

Lab Test/Category	PCS	Cohort 1 (N=XXX)	Cohort 2 (N=XXX)
Lab #1	No	X (XX.X)	X (XX.X)
	Yes	X (XX.X)	X (XX.X)
Lab #2	No	X (XX.X)	X (XX.X)
	Yes	X (XX.X)	X (XX.X)
Etc.			

Table 14.3.3.1 Vital Signs – Day 0 – Safety Population

Age Group	Vital Sign	Time Point	Statistic/ Category	Cohort 1 (n=XXX)	Cohort 2 (n=XXX)
All Subjects	Sitting Diastolic BP (mmHg)	Day 0 Pre-Treatment	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Day 0 Immediately Post-Treatment	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Change from Pre-Treatment to Immediately Post-Treatment	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Day 0 30 Minutes Post-Treatment	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Change from Pre-Treatment to 30 Minutes Post-Treatment	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX

Note to programmer, repeat above for all Systolic BP and Heart Rate and for two age stratum: 1 - < 6 years, and 6 – 17 years

Table 14.3.3.2 Vital Signs – All Visits – Safety Population

Age Group	Vital Sign	Time Point	Statistic/ Category	Cohort 1 (n=XXX)	Cohort 2 (n=XXX)
All Subjects	Sitting Diastolic BP (mmHg)	Screening	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Day 0 Initial (Baseline)	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		72hr / Day 3	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Change from Baseline at 72hr / Day 3	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Day 14	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Change from Baseline at Day 14	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Day 28	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Change from Baseline at Day 28	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Day 35 (End of Study)	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX
		Change from Baseline at Day 35 (End of Study)	N	XX	XX
			Mean (SD)	XX (XX.X)	XX (XX.X)
			Median	XX	XX
			Range	XX, XX	XX, XX

Age Group	Vital Sign	Time Point	Statistic/ Category	Cohort 1 (n=XXX)	Cohort 2 (n=XXX)
Note to programmer, repeat above for Systolic BP, Heart Rate, and for two age stratum: 1 - < 6 years, and 6 – 17 years. Note also that height and weight are only measured at Day 0.					

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Listing 16.2.1.1 Completion/Discontinuation

ite/ bject	Safety	PK	Group	Date of First Dose	Date of Completion or Discontin-uation (RxDay)	Subject Status	Physician Decision, Specify	If Other, Specify	Date of Death (RxDay)	Autopsy	Primary Cause of Death	Pregnant During Study	Lactation Exposure	Inter-vention	Date	Increase in Dose of Erythrop-oletin for any Reason

Listing 16.2.1.2 Identification of Subjects with Clinically Important Protocol Violations

Site/ Subject	Safety	PK	Group	Clinically Important Protocol Violation

Listing 16.2.1.3 Inclusion/Exclusion Criteria

Site/ Subject	Safety	PK	Group	Did subject meet all inclusion and exclusion criteria?	Inclusion/Exclusion Category Not Met	Inclusion/Exclusion Number Not Met	Waiver Granted? Y/N	Waiver Date	Waiver Granted by:

Listing 16.2.1.4 Patient Populations

Site/ Subject	Group	Safety Population	PK/PD Population

Listing 16.2.1.5 Demographics

Site/ Subject	Safety	PK	Group	Birth Date	Age (yrs) at Date of Screening	Sex	Ethnicity (Hispanic or Latino)	American Indian/Alaska Native	Asian	Black/African American	Native Hawaiian/Other Pacific Islander	White

Listing 16.2.1.6 Medical/Surgical History

Site/ Subject	Safety	PK	Group	Body System	Medical Condition/Past Surgery	Start Date	End Date	Ongoing?

Listing 16.2.1.7 Drug Allergy/Intolerance at Screening

Site/ Subject	Safety	PK	Group	Does the subject have any drug allergies/intolerance	Drug/Drug Class	Reaction Symptom

Listing 16.2.1.8 IV Iron Intolerance

Site/ Subject	Safety	PK	Group	Does the subject have any known IV iron intolerance?	If yes, Name	Itching	Rash	Bronchospasm	Hypotension	Other	Sodium Ferric Gluconate Other Symptom, Specify

Listing 16.2.1.9 Physical Examination

Site/ Subject	Group	Visit	Exam Performed?	Body System	Not Done	Result	Specify Abnormalities

Listing 16.2.1.10 Iron Deficiency

Site/ Subject	Safety	PK	Group	Heavy Uterine Bleeding Type	Polyps	Endo-crine Dys-function	Heavy Uterine Bleeding Other	Heavy Uterine Bleeding Specify	Gastro-intestinal Related Symptom	Mal-absorp-tion	Celiac Disease	GI Bleed-ing	Gastro-intestinal Other	Gastro-intestinal Specify	Cancer Specify	Trauma Specify	Surgery Specify	Other Specify

Listing 16.2.2.1 Erythropoiesis Stimulating Agent

Site/ Subject	Safety	PK	Group	Is subject using Erythropoiesis Stimulating Agent (ESA)?	Has the dose been stable per inclusion criteria?

Listing 16.2.2.2 Ferric Carboxymaltose Administration

Site/ Subject	Safety	PK	Group	Date	Total Dose Required for Injection	Start Time	Stop Time	Total Dose of Elemental Iron Administered	IV Administration	Reason Not Administered	Other Specify

Listing 16.2.2.3 Pharmacokinetic Samples

Site/ Subject	Safety	PK	Group	Timepoint Not Done	Date (RxDay)	Time

Listing 16.2.3.1 Concomitant Medications

Site/ Subject	Safety	PK	Group	Were any medications taken from 30 days prior to consent through end of study or Day 35?	Drug Name	Dose	Unit	Route	Other Route	Indication	Start Date (RxDay)	Stop Date (RxDay)	Ongoing

Listing 16.2.3.2.1 Central Laboratory Values - CFR

Site/ Subject	Safety	PK	Group	Visit	Were labs performed?	Date (RxDay)	Collection Time	Accession #

Listing 16.2.3.2.2 Central Laboratory Values – Lab Transfer

Site/ Subject	Safety	PK	Group	Visit	Date (RxDay)	Lab	Result	Normal Range	H/L Flag

Listing 16.2.3.2.3 Potentially Clinically Significant Central Laboratory Values – Lab Transfer

Site/ Subject	Safety	PK	Group	Visit	Date (RxDay)	Lab	Result	Normal Range	H/L Flag

Listing 16.2.3.3.1 Vital Signs

Site/ Subject	Safety	PK	Group	Visit	Vital Signs Collected?	Date (RxDay)/Time	Test	Not Done	Result	Units

Listing 16.2.3.4 Adverse Event Details

Site/ Subject	Safety	PK	Group	Any AE?	Verbatim Term	Serious	Onset Date (RxDay) / Time	Resolution Date (RxDay) / Time	Continuing	CTC Toxicity Criteria Grade	Action Taken With Study Drug	Treatment	Other Treatment, Specify	Final Outcome	Causality	Did the AE result in the subject being discontinued form the study?