FRESENIUS KABI USA, LLC

STATISTICAL ANALYSIS PLAN

Device:	AMICUS Separator
Clinical Study Protocol:	AMIC-003-CMD
Study Title:	Evaluation of the AMICUS Red Blood Cell Exchange (RBCx) System in Sickle Cell Patients
Version Date:	21 Feb 2018

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Clinical Study Protocol AMIC-003-CMD

Evaluation of the AMICUS Red Blood Cell Exchange (RBCx) System in Sickle Cell Patients

Signature Page

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1 STUDY DESIGN

The AMICUS Red Blood Cell Exchange (RBCx) procedure will be evaluated using a multi-center, single-arm, open label study design. Up to a total of 100 subjects meeting all eligibility criteria will be enrolled to complete a minimum of 62 evaluable RBCx procedures.

The RBCx is a type of therapeutic procedure used to remove red blood cells (RBCs) from sickle cell disease (SCD) subjects, exchanging them for healthy donor RBCs and/or crystalloid or colloid solutions to maintain fluid balance. Depending upon the replacement fluid(s) (RF) used, the procedure can be considered an RBC Exchange or an RBC Depletion/Exchange procedure. The RBC Depletion/Exchange procedure is a modification of the RBC Exchange procedure. Removal of RBCs may be performed manually or using an apheresis device. The removal of RBCs and replacement with healthy donor RBCs is most frequently used in the treatment of patients with complications of sickle cell disease. The type of procedure performed (RBC Exchange or RBC Depletion/Exchange) will be prescribed by the physician.

The study will have a lead-in phase for training purposes and the lead-in subjects will not be included in the evaluable population. Evaluable subjects will be obtained in two stages. In the first stage up to 40 subjects 18 years old or older will be enrolled to complete 31 evaluable procedures. An interim report including summary statistics and safety-related data will be reviewed by a Data Safety Monitoring Board (DSMB). The DSMB primary responsibilities are to monitor the safety of the trial participants, to review safety-related data, to evaluate the frequency and severity of adverse events, and to judge the quality and integrity of study data. A separate analysis plan is written for the interim report.

Following the DSMB review the report will be submitted to the FDA for review as an IDE supplement. This supplement must be approved before the start of the second stage of the study. This stage will enroll pediatric subjects 6 to 17 years old.

1.1 Study Objectives

The primary objective of the study is to evaluate the accuracy of the subject's original RBCs remaining (Actual FCR) as measured by subject's post-procedure Hb S at the end of the procedure to the Target FCR.

The secondary objectives are:

- To evaluate the accuracy of subject hematocrit (Hct) post-procedure (End Hct)
- To evaluate subject cellular loss (white blood cells, platelets) post-procedure
- To evaluate the cellular content of the waste material

- To evaluate device related serious adverse events during the procedure and approximately 18 to 24 hours post-procedure

1.2 Statistical Hypothesis

Hypothesis testing will be performed to evaluate the primary objective of the 95% confidence interval around the mean ratio of actual to target FCR as measured by Hb S in the subjects pre- and post-procedure to a pre-defined FCR range of 0.75 to 1.25.

The primary hypothesis set for the 2-sided test is given as:

H_0: P_T LL<0.75 and/or P_T UL>1.25

Versus

H_1: 0.75 ≤ LL P_T UL ≤ 1.25

Where P_T = the 95% CI for AMICUS mean ratio; LL = Lower limit; and UL = Upper limit.

We will reject H_o at the alpha level of significance if the entire 95% confidence interval around the mean ratio is within the predefined range. Stated explicitly, if the lower limit of the 95% confidence interval around the mean ratio is greater than or equal to the lower predefined range boundary (0.75) and simultaneously the upper limit of the 95% confidence interval around the mean ratio is less than or equal to the upper predefined range boundary (1.25).

Hypothesis testing is not planned for secondary objectives. Summary statistics (mean, standard deviation, minimum, median, maximum, and count) of the RBC Exchange and RBC Depletion/Exchange procedure data will be used to evaluate the secondary objectives: evaluation of the accuracy of subject End Hct, accuracy of Fluid Balance, subject cellular loss post-procedure, and serious device related adverse events.

Hypothesis testing is not planned for the interim report. Summary statistics (mean, standard deviation, minimum, median, maximum, and count) of the RBC Exchange and RBC Depletion/Exchange procedure data will be used to evaluate the primary and secondary objectives.

2 STATISTICAL METHODOLOGY

2.1 Sample Size Calculation

The sample size needed for the study design is given as:

$N= 2(Z_1-\alpha + Z_1-\beta)^2 \sigma^2 \div \delta^2$

Where Z_1-α and Z_1-β are the standard normal deviates corresponding to 1 minus significance level (α) and 1 minus the type II error (β) respectively, σ^2 is the variance or squared standard deviation of the outcome and δ is the margin.

Since we planned to have a 90% power at the 0.025 significance level to detect equivalence to a ratio of 1, then the sample size with the margin of 0.25 and observed standard deviation of the difference of 0.43 with β =0.10 will yield:

$N= 2(1.96 +1.28)^2\ 0.43^2 \div .25^2 = 2(10.4976)\ 0.185 \div 0.0625 = 62.$

Therefore, a sample size of 62 evaluable procedures will be used to demonstrate that AMICUS is within a margin of 25% with at least 95% (2-sided) confidence and at least 90% power.

2.2 Analysis Population

2.2.1 All Subjects Enrolled Population

The All Subjects Enrolled population will consist of those subjects who signed an informed consent. The safety population will consist of all enrolled subjects.

2.2.2 Intent-to-Treat Subjects Population

The Intent-to-Treat population will consist of those enrolled subjects who successfully complete the AMICUS Separator procedures, and exclude subjects who participated in a Lead-in procedure.

2.2.3 Evaluable Population

The Evaluable population will consist of those enrolled subjects who successfully complete the AMICUS Separator procedures, have values reported for parameters required to calculate the primary endpoint (e.g., day of procedure pre- and post-procedure Hb S results are obtained) and the evaluability criteria are met. These are circumstances during or associated with a RBCx procedure that may cause the primary or secondary endpoint to be non-evaluable. These are stated in Section 13.6 of the protocol. Primary and secondary objectives will be evaluated using the Evaluable population.

If the data required for determining the evaluability of this population is missing, the subject will be non-evaluable. Reasons for non-evaluability of this population will be revisited by the Sponsor prior to database lock. If additional reasons for non-evaluability are identified at this time, all affected statistical documents and SAS programs will be updated accordingly.

Evaluability Criterion 1: Procedure Completion

This Criterion indicates whether or not subjects have a completed collection procedure.

Evaluability Criterion 2: If reinfusion was performed, post-procedure blood sample must be taken prior to reinfusion.

Evaluability Criterion 3: Did operator change subject HCT, Avg RF Hct or Total Blood Volume after procedure start

Evaluability Criterion 4: Average RF Hct Accuracy

This Criterion indicates If the absolute difference of the Average Replacement Fluid Hematocrit (%) and Calculated Average Replacement Fluid Hematocrit (%) values is less than or equal to 5 Hematocrit points the calculated A:T FCR Ratio and Calculated End Hct Accuracy are evaluable. If the absolute difference of the Average Replacement Fluid Hematocrit (%) and Calculated Average Replacement Fluid Hematocrit (%) values is less than or equal to 5 Hematocrit points the Calculated A: T FCR Ratio, Calculated Depletion Hct Accuracy and Calculated End Hct Accuracy are evaluable, where Calculated Average Replacement Fluid Hematocrit (%) is equal to the sum of the red cell volume in the RBC units divided by the sum of the total volume in the RBC units. The red cell volume of each unit is defined as the product of the hematocrit and the volume of each individual unit. N is equal to the number RBC units transfused. If the absolute difference of the Average Replacement Fluid Hematocrit (%) and Calculated Average Replacement Fluid Hematocrit (%) values is greater than 5 Hematocrit points then calculated A:T FCR Ratio and Calculated End Hct Accuracy are non-evaluable.

Evaluability Criterion 5: Input Hematocrit Difference

If absolute difference of Subject Hematocrit (%) and Pre-procedure Hematocrit (%) value is less than or equal to 5 Hematocrit points then Calculated A:T FCR Ratio, Calculated Depletion Hct Accuracy and Calculated End Hct Accuracy are evaluable. If absolute difference of Subject Hematocrit (%) and Pre-procedure Hematocrit (%) value is greater than 5 Hematocrit points then Calculated A:T FCR Ratio, Calculated Depletion Hct Accuracy and Calculated End Hct Accuracy are non-evaluable.

Evaluability Criterion 6: Input FCR Difference

For procedure in which the Fraction of Cells Remaining (%) instead of Replacement Volume (mL) is used to program the inputs, apply the following Evaluability criteria. If the absolute difference of the Fraction of Cells Remaining (%) and Calculated Fraction of Cells Remaining (%) value is less than or equal to 6 percent points then the Calculated A:T FCR Ratio, Calculated Depletion Hct Accuracy and Calculated End Hct are evaluable. . If the absolute difference of the Fraction of Cells Remaining (%) and Calculated Fraction of Cells Remaining (%) value is greater than 6 percent points then the Calculated A:T FCR Ratio is not evaluable.

Check if Fraction of Cells Remaining was used as an input. If the following is true then continue on to the evaluability criteria. If the following is not true Fraction of Cells Remaining was not used as an input and the evaluability criterion is not applicable. Note that the evaluability criterion also does not apply if NA is entered for Target Hemoglobin S (%) and/or Actual Hemoglobin S (%).

2.3 Methods of Statistical Analysis

Summary statistics (N, mean, standard deviation, median, minimum, and maximum) will be reported on all continuous (numeric) parameters. Descriptive statistics (e.g., counts and percentages) will be reported on categorical (non-numeric) parameters. All summary statistics will be presented at rounded precision. No estimates will be truncated.

Hypothesis testing will be performed at the conclusion of the study to evaluate the primary objective of 95% confidence interval around the mean ratio of actual to target FCR as measured by Hb S in the subjects' pre- and post-procedure to a pre-defined FCR range of 0.75 to 1.25.

Hypothesis testing will not be performed for the interim analyses and summary statistics will be performed for the Interim report.

All calculations will be performed using SAS 9.4 (Windows platform).

3 ANALYSIS PARAMETERS

All parameters are reported as "[measured]" or "[calculated]". The former indicates that the parameter was collected on a CRF. The latter indicates that the parameter was calculated based on CRF data. The details of all parameter calculations will be provided in the study Algorithms Document.

As a general rule, any parameter values that are censored (left or right) will be analyzed as the numeric version of the observed detection limit (e g, <1.0 will be analyzed as 1.0). The parameters associated with the depletion phase data are only applicable for RBC Depletion/Exchange procedures.

All parameters will be listed for all enrolled subjects. All procedures results summarized will be presented for the evaluable subjects. Summary statistics (mean, standard deviation, minimum, median, maximum, and count) will be presented.

All parameters documented will be available in SAS analysis datasets.

3.1 Primary Efficacy Parameters

The primary efficacy parameter is the subject's original RBCs remaining (Actual FCR) as measured by subject's post-procedure Hb S at the end of the procedure to the target FCR. Hypothesis testing will be performed to evaluate the primary objective of 95% confidence interval around the mean ratio of actual to target FCR as measured by Hb S in the subjects' pre- and post-procedure to a pre-defined FCR 0.75 to 1.25.This parameter will be provided in a listing for the All Enrolled Subjects population.

3.2 Secondary Outcome Parameters

The following secondary objectives will be assessed using the appropriate Evaluable Subject population. The overall procedure subject cellular percent losses, plasma hemoglobin delta, and calculated target End Hct will be calculated. The Exchange procedures and Depletion/Exchange procedures total cell losses, plasma hemoglobin delta, and calculated target End Hct accuracy will be presented.

The waste material for the exchange procedures and Depletion/Exchange procedures will be evaluated for volume, total WBC and platelet counts. For the Depletion/Exchange procedures the depletion phase and exchange phase will be evaluated separately.

A. Overall Procedures:

- Subject WBC Percent Loss (%)
- Subject RBC Percent Loss (%)
- Subject Platelet Percent Loss (%)
- Subject Plasma Hemoglobin Delta (mg/dL)
- Calculated Target End Hct Accuracy.

B. Exchange Procedures:

- Exchange Procedure Waste Material Volume (mL)
- Exchange Procedure Waste WBC Count ($x10^{10}$)
- Exchange Procedure Waste RBC Count ($x10^{10}$)
- Exchange Procedure Waste Platelet Count ($x10^{11}$)

- Calculated Target End Hct Accuracy

Primary and secondary parameters calculations are in the Algorithm Document.

C. Depletion/Exchange Procedures:

Depletion Phase

- Depletion Phase Waste Material Volume (mL)
- Depletion Phase Waste WBC Count ($x10^{10}$)
- Depletion Phase Waste Platelet Count ($x10^{11}$)
- Calculated Depletion Hct Accuracy
- Subject Depletion Phase Plasma Hemoglobin Delta (mg/dL)

Exchange Phase

- Exchange Phase Waste WBC Count ($x10^{10}$)
- Exchange Phase Waste Platelet Count ($x10^{11}$)
- Calculated Target End Hct Accuracy

3.3 Subject and Procedure Parameters

3.3.1 Procedure Selection (CRF 1)

The procedure selection parameters to be presented are:

Is this a lead-in procedure? (Yes / No)
- If Yes,

- Lead-in RBC Exchange
- Lead-in RBC Depletion Exchange

- If No,

- RBC Exchange
- RBC Depletion/Exchange

Listing and summary statistics for all parameters will be reported.

3.3.2 Inclusion/Exclusion Criteria and Eligibility (CRF 2, 3)

Listing of all inclusion/exclusion and subject eligibility will be reported.

3.3.3 Demographics (CRF 4)

The demographics parameters to be presented are:

1. Date of birth [measured]
2. Sex
3. Ethnicity
4. Race
5. Subject age (years) at the time informed consent is obtained.
6. Subject age (years) at the time of procedure

Listing and summary statistics for all parameters will be reported.

3.3.4 Routine Pre-procedure Testing Data (CRF 5)

The routine pre-procedure testing data to be presented are:

1. Sample date (Mmm-dd-yyyy)
2. Sample time (hh:mm)
3. Actual Hb S (%)
4. Target Hb S (%)
5. Hct (%)

Listing and summary statistics for all parameters will be reported.

3.3.5 Subject Evaluations Parameters (CRF 5)

The subject evaluations parameters to be presented for all procedures are:

1. Primary Diagnosis (1=SS, 2=SB-0 thal, 3=SCD, 4=Other (specify))
2. Weight (lbs) [measured] [Pre-Procedure]
3. Height (in) [measured] [Pre-Procedure]
4. Systolic Blood Pressure (mmHg) [measured] [Pre, End of Depletion Phase, and Post-procedure]
5. Diastolic Blood Pressure (mmHg) [measured] [Pre, End of Depletion Phase, and Post-procedure]
6. Temperature (°F) [measured] [Pre, End of Depletion Phase, and Post-procedure]
7. Pulse (bpm) [measured] [Pre, End of Depletion Phase, and Post-procedure]
8. Respiration Rate (breaths/min) [measured] [Pre, End of Depletion Phase, and Post-procedure]

Listing and summary statistics for all parameters will be reported.

3.3.6 Subject Laboratory Analysis Parameters (CRF 6)

The subject laboratory parameters to be presented are:

1. White Blood Cell Count (WBC) ($x10^3/\mu L$) [measured] [Pre-procedure, End of Depletion, and Post-procedure]
2. Red Blood Cell Count (RBC) ($x10^6/\mu L$) [measured]][Pre- procedure, End of Depletion, and Post-procedure]
3. Platelet Count ($x10^3/\mu L$) [measured] [Pre- procedure, End of Depletion, and Post-procedure]
4. Hct (%) [measured]][Pre- procedure, End of Depletion, and Post-procedure]
5. Plasma Hb (mg/dL) [measured] [Pre- procedure, End of Depletion, and Post-procedure
6. Hb A (%) [measured] [Pre- and Post-procedure]
7. Hb S (%) [measured] [Pre- and Post-procedure]
8. Hb C (%) [measured] [Pre- and Post-procedure]
9. Hb F (%) [measured] [Pre- and Post-procedure]
10. Hb A2 (%) [measured] [Pre- and Post-procedure]
11. Pregnancy test [measured] [Pre-procedure]

Listing and summary statistics for all parameters will be reported.

3.4 Concomitant Medications (CRF 7)

Concomitant medications used by the subjects for seven days prior to and during the study procedures will be listed in data listings only using the Medical Dictionary for Regulatory Activities (MedDRA) version 18.0 and World Health Organization Drug Dictionary (WHO Drug) version March 2015 dictionaries. No formal summary table will be generated.

3.5 Procedure Parameters

3.5.1 Procedure Evaluations (CRF 8 & 9)

The measured procedure evaluation parameters are:

1. Procedure Date (Mmm-dd-yyyy)
2. End Time (hh:mm)
3. Venous Access Used (Peripheral IV, Temporary Catheter, Long Term/Permanent Catheter(Two single lumen ports/One double lumen port)
4. Replacement Fluid Used (Saline/Albumin/Custom (specify))
5. Anticoagulant Type: (ACD-A/Custom (specify))
6. Was reinfusion selected prior to the start of the procedure? (Yes/No)

7. Subject Total Sample Volume Removed (mL)
8. Custom Prime (Full/Partial/None)
9. Was Prime diverted? (Yes/No)
10. Was a blood warmer used during the procedure? (Yes/No). If Yes, provide the prime volume (mL)
11. Was Saline bolus performed? (Yes/No)
12. Was the procedure ended prior to or extended beyond (± 50 mls) of the Target RF Volume? (Yes/No)
13. At the end of the procedure, was reinfusion performed? (Yes/No). If Yes, was a sample taken prior to reinfusion? (Yes/No)

Listing and summary statistics for all parameters will be reported.

3.5.2 Adverse Events (CRF 10 and 21)

Adverse events (AE) will be recorded through the completion of each Procedure type (during and approximately 18 to 24 hours post procedure). AEs will be presented using MedDRA coding for AEs which requires the site to record the descriptors. Events classified as "Other" will be presented as verbatim terms. An AE type occurring multiple times per subject will be counted once for subject-reported frequencies.

The frequency of subjects who reported AEs and the frequency of AEs reported by and across severity, seriousness, relationship to procedure, and relationship to device will be presented overall, and by site for all subjects enrolled in the study.

Listings and summary tables of AEs/SAEs, and incidence of AEs/SAEs will be reported during the procedure and at post-procedure follow-up of the study.

3.5.3 Adverse Events Post-procedure Assessment (CRF 20)

The sites have up to 2 attempts to contact each subject and record the following:

1. Was subject contacted on the first attempt? (Yes/No/Not Done).
2. Date of first attempt (Mmm-dd-yyyy) / Time of first attempt (hh:mm).
    a. Was subject contacted on the second attempt? (Yes/No/Not Done).
    b. Date of second attempt (Mmm-dd-yyyy) / Time of second attempt (hh:mm).
    c. If No contact by telephone, was a certified letter sent? (Yes/No)
3. Was there an AE that occurred during procedure with an outcome of continuing? (Yes/No). If Yes, record all the AE numbers as referenced on the AE page.
4. Current outcome of continuing adverse event are:

a. Recovered (End Date) (Mmm-dd-yyyy)
b. Recovered with Sequela(e) (End Date) (Mmm-dd-yyyy)
c. Continuing
d. Death (Date of Death) (Mmm-dd-yyyy)

5. Did the subject experience any AE post-procedure? (Yes/No/Unknown). If Yes, record AE on the AE-post procedure form

Listing of adverse event post-procedure assessment will be reported

3.5.4 Procedure Parameters –Pre-procedure (CRF 11)

The procedure parameter results are:

Input Parameter

1. Fraction Cells Remaining (%)
2. End Hct (%)
3. Depletion Hct (%)*
4. Replacement Volume (mL)
5. Fluid Balance (mL)
6. AC Ratio
7. Start Prime Hct (%)
8. End Prime Hct (%)

Estimator Parameter

1. Whole Blood Flow Rate (mL/min)
2. Procedure Time (min)
3. Anticoagulant to Subject (mL)
4. Anticoagulant Used (mL)
5. Other Replacement Fluid (mL)
6. Depletion Red Cell Volume (mL)

Input Parameter

1. Subject Hct (%)
   Was value changed during Procedure? (Yes/No) If Yes Final value---------
2. Average Replacement Fluid Hct (%)
   Was value changed during Procedure? (Yes/No) If Yes Final value---------
3. Total Blood Volume (mL)
   Was value changed during Procedure? (Yes/No) If Yes Final value---------

4. Maximum Whole Blood Flow Rate (mL/min)
   Was value changed during Procedure? (Yes/No) If Yes Final value---------
5. Citrate Infusion Rate (CIR) (mg/kg/min)
   Was value changed during Procedure? (Yes/No) If Yes Final value---------

Listing and summary statistics of all parameters will be reported.

3.5.5 Procedure Parameters –End of Depletion Phase (CRF 12)

The end of depletion phase parameter results are:

1. Fluid Balance (mL)
2. Depletion Hct (%)
3. Whole Blood Processed (mL)
4. Replacement Fluid Albumin Returned (mL)
5. Replacement Fluid Saline Returned (mL)
6. Custom Replacement Fluid Returned (mL)
7. Plasma Returned (mL)
8. Procedure Time (min)
9. Anticoagulant Used (mL)
10. Anticoagulant to Subject (mL)
11. Saline to Subject (mL)

Listing and summary statistics of all parameters will be reported.

3.5.6 Procedure Results (CRF 13)

The procedure parameter results are:

1. Procedure Time (min)
2. Fraction Cells Remaining (%)
3. End Hct (%)
4. Fluid Balance (mL)
5. Red Blood Cell Mass Balance
6. Whole Blood Processed (mL)
7. Replacement Fluid to Subject (mL)
8. Anticoagulant to Subject (mL)
9. Anticoagulant Used (mL)
10. Saline to Subject (mL)
11. Replacement Fluid Albumin Returned (mL)
12. Replacement Fluid RBC Returned (mL)

13. Replacement Fluid Saline Returned (mL)
14. Custom Replacement Fluid Returned (mL)

Listing and summary statistics of all parameters will be reported.

3.5.7 Replacement RBC Unit Parameters (CRF 14)

Replacement RBC unit parameters to be presented are:

1. Type of RBC Unit
2. Unit Identification Number
3. Sample Date (Mmm-dd-yyyy)
4. Sample Time (hh:mm)
5. Hct (%)
6. Volume (mL)
7. ABO Type/Rh Factor
8. Expiration Date
9. Plasma Hb (mg/dL)
10. Confirmation of Sickle Trait Negative
11. Confirmation of Leukoreduction
12. Confirmation of Rh(D) compatibility

Listing and summary statistics of all parameters will be reported.

3.5.8 Device Alarms (CRF 15)

Device alarms as it occurs during the procedure will be reported with its frequency.

Did alarm(s) occur during the procedure? (Yes/No)
- If yes, record all alarms that occurred and their frequency.

Listings and summary table of all device alarm will be reported by the alarm code, description and frequency.

3.5.9 Waste Material – RBC Depletion/Exchange (CRF 16)

The RBC waste material parameters to be presented are:

1. Gross Weight (g)
2. Tare Weight (g)
3. Volume (mL)
4. White Blood Cell Count (WBC) ($x10^3/\mu L$)
5. Total WBC Count ($x10^9$)

6. Platelet Count ($x10^3/\mu L$)
7. Total Platelet Count ($x10^{11}$)
8. Hct (%)

Listing and summary statistics of all parameters will be reported.

3.5.10 Waste Material – RBC Exchange (CRF 16)

The RBC waste material parameters to be presented are:

1. Gross Weight (g)
2. Tare Weight (g)
3. Volume (mL)
4. White Blood Cell Count (WBC) ($x10^3/\mu L$)
5. Total WBC Count ($x10^9$)
6. Platelet Count ($x10^3/\mu L$)
7. Total Platelet Count ($x10^{11}$)
8. Hct (%)

Listing and summary statistics of all parameters will be reported.

3.6 Procedure Evaluation and End of Study Parameters (CRF 8, 9 and 17)

The evaluability criteria in section 13.6 of the protocol to be presented are:

- If procedure is terminated prior to completion, the procedure is non-evaluable.
- If reinfusion is performed, the post-procedure blood sample must be drawn prior to reinfusion or it is not evaluable.
- Operator should not change subject Hct, Avg RF Hct, or Total Blood Volume after procedure start or it is not evaluable.
- If a saline bolus is performed, End Hct is not evaluable.

The End of Study parameters to be presented are:

Was the procedure completed? (Yes / No)
- If No, the primary reason will be presented:

  - Adverse Events
  - Venous Access Issue (Non-Adverse Event)
  - Instrument Alarm (specify)
  - Disposable Issue:

  - Leak
  - Kink
  - Misassembly
  - Other

- Hardware Issue
- Investigator Decision
- Subject Decision
- Protocol Deviation/Violation
- Other (please describe)

Listing of all subjects that completed the procedure will be presented and subjects that did not complete the procedure will be reported as per a reason above.

3.7 Protocol Deviation (CRF 18)

Protocol deviations will be presented in data listings only. No formal summary table will be generated.

Listing of protocol deviation will include:

1. Was a protocol deviation recorded? (Yes/No)
2. Date of the deviation
3. Protocol deviation

    a. Inclusion criteria
    b. Exclusion criteria
    c. Sampling /testing issues
    d. Procedure related issues
    e. Subject receives wrong treatment or incorrect dose
    f. Informed consent issues
    g. Follow-up not performed
    h. Follow-up outside of window
    i. Other

4 DATA CONVENTIONS

4.1 Data Collection, Verification, and Monitoring

Refer to protocol Section 12, Data Quality Assurance.

4.2 Data Handling

4.2.1 Handling of Missing Values

No missing or incomplete dates will be imputed for this study. No missing or incomplete parameter results will be imputed for this study.

4.2.2 Relative Day Ranges

Not applicable to this study.

4.3 Time and Events Schedule for Study Evaluation Testing Parameters

Refer to protocol Section 8.2, Study Procedures/Methodology, Tables 2 to 6.

5 TRIAL TERMINATION PROCEDURES

There are no plans for prematurely terminating this study. However, site closure or study termination may be decided at any time by the sponsor or site investigator due to safety concerns, inadequate study subject enrollment, and failure to comply with the study protocol, regulatory requirements, and Good Clinical Practices.

6 RANDOMIZATION SCHEDULE

Not applicable for this study

7 STATISTICAL REFERENCES

Base SAS 9.4 Procedures Guide, Second Edition, Volumes 1-4 (March 2013). SAS Publishing: Cary, NC.

8 STATISTICAL CODE FOR HYPOTHESIS TESTING

A SAS macro will be written for generating the applicable output. The macro will be located in the I drive.

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Table 14.15	Device Alarms Section 3.5.8	Summary of Device Alarms (All Subjects Enrolled)
Table 14.16.1	Waste Material-RBC Depletion/Exchange Section 3.5.9	Summary of Waste Material-RBC Depletion/Exchange Procedure (All Evaluable Subjects)
Table 14.16.2	Waste Material-RBC Exchange Section 3.5.10	Summary of Waste Material-RBC Exchange Procedure (All Evaluable Subjects)
Table 14.17	End Hematocrit Section 3.5.4	Summary of End Hematocrit (All Evaluable Subjects)

[1]Titles for pediatric and adult subjects should be used for populating their respective output.
[2]Summary of Empirical RBC Mass Balance Excluding Outlier(s) Table is provided for overall population only.

9.2 Planned Listings

Listing Number	Section	Description of Output
Listing 16.1	Patients Disposition	Listing of Subjects Disposition (All Subjects Enrolled)
Listing 16.2	Procedure Evaluability/End of Study	Listing of Procedure Evaluability/End of Study (All Subjects Enrolled)
Li sting 16.3.1	Inclusion/Exclusion and Eligibility	Listing of Inclusion Criteria (All Subjects Enrolled)
Listing 16.3.2	Inclusion/Exclusion and Eligibility	Listing of Exclusion Criteria (All Subjects Enrolled)
Listing 16.3.3	Inclusion/Exclusion and Eligibility	Listing of Subject Eligibility All Subjects Enrolled)
Listing 16.4	Demographic Parameters	Listing of Demographic Parameters (All Subjects Enrolled)
Listing 16.5	Routine Pre-procedure Testing Data	Listing of Routine Pre-procedure Testing Data (All Subjects Enrolled)
Listing 16.6	Subject Evaluation Parameters	Listing of Subject Evaluation Parameters (All Subjects Enrolled)
Listing 16.7	Subject Laboratory Parameters	Listing of Subject Laboratory Analysis Parameters (All Subjects Enrolled)
Listing 16.8	Concomitant Medications	Listing of Concomitant Medications (All Subjects Enrolled)
Listing 16.9	Procedure Evaluation	Listing of Procedure Evaluation Parameters (All Subjects Enrolled)
Listing 16.10.1	Adverse Events During the Procedure	Listing of Adverse Events during Procedure (All Subjects Enrolled)
Listing 16.10.2	MedDRA coding During the Procedure	Listing of MedDRA coding AE during Procedure (All Subjects Enrolled)
Listing 16.11	Adverse Events Post-procedure Assessment	Listing of Adverse Events Post-procedure Assessment (All Subjects Enrolled)
Listing 16.12.1	Adverse Events Post-procedure	Listing of Adverse Events Post-procedure (All Subjects Enrolled)
Listing 16.12.2	MedDRA coding Post Procedure	Listing of MedDRA coded Adverse Events Post-Procedure (All Subjects Enrolled)
Listing 16.13.1	Procedure Parameters-Pre-procedure	Listing of Input Parameters Pre-procedure (All Subjects Enrolled)
Listing 16.13.2	Procedure Parameters-Pre-procedure	Listing of Estimator Parameters Pre-procedure (All Subjects Enrolled)
Listing 16.13.3	Input Parameter	Listing of Input Procedure Parameters (All Subjects Enrolled)
Listing 16.14	Procedure Parameters-End of Depletion Phase	Listing of End of Depletion Phase Parameters (All Subjects Enrolled)
Listing 16.15.1	Procedure Results	Listing of Procedure Results (All Subjects Enrolled)
Listing 16.15.2	Procedure Results	Listing of Procedure Results (All Subjects Enrolled)
Listing 16.16	Primary Endpoint	Listing of Primary Endpoint (All Subjects Enrolled)
Listing 16.17.1	Secondary Endpoint	Listing of Secondary Endpoints (All Subjects Enrolled)
Listing 16.17.2	Secondary Endpoint	Listing of Waste Material for Secondary Endpoints (All Subjects Enrolled)
Listing 16.17.3	End Hematocrit	Listing of End Hematocrit (All Subject Enrolled)
Listing 16.18	Replacement RBC Unit Parameters	Listing of Replacement RBC Unit Parameters (All Subject Enrolled)

Listing Number	Section	Description of Output
Listing 16.19	Device Alarms	Listing of Device Alarms (All Subjects Enrolled)
Listing 16.20	Waste Material-RBC Depletion/Exchange	Listing of Waste Material-RBC Depletion/Exchange Procedures (All Subjects Enrolled)
Listing 16.21	Waste Material-RBC Exchange	Listing of Waste Material-RBC Exchange (All Subjects Enrolled)
Listing 16.22	Protocol Deviations	Listing of Protocol Deviation (All Subjects Enrolled)

10 MOCK TABLES AND LISTINGS

Table 14.1
Summary of Subject Disposition
All Subjects Enrolled (N=xx)

Parameter	Overall
Total Subjects	xx
Lead-In Subjects	xx
Intent-to-Treat Subjects	xx
Evaluable Subjects	xx
RBC Exchange Procedure	xx
RBC Depletion/Exchange Procedure	xx
Non-Evaluable Subjects	xx
RBC Exchange Procedure	xx
RBC Depletion/Exchange Procedure	xx

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.1.sas
Cross reference: Listing 16.1

Table 14.2.1
Summary of Procedure Evaluability
Intent-to-Treat Subjects[1] (N=xx)

	Overall n (%)
Was the procedure completed?	
Yes	xx (%)
No	xx (%)
If No, check the primary reason:	
Adverse Event	xx (%)
Venous Access Issue (Non-Adverse Event)	xx (%)
Instrument Alarm	xx (%)
Disposable Issue	xx (%)
Leak	xx (%)
Kink	xx (%)
Misassembly	xx (%)
Other	xx (%)
Investigator Decision	xx (%)
Subject Decision	xx (%)
Protocol Deviation/Violation	xx (%)
Other	xx (%)
At the end of procedure, was reinfusion performed?	
Yes	xx (%)
No	xx (%)
NA	xx (%)
If Yes, was the subject's post-procedure blood sample taken prior to reinfusion?	
Yes	xx (%)
No	xx (%)
Did operator change subject Hct, Avg RF Hct, or Total Blood Volume after procedure start?	
Yes	xx (%)
No	xx (%)
NA	xx (%)
Was saline bolus performed?[2]	
Yes	xx (%)
No	xx (%)
NA	xx (%)
Is absolute difference of Average RF Hct and calculated Avg RF Hct ≤ 5 Hct points?	
Yes	xx (%)
No	xx (%)
NA	xx (%)
Is absolute difference of subject Hct and pre-procedure Hct value ≤ 5 Hct points?	
Yes	xx (%)
No	xx (%)
NA	xx (%)
Is absolute difference of the FCR and calculated FCR value ≤ 6 FCR points?[3]	
Yes	xx (%)
No	xx (%)
NA	xx (%)

Clinical Study Protocol: AMIC-003-CMD
[1]Intent-to-Treat population is all subjects enrolled minus Lead-In subjects.
[2]If a saline bolus is given during the procedure, the end Hct is not evaluable.
[3]If Fraction of Cells Remaining was not used as an input, the evaluability criterion is not applicable.

Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.2.1sas
Cross reference: Listing 16.2 and 16.13.3

Table 14.2.2
Summary of Procedure Selection Parameters
All Subjects Enrolled (N=xx)

	Overall n (%)
Is this a Lead-In procedure?	
Yes	xx (%)
No	xx (%)
If Yes	
Lead-in RBC Exchange	xx (%)
Lead-in RBC Depletion /Exchange	xx (%)
If No	
RBC Exchange	xx (%)
RBC Depletion/ Exchange	xx (%)

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.2.2sas
Cross reference: Listing 16.1

Table 14.3
Summary of Demographic Parameters
All Subjects Enrolled (N=xx)

Parameter	Overall
Age at Consent (years)	
N	xx
Mean (SD)	xx.x (xx.xx)
Median	xx.x
Min, Max	xx, xx
Age at Procedure (years)[1]	
N	xx
Mean (SD)	xx.x (xx.xx)
Median	xx.x
Min, Max	xx, xx
Sex [n (%)]	
Male	xx (%)
Female	xx (%)
Ethnicity [n (%)]	
Hispanic or Latino	xx (%)
Not Hispanic or Latino	xx (%)
Decline to Respond	xx (%)
Race [n (%)]	
American Indian or Alaska Native	xx (%)
Asian	xx (%)
Black or African American	xx (%)
Native Hawaiian or Other Pacific Islander	xx (%)
White	xx (%)
Decline to Respond	xx (%)

Clinical Study Protocol: AMIC-003-CMD
[1] For calculated parameters refer to algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.3.sas
Cross reference: Listing 16.4

Table 14.4
Summary of Routine Pre-Procedure Testing Data
Intent-to-Treat Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Actual Hemoglobin S (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Target Hemoglobin S (%)[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx
Hematocrit (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx

Clinical Study Protocol: AMIC-003-CMD
[1]Operator may input either Replacement Volume or FCR. For those that enter by Replacement Volume, a Target HbS value is not necessary
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.4.sas
Cross reference: Listing 16.5

Table 14.5
Summary of Subject Evaluations Parameters
All Subjects Enrolled (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Weight (lb)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Height (in)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Systolic Blood Pressure (mmHg)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Diastolic Blood Pressure (mmHg)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Temperature (°F)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Pulse (bpm)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Respiration Rate (breaths/min)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x

Clinical Study Protocol: AMIC-003-CMD
[1]Additional analysis recorded at end of Depletion Phase for RBC Depletion/Exchange procedures
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.5.sas
Cross reference: Listing 16.6

Table 14.6
Summary of Subject Laboratory Parameters
All Subjects Enrolled (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
White Blood Cell Count (WBC) ($x10^3/\mu L$)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Red Blood Cell Count (RBC) ($x10^6/\mu L$)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Platelet Count ($x10^3/\mu L$)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Hematocrit (%)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Plasma Hemoglobin (mg/dL)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
End of Depletion Phase[1]	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Hemoglobin A[2] (%)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Hemoglobin S[2] (%)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post -Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Hemoglobin C[2] (%)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post -Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Hemoglobin F[2] (%)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post -Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Hemoglobin A2[2] (%)				
Pre-Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x
Post -Procedure	xx	xx.xx (xx.xxx)	xx.xx	xx.x, xx.x

Clinical Study Protocol: AMIC-003-CMD
[1]Additional analysis recorded at end of Depletion Phase for RBC Depletion/Exchange procedures
[2]Only Hemoglobin values that could be quantified were entered into the database.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.6.sas
Cross reference: Listing 16.7

Table 14.7
Analysis of Primary Endpoint Parameters
All Evaluable Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min,Max	95% CI
Post-Procedure Hemoglobin S (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx	
Pre-Procedure Hemoglobin S (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx	
Actual FCR[1] (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx	
FCR (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx	
Calculated A:T FCR Ratio[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx	x.xx, x.xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to the algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.7.sas
Cross reference: Listing 16.16

Table 14.8
Summary of Secondary Endpoint Parameters
All Evaluable Subjects (N=xx)

Parameter[1]	N	Mean (SD)	Median	Min,Max
Overall Procedures				
Subject WBC Percent Loss[2] (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Subject RBC Percent Loss[2] (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Subject Platelet Percent Loss[2] (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Subject Plasma Hemoglobin Delta (mg/dL)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Calculated Target End Hct Accuracy (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Exchange Procedures				
Waste Material Volume (mL)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Waste WBC Count ($x10^{10}$)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Waste Platelet Count ($x10^{11}$)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Calculated Target End Hct Accuracy (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Depletion/Exchange Procedure				
Depletion Phase				
Waste Material Volume (mL)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Waste WBC Count ($x10^{10}$)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Waste Platelet Count ($x10^{11}$)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Calculated Depletion Hct Accuracy (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Exchange Phase				
Waste Material Volume (mL)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Waste WBC Count ($x10^{10}$)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Waste Platelet Count ($x10^{11}$)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Calculated Target End Hct Accuracy (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to algorithm document (AD)
[2]For Subject Percent Loss, negative values indicate a gain
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.8.sas
Cross reference: Listing 16.17.1 and 16.17.2

Table 14.9
Summary of Procedure Evaluation Parameters
All Evaluable Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Blood Warmer Prime Volume (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Subject Total Sample Volume Removed (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.9.sas
Cross reference: Listing 16.9

Table 14.10.1
Summary of Adverse Events During the Procedure
All Subjects Enrolled (N=xx)

Adverse Event Parameter Level	**Subjects[1] n (%)**	**Events n**
Total	xx (xx.x)	xx
Severity[2]		
Mild	xx (xx.x)	xx
Moderate	xx (xx.x)	xx
Severe	xx (xx.x)	xx
Serious		
Yes	xx (xx.x)	xx
No	xx (xx.x)	xx
Relationship to Procedure		
Not Related	xx (xx.x)	xx
Unlikely Related	xx (xx.x)	xx
Possibly Related	xx (xx.x)	xx
Related	xx (xx.x)	xx
Relationship to Device		
Not Related	xx (xx.x)	xx
Unlikely Related	xx (xx.x)	xx
Possibly Related	xx (xx.x)	xx
Related	xx (xx.x)	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Number of subjects experiencing one or more adverse events.
[2]Subjects experiencing multiple events with different severity levels are counted only once for the most severe condition.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.10.1.sas
Cross reference: Listing 16.10.1

Table 14.10.2
Summary of Adverse Events During the Procedure by Site
All Subjects Enrolled (N=xx)

Site	Adverse Event Parameter Level	Subjects[1] n (%)	Events n
BCW (N=xx)	**Total**	**xx (xx.x)**	**xx**
	Severity[2]		
	Mild	xx (xx.x)	xx
	Moderate	xx (xx.x)	xx
	Severe	xx (xx.x)	xx
	Serious		
	Yes	xx (xx.x)	xx
	No	xx (xx.x)	xx
	Relationship to Procedure		
	Not Related	xx (xx.x)	xx
	Unlikely Related	xx (xx.x)	xx
	Possibly Related	xx (xx.x)	xx
	Related	xx (xx.x)	xx
	Relationship to Device		
	Not Related	xx (xx.x)	xx
	Unlikely Related	xx (xx.x)	xx
	Possibly Related	xx (xx.x)	xx
	Related	xx (xx.x)	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Number of subjects experiencing one or more adverse events.
[2]Subjects experiencing multiple events with different severity levels are counted only once for the most severe condition.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.10.2.sas
Cross reference: Listing 16.10.1

Table 14.10.3
Incidence of Adverse Events During the Procedure
All Subjects Enrolled (N=xx)

Adverse Events Reported[1]			
MedDRA			
System Organ Class	**Preferred Term**	**Subjects[2] n (%)**	**Events n**
Chills	Chills	xx (xx.x)	xx
Headache	Headache	xx (xx.x)	xx
Muscle Discomfort	Muscle Discomfort	xx (xx.x)	xx
Skin Irritation	Skin Irritation	xx (xx.x)	xx
Fainting	Fainting	xx (xx.x)	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Adverse events are sorted in descending frequency of events
[2]Subjects experiencing multiple episodes of a given adverse event are counted only once for each adverse event term.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.10.3.sas
Cross reference: Listing 16.10.2

Table 14.10.4
Incidence of Adverse Events during the Procedure by Site
All Subjects Enrolled (N=xx)

Site	Adverse Events Reported1			
	MedDRA			
	System Organ Class	Preferred Term	Subjects[2] n (%)	Events n
BCW (N=xx)	Nervous system disorders	Dizziness	xx (xx.x)	xx
	Eye disorders	Vision blurred	xx (xx.x)	xx
	Gastrointestinal disorders	Nausea	xx (xx.x)	xx
	General disorders and administration site conditions	Chest pain	xx (xx.x)	xx
	Investigations	Blood pressure decreased	xx (xx.x)	xx
	Musculoskeletal and connective tissue disorders	Back pain	xx (xx.x)	xx

Clinical Study Protocol: AMIC-003-CMD
[1] Adverse events are sorted in descending frequency of events
[2]Subjects experiencing multiple episodes of a given adverse event are counted once for each adverse event term.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.10.4.sas
Cross reference: Listing 16.10.2

Table 14.11.1
Summary of Adverse Events Post-Procedure
All Subjects Enrolled (N=xx)

Adverse Event Parameter **Level**	**Subjects[1]** **n (%)**	**Events** **n**
Total	xx (xx.x)	xx
Severity[2]		
Mild	xx (xx.x)	xx
Moderate	xx (xx.x)	xx
Severe	xx (xx.x)	xx
Serious		
Yes	xx (xx.x)	xx
No	xx (xx.x)	xx
Relationship to Procedure		
Not Related	xx (xx.x)	xx
Unlikely Related	xx (xx.x)	xx
Possibly Related	xx (xx.x)	xx
Related	xx (xx.x)	xx
Relationship to Device		
Not Related	xx (xx.x)	xx
Unlikely Related	xx (xx.x)	xx
Possibly Related	xx (xx.x)	xx
Related	xx (xx.x)	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Number of subjects experiencing one or more adverse events.
[2]Subjects experiencing multiple events with different severity levels are counted only once for the most severe condition.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.11.1.sas
Cross reference: Listing 16.12.1

Table 14.11.2
Summary of Adverse Events Post-Procedure by Site
All Subjects Enrolled (N=xx)

Site	Adverse Event Parameter Level	Subjects[1] n (%)	Events n
BCW (N=xx)	**Total**	**xx (xx.x)**	**xx**
	Severity[2]		
	Mild	xx (xx.x)	xx
	Moderate	xx (xx.x)	xx
	Severe	xx (xx.x)	xx
	Serious		
	Yes	xx (xx.x)	xx
	No	xx (xx.x)	xx
	Relationship to Procedure		
	Not Related	xx (xx.x)	xx
	Unlikely Related	xx (xx.x)	xx
	Possibly Related	xx (xx.x)	xx
	Related	xx (xx.x)	xx
	Relationship to Device		
	Not Related	xx (xx.x)	xx
	Unlikely Related	xx (xx.x)	xx
	Possibly Related	xx (xx.x)	xx
	Related	xx (xx.x)	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Number of subjects experiencing one or more adverse events.
[2]Subjects experiencing multiple events with different severity levels are counted only once for the most severe condition.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.11.2.sas
Cross reference: Listing 16.12.1

Table 14.11.3
Incidence of Adverse Events Post-Procedure
All Subjects Enrolled (N=xx)

Adverse Events Reported[1]			
MedDRA			
System Organ Class	**Preferred Term**	**Subjects[2] n (%)**	**Events n**
Chills	Chills	xx (xx.x)	xx
Headache	Headache	xx (xx.x)	xx
Muscle Discomfort	Muscle Discomfort	xx (xx.x)	xx
Skin Irritation	Skin Irritation	xx (xx.x)	xx
Fainting	Fainting	xx (xx.x)	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Adverse events are sorted in descending frequency of events.
[2]Subjects experiencing multiple episodes of a given adverse event are counted once for each adverse event term.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.11.3.sas
Cross reference: Listing 16.12.2

Table 14.11.4
Incidence of Adverse Events Post-Procedure by Site
All Subjects Enrolled (N=xx)

Site	Adverse Events Reported[1]			
	MedDRA			
	System Organ Class	Preferred Term	Subjects[2] n (%)	Events n
BCW (N=xx)	Nervous system disorders	Dizziness	xx (xx.x)	xx
	Eye disorders	Vision blurred	xx (xx.x)	xx
	Gastrointestinal disorders	Nausea	xx (xx.x)	xx
	General disorders and administration site conditions	Chest pain	xx (xx.x)	xx
	Investigations	Blood pressure decreased	xx (xx.x)	xx
	Musculoskeletal and connective tissue disorders	Back pain	xx (xx.x)	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Adverse events are sorted in descending frequency of events.
[2]Subjects experiencing multiple episodes of a given adverse event are counted once for each adverse event term.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.11.4.sas
Cross reference: Listing 16.12.2

Table 14.12.1
Summary of Input and Estimator Parameters
All Evaluable Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Input Pre-Procedure				
FCR (%)	xx	xx.x (xx.xx)	xx.x	xx, xx
End Hematocrit (%)	xx	xx.x (xx.xx)	xx.x	xx, xx
Depletion Hematocrit (%)[1]	xx	xx.x (xx.xx)	xx.x	xx, xx
Replacement Volume (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Fluid Balance (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
AC Ratio	xx	xx.x (xx.xx)	xx.x	xx, xx
Start Prime Hematocrit (%)	xx	xx.x (xx.xx)	xx.x	xx, xx
End Prime Hematocrit (%)	xx	xx.x (xx.xx)	xx.x	xx, xx
Estimator				
Whole Blood Flow Rate (mL/min)	xx	xx.x (xx.xx)	xx.x	xx, xx
Procedure Time (min)	xx	xx.x (xx.xx)	xx.x	xx, xx
Anticoagulant to Subject (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Anticoagulant Used (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Other Replacement Fluid (mL)[1]	xx	xx.x (xx.xx)	xx.x	xx, xx
Depletion Red Cell Volume (mL)[1]	xx	xx.x (xx.xx)	xx.x	xx, xx
Input				
Subject Hematocrit (%)	xx	xx.x (xx.xx)	xx.x	xx, xx
Was value changed during procedure?				
Yes	xx			
No	xx			
Total Blood Volume (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Was value changed during procedure?				
Yes	xx			
No	xx			
Maximum Whole Blood Flow Rate (mL/min)	xx	xx.x (xx.xx)	xx.x	xx, xx
Was value changed during procedure?				
Yes	xx			
No	xx			
Citrate Infusion Rate (CIR) (mg/kg/min)	xx	xx.x (xx.xx)	xx.x	xx, xx
Was value changed during procedure?				
Yes	xx			
No	xx			
Average Replacement Fluid Hematocrit (%)	xx	xx.x (xx.xx)	xx.x	xx, xx
Was value changed during procedure?				
Yes	xx			
No	xx			

Clinical Study Protocol: AMIC-003-CMD
[1]Parameter applies to RBC Depletion/Exchange procedures
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done; AC=anticoagulant
Table Status: DRAFT; SAS Program: Table 14.12.1.sas
Cross reference: Listing 16.13.1, 16.13.2 and 16.13.3

Table 14.12.2
Summary of Procedure Parameters End of Depletion Phase[1]
All Evaluable Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Fluid Balance (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Depletion Hematocrit (%)	xx	xx.x (xx.xx)	xx.x	xx, xx
Whole Blood Processed (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Replacement Fluid Albumin Returned (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Replacement Fluid Saline Returned (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Custom Replacement Fluid Returned (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Plasma Returned (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Procedure Time (minutes)	xx	xx.x (xx.xx)	xx.x	xx, xx
Anticoagulant Used (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Anticoagulant to Subject (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Saline to Subject (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx

Clinical Study Protocol: AMIC-003-CMD
[1]Applicable for RBC Depletion/Exchange procedures
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.12.2.sas
Cross reference: Listing 16.14

Table 14.13.1
Summary of Procedure Results
All Evaluable Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Procedure Time (minutes)	xx	xx.x (xx.xx)	xx.x	xx, xx
FCR (%)	xx	xx.x (xx.xx)	xx.x	xx, xx
A:T FCR Ratio[1]	xx	xx.x (xx.xx)	xx.x	xx, xx
End Hematocrit (%)	xx	xx.x (xx.xx)	xx.x	xx, xx
Fluid Balance (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Theoretical RBC Mass Balance (mL)[1]	xx	xx.x (xx.xx)	xx.x	xx, xx
Empirical RBC Mass Balance (mL)[1]	xx	xx.x (xx.xx)	xx.x	xx, xx
Whole Blood Processed (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Replacement Fluid to Subject (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Anticoagulant to Subject (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Anticoagulant Used (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Saline to Subject (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Replacement Fluid Albumin Returned (mL)[2]	xx	xx.x (xx.xx)	xx.x	xx, xx
Replacement Fluid RBC Returned (mL)	xx	xx.x (xx.xx)	xx.x	xx, xx
Replacement Fluid Saline Returned (mL)[2]	xx	xx.x (xx.xx)	xx.x	xx, xx
Custom Replacement Fluid Returned (mL)[2]	xx	xx.x (xx.xx)	xx.x	xx, xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to algorithm document (AD)
[2]Applicable for RBC Depletion/Exchange Procedures
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.13.1.sas
Cross reference: Listing 16.15.1 and 16.15.2

Table 14.13.2
Summary of Empirical RBC Mass Balance Excluding Outlier(s)
All Evaluable Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Empirical RBC Mass Balance (mL)[1,2]	xx	xx.xxx (xxxx.xxxx)	xx.xxx	xx.xx,xx.xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to the algorithm document (AD)
[2]Excludes xx subjects with outlier values using Box and Whisker plot (Subject IDs xxxxx, …)
Note: NA=Not Applicable: UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.13.2.sas
Cross reference: Listing 16.15.1 and 16.15.2

Table 14.14
Summary of Replacement RBC Unit Parameters
All Evaluable Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Hematocrit (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Volume (mL)[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx
Plasma Hemoglobin (mg/dL)	xx	xx.x (xx.xx)	xx.xx	xx, xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to the algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.14.sas
Cross reference: Listing 16.18

Table 14.15
Summary of Device Alarms
All Subjects Enrolled (N=xx)

Alarm	**Frequency (Occurrence per Procedure) x**	**Total Number of Procedures n (%)**
ACD Flow Problem	xx	xx (%)
Air Detected	xx	xx (%)
Blood Warmer Prime Flow Problem	xx	xx (%)
Cassette Pressure Limit Exceeded	xx	xx (%)
Centrifuge Line Blockage	xx	xx (%)
Check Replacement Fluids	xx	xx (%)
Empty ACD	xx	xx (%)
Return Line Occlusion	xx	xx (%)
Empty Saline	xx	xx (%)
Inlet Line Occlusion	xx	xx (%)
Other	xx	xx (%)

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.15.sas
Cross reference: Listing 16.19

Table 14.16.1
Summary of Waste Material-RBC Depletion/Exchanges
All Evaluable Subjects (N=xx)

Parameter	RBC Depletion Phase				RBC Exchange Phase			
	N	Mean (SD)	Median	Min, Max	N	Mean (SD)	Median	Min, Max
Volume (mL)[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx	xx	xx.x (xx.xx)	xx.xx	xx, xx
WBC ($x10^3/\mu L$)	xx	xx.x (xx.xx)	xx.xx	xx, xx	xx	xx.x (xx.xx)	xx.xx	xx, xx
Total WBC Count ($x10^{10}$)[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx	xx	xx.x (xx.xx)	xx.xx	xx, xx
Platelet Count ($x10^3/\mu L$)	xx	xx.x (xx.xx)	xx.xx	xx, xx	xx	xx.x (xx.xx)	xx.xx	xx, xx
Total Platelet Count ($x10^{11}$)[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx	xx	xx.x (xx.xx)	xx.xx	xx, xx
Hematocrit (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx	xx	xx.x (xx.xx)	xx.xx	xx, xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to the algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.16.1.sas
Cross reference: Listing 16.20

Table 14.16.2
Summary of Waste Material - RBC Exchange Procedures
All Evaluable Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Volume (mL)[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx
WBC ($x10^3/\mu L$)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Total WBC Count ($x\ 10^{10}$)[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx
Platelet Count ($x10^3/\mu L$)	xx	xx.x (xx.xx)	xx.xx	xx, xx
Total Platelet Count ($x10^{11}$)[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx
Hematocrit (%)	xx	xx.x (xx.xx)	xx.xx	xx, xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to the algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.16.2.sas
Cross reference: Listing 16.21

Table 14.17
Summary of End Hematocrit
All Evaluable Subjects (N=xx)

Parameter	N	Mean (SD)	Median	Min, Max
Target Depletion Hct (%)[3]	xx	xx.x (xx.xx)	xx.xx	xx, xx
Procedure Results Depletion Hct (%)[1]	xx	xx.x (xx.xx)	xx.xx	xx, xx
Subject Post-Depletion Phase Hct (%)[2]	xx	xx.x (xx.xx)	xx.xx	xx, xx
End of Depletion Phase Hct Accuracy (%)[5]	xx	xx.x (xx.xx)	xx.xx	xx, xx
Target Exchange End Hct (%)[3]	xx	xx.x (xx.xx)	xx.xx	xx, xx
Procedure Results End Hct (%)[4]	xx	xx.x (xx.xx)	xx.xx	xx, xx
Subject Post-Procedure Hct (%)[2]	xx	xx.x (xx.xx)	xx.xx	xx, xx
End of Exchange Phase Hct Accuracy (%) [5]	xx	xx.x (xx.xx)	xx.xx	xx, xx

Clinical Study Protocol: AMIC-003-CMD
[1]Depletion Hct (%) results reported Post-Depletion Phase
[2]Subject laboratory measured values
[3]Target Depletion Hct and Exchange End Hct values entered Pre-Procedure
[4]End Hct (%) results reported Post-Procedure
[5]For calculated parameters refer to algorithm document (AD)
Note: NA=Not Applicable: UNK=Unknown; ND=Not Done
Table Status: DRAFT; SAS Program: Table 14.17.sas
Cross reference: Listing 16.17.3

Listing 16.1
Listing of Patient Disposition
All Subjects Enrolled (N=xx)

Subject ID	Intent-to-Treat subjects[1]	Evaluable RBC Exchange Subjects	Evaluable RBC Depletion/Exchange Subjects
xxxxx	Yes		Yes
xxxxx	Lead-in	No	

Clinical Study Protocol: AMIC-003-CMD
[1]Intent-to-Treat is defined as all subjects enrolled minus the Lead-In subjects.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Listing Status: DRAFT; SAS Program: Listing 16.1.sas

Listing 16.2
Listing of Procedure Evaluability/End of Study
All Subjects Enrolled (N=xx)

Subject ID	Was procedure completed?	If No, reason procedure not completed	At the end of the procedure, was reinfusion performed?	If Yes, was the subject's post-procedure blood sample taken prior to reinfusion?	Did operator change subject Hct, Avg RF Hct, or TBV after procedure start?	Was saline bolus performed?[1]	Is absolute difference of Average RF Hct and calculated Avg RF Hct value ≤ 5 Hct points?[2]	Is absolute difference of subject Hct and pre-procedure Hct ≤ 5 Hct points?[2]	Is absolute difference of the FCR and calculated FCR value ≤ 6 FCR points?[2,4]	A:T FCR Ratio Evaluable[3]	Calculated Depletion Hct Accuracy Evaluable[3]	Calculated End Hct Accuracy Evaluable[3]
xxxxx	No	NA	No	NA	No	No	Yes	Yes	Yes	Evaluable	Evaluable	Evaluable
xxxxx	Yes	Adverse Event	No	NA	No	No	Yes	Yes	Yes	Non Evaluable	Non Evaluable	Non Evaluable
xxxxx	Yes	NA		No	No	No	Yes	Yes	Yes	Evaluable	Evaluable	Evaluable
xxxxx	No	NA		NA	Yes	No	Yes	Yes	Yes	Non Evaluable	Non Evaluable	Non Evaluable
xxxxx	Yes	NA		NA	No	Yes	Yes	Yes	Yes	Evaluable	Evaluable	Evaluable
xxxxx	No	NA		NA	No	No	Yes	Yes	Yes	Evaluable	Evaluable	Evaluable
xxxxx	No	NA		NA	No	No	Yes	Yes	Yes	Evaluable	Evaluable	Evaluable
xxxxx	No	NA		NA	No	No	Yes	No	NA	Evaluable	Evaluable	Evaluable
xxxxx	No	NA		NA	No	No	Yes	Yes	No	Evaluable	Evaluable	Evaluable

Clinical Study Protocol: AMIC-003-CMD
[1]If saline bolus is given during the procedure, the end Hct is not evaluable.
[2]For calculated parameters refer to algorithm document (AD)
[3]Lead-In subjects are not included in the evaluable population for this protocol
[4]If Fraction of Cells Remaining was not used as an input, the evaluability criterion is not applicable.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
FCR=fraction of cells remaining; Hb=hemoglobin; Hct=hematocrit; RF=replacement fluid
Listing Status: DRAFT; SAS Program: Listing 16.2.sas

Listing 16.3.1
Listing of Inclusion Criteria
All Subjects Enrolled (N=xx)

Subject ID	Subject >6 years old	Subject with SCD who require RBC Exchange or RBC Depletion/Exchange treatment	Medically stable subjects treated for SCD with RBC Exchange or RBC Depletion/Exchange	Subjects who have provided signed IC/assent prior to participation	Adequate availability of sickle trait negative, leukoreduced, ABO blood group, Rh (D) compatible, unexpired replacement RBC products	Subjects with sufficient vascular access for RBC procedure	Subject is able and agrees to report AEs during the required reporting period
xxxxx	Yes	Yes	Yes	Yes	Yes	Yes	Yes
xxxxx	Yes	Yes	Yes	Yes	Yes	Yes	Yes
xxxxx	No	No	No	No	No	No	No
xxxxx	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
IC=informed consent; RBC=red blood cell; SCD=sickle cell disease
Listing Status: DRAFT; SAS Program: Listing 16.3.1.sas

Listing 16.3.2
Listing of Exclusion Criteria
All Subjects Enrolled (N=xx)

Subject ID	Procedures that occur during acute hospitalization	Procedures prescribed within 1 wk of hospital discharge	Subjects with AMS that prohibit giving IC and assent and do not have LAR	Drug/alcohol abuse or other factors that could affect the ability of subject to comply with protocol requirements	Subjects who had an SAE associated with an RBCx procedure in the past	Subjects who have a life expectancy < 30 days	Subjects who refuse blood products	Subjects who are pregnant	Subjects who fail to comply with site requirements for cessation of medication that interfere or increase procedure risk
xxxxx	No	No	No	No	No	No	No	No	No
xxxxx	No	No	No	No	No	No	No	No	No
xxxxx	No	No	No	No	No	No	No	No	No
xxxxx	No	No	No	No	No	No	No	No	No

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
AMS=altered mental status; IC=informed consent; LAR=legally authorized representative; SAE=serious adverse event; wk=week
Listing Status: DRAFT; SAS Program: Listing 16.3.2.sas

Listing 16.3.3
Listing of Subject Eligibility
All Subjects Enrolled (N=xx)

Subject ID	Has the subject met all eligibility criteria according to the protocol?	Date Informed Consent Signed
xxxxx	Yes, subject has met all eligibility criteria	Mmm-dd-yyyy
xxxxx	No, subject has not met all eligibility criteria	Mmm-dd-yyyy
xxxxx	Yes, subject has met all eligibility criteria	Mmm-dd-yyyy
xxxxx	No, subject has not met all eligibility criteria	Mmm-dd-yyyy

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Listing Status: DRAFT; SAS Program: Listing 16.3.3.sas

Listing 16.4
Listing of Demographic Parameters
All Subjects Enrolled (N=xx)

Subject ID	Date of Birth	Age at Consent (years)	Age at Procedure (years)[1]	Sex	Ethnicity	Race
xxxxx	Mmm-dd-yyyy	xx	xx	Male	Hispanic or Latino	White
xxxxx	Mmm-dd-yyyy	xx	xx	Female	Not Hispanic or Latino	Black or African American
xxxxx	Mmm-dd-yyyy	xx	xx	Female	Hispanic or Latino	Asian
xxxxx	Mmm-dd-yyyy	xx	xx	Male	Hispanic or Latino	Asian
xxxxx	Mmm-dd-yyyy	xx	xx	Female	Not Hispanic or Latino	American Indian or Alaska Native
xxxxx	Mmm-dd-yyyy	xx	xx	Female	Hispanic or Latino	Asian
xxxxx	Mmm-dd-yyyy	xx	xx	Male	Hispanic or Latino	Decline to Respond
xxxxx	Mmm-dd-yyyy	xx	xx	Female	Not Hispanic or Latino	White
xxxxx	Mmm-dd-yyyy	xx	xx	Female	Hispanic or Latino	Black or African American

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to algorithm document (AD)
Note: NA= Not Applicable; UNK= Unknown; ND= Not Done
Listing Status: DRAFT; SAS Program: Listing 16.4.sas

Listing 16.5
Listing of Routine Pre-Procedure Testing Data
All Subjects Enrolled (N=xx)

Subject ID	Sample Date	Sample Time (24 hour clock)	Actual Hb S (%)	Target Hb S[1] (%)	Hct (%)
xxxx	Mmm-dd-yyyy	hh:mm	xx.x	xx.x	xx.x
xxxx	Mmm-dd-yyyy	hh:mm	xx.x	xx.x	xx.x
xxxx	Mmm-dd-yyyy	hh:mm	xx.x	xx.x	xx.x
xxxx	Mmm-dd-yyyy	hh:mm	xx.x	xx.x	xx.x
xxxx	Mmm-dd-yyyy	hh:mm	xx.x	xx.x	xx.x

Clinical Study Protocol: AMIC-003-CMD
[1]Operator may input either Replacement Volume or FCR. For those that enter by Replacement Volume, a Target HbS value is not necessary.
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done; Hb=hemoglobin; Hct=hematocrit
Listing Status: DRAFT; SAS Program: Listing 16.5.sas

Listing 16.6
Listing of Subject Evaluations Parameters
All Subjects Enrolled (N=xx)

Subject ID	Primary Diagnosis	Procedure[1]	Weight (lb)	Height (in)	Systolic BP (mmHg)	Diastolic BP (mmHg)	Temp (°F)	Pulse (bpm)	Respiration Rate (breaths/min)
xxxxx	SS	Pre	xxx	xx	xxx	xxx	xx.x	xx	xxx
		End of Depletion Phase			xxx	xxx	xx.x	xx	xxx
		Post			xxx	xxx	xx.x	xx	xxx
xxxxx	SB-0 thal	Pre	xxx	xx	xxx	xxx	xx.x	xx	xxx
		End of Depletion Phase	xxx	xxx	xxx	xxx	xx.x	xxx	xxx
		Post	xxx	xx	xxx	xxx	xx.x	xx	xxx
xxxxx	SC	Pre	xxx	xx	xxx	xxx	xx.x	xx	xxx
		End of Depletion Phase	xxx	xx	xxx	xxx	xx.x	xx	xxx
		Post	xxx	xx	xxx	xxx	xx.x	xx	xxx
xxxxx	Other	Pre	xxx	xx	xxx	xxx	xx.x	xx	xxx
		End of Depletion Phase	xxx	xx	xxx	xxx	xx.x	xx	xxx
		Post	xxx	xx	xxx	xxx	xx.x	xx	xxx
xxxxx	SS	Pre	xxx	xx	xxx	xxx	xx.x	xx	xxx
		End of Depletion Phase	xxx	xx	xxx	xxx	xx.x	xx	xxx
		Post	xxx	xx	xxx	xxx	xx.x	xx	xxx
xxxxx	SS	Pre	xxx	xx	xxx	xxx	xx.x	xx	xxx
		End of Depletion Phase	xxx	xx	xxx	xxx	xx.x	xx	xxx
		Post	xxx	xx	xxx	xxx	xx.x	xx	xxx

Clinical Study Protocol: AMIC-003-CMD
[1]Additional analysis recorded at end of Depletion Phase for RBC Depletion/Exchange procedures
Note: NA= Not Applicable; UNK= Unknown; ND= Not Done
BP=blood pressure; SB-0 thal= sickle beta 0 thalassemia; SC=sickle hemoglobin C disease; SS=sickle cell anemia; Temp=temperature
Listing Status: DRAFT; SAS Program: Listing 16.6.sas

Listing 16.7
Listing of Subject Laboratory Analysis Parameters
All Subjects Enrolled (N=xx)

Subject ID	Procedure[1]	WBC ($x10^3/\mu L$)	RBC ($x10^6/\mu L$)	Platelet Count ($x10^3/\mu L$)	Hct (%)	Post-Procedure Sample Time[3]	Plasma Hb (mg/dL)	Post-Procedure Sample Time[3]	Hb A[4] (%)	Hb S[4] (%)	Actual FCR[2] (%)	Hb C[4] (%)	Hb F[4] (%)	Hb A2[4] (%)	Post-Procedure Sample Time[3]	Pregnancy Test
xxxx	Pre	xxx	xxx	xxx	xx		xx.x		xx.x	xx.x		xx.x	xx.x	xx.x		Neg
x	Post	xxx	xxx	xxx	xx	hh:mm	xx.x	hh:mm	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	hh:mm	
xxxx	Pre	xxx	xxx	xxx	xx		xx.x		xx.x	xx.x		xx.x	xx.x	xx.x		ND
x	Post	xxx	xxx	xxx	xx	hh:mm	xx.x	hh:mm	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	hh:mm	
xxxx	Pre	xxx	xxx	xxx	xx		xx.x		xx.x	xx.x		xx.x	xx.x	xx.x		Pos
x	End of Depletion Phase	xxx	xxx	xxx	xx		xx.x									
	Post	xxx	xxx	xxx	xx	hh:mm	xx.x	hh:mm	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	hh:mm	
xxxx	Pre	xxx	xxx	xxx	xx		xx.x		xx.x	xx.x		xx.x	xx.x	xx.x		Male, N/A
x	Post	xxx	xxx	xxx	xx	hh:mm	xx.x	hh:mm	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	hh:mm	
xxxx	Pre	xxx	xxx	xxx	xx		xx.x		xx	xx.x		xx.x	xx.x	xx.x		ND
x	Post	xxx	xxx	xxx	xx	hh:mm	xx.x	hh:mm	xx	xx.x	xx.x	xx.x	xx.x	xx.x	hh:mm	
xxxx	Pre	xxx	xxx	xxx	xx		xx.x		xx	xx.x		xx.x	xx.x	xx.x		Pos
	End of Depletion Phase	xxx	xxx		xx		xx.x									
	Post	xxx	xxx	xxx	xx	hh:mm	xx.x	hh:mm	xx	xx.x	xx.x	xx.x	xx.x	xx.x	hh:mm	

Clinical Study Protocol: AMIC-003-CMD
[1]Additional analysis recorded at end of Depletion Phase for RBC Depletion/Exchange procedures
[2]For calculated parameters refer to algorithm document (AD)
[3]Sample time is 24 Hour clock
[4]Only Hemoglobin values that could be quantified were entered into the database.
Note: NA= Not Applicable; UNK= Unknown; ND= Not Done
FCR=fraction of cells remaining; Hb=hemoglobin; Hct=hematocrit; Neg=negative; Pos=positive; RBC=red blood cell; WBC=white blood cell
Listing Status: DRAFT; SAS Program: Listing 16.7.sas

Listing 16.8
Listing of Concomitant Medications
All Subjects Enrolled (N=xx)

Subject ID	Any Con Meds?[1]	Medication Verbatim[2]	Medication (WHO Term)[3]	Drug Class	Start Date	Continuing	End Date	Dose/ Unit	Route	Frequency	Indication
xxxxx	Yes	Ca Gluconate	CALCIUM	CALCIUM GLUCONATE	Mmm-dd-yyyy	Yes	Mmm-dd-yyyy		Topical	Morning	
xxxxx	Yes	Albuterol			Mmm-dd-yyyy	No	Mmm-dd-yyyy		Inhaled	As Needed	Asthma
	Yes	Benadryl	Benadryl		Mmm-dd-yyyy	No	Mmm-dd-yyyy		IV	Other	

Clinical Study Protocol: AMIC-003-CMD
[1]Concomitant medications were not recorded for enrolled subjects that did not start a procedure.
[2]Medication is reported verbatim from the CRF.
[3]The medical terms are from WHO Drug Dictionary (version 2015).
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Listing Status: DRAFT; SAS Program: Listing 16.8.sas

Listing 16.9
Listing of Procedure Evaluation Parameters
All Subjects Enrolled (N=xx)

Subject ID	Procedure Date	End Time[1]	Venous Access Used	RF Used[2]	AC Type	Was reinfusion selected prior to start of procedure?	STSVR (mL)	CP[3]	Was prime diverted ?	Was a blood warmer used during procedure?	If Yes, provide the prime volume (mL)	Was procedure ended prior to or extended beyond (±50mLs) of the Target RF Volume?
xxxxx	Mmm-dd-yyyy	hh:mm	Central	Saline	ACD-A	Yes	xx	Full	Yes	xx	Yes	Yes
xxxxx	Mmm-dd-yyyy	hh:mm	Peripheral	Albumin	Custom	Yes	xx	Partial	Yes	xx	No	No
xxxxx	Mmm-dd-yyyy	hh:mm	Central and Peripheral	Saline	Custom	No	xx	Full	No	xx	Yes	Yes
xxxxx	Mmm-dd-yyyy	hh:mm	Central	Custom	ACD-A	Yes	xx	None	No	xx	Yes	Yes

Clinical Study Protocol: AMIC-003-CMD
[1]End time is 24 Hour clock
[2] Applicable for Depletion/Exchange procedures
[3]Applicable for Exchange procedures
Note: NA= Not Applicable; UNK= Unknown; ND= Not Done
AC=anticoagulant; ACD-A=Anticoagulant Citrate Dextrose Formula A; CP= Custom Prime; RF=Replacement Fluid; STSVR=Subject Total Sample Volume Removed
Listing Status: DRAFT; SAS Program: Listing 16.9.sas

Listing 16.10.1
Listing of Adverse Events During Procedure
All Subjects Enrolled (N=xx)

Subject ID	Study Site	Any AEs?	AE Number	Description of Event	Start Date	Severity	Episode Pattern	Action Taken (Procedure)	Action Taken (Subject)	Relationship to Procedure	Relationship to Device	Serious /Reason	Outcome/ End Date
xxxxx	BCW	Yes		Nausea	Mmm-dd-yyyy	Mild	Single	No Change	No	Possibly Related	Not Related	No	Recovered/ Mmm-dd-yyyy
xxxxx	BCW	Yes		Chills	Mmm-dd-yyyy	Mild	Single	No Change	No	Possibly Related	Not Related	No	Continuing
xxxxx	NCH	Yes		Chills	Mmm-dd-yyyy	Severe	Cont	Interrupted	Yes	Not Related	Possibly Related	Yes/ Hospitalization	Continuing
xxxxx	UT	Yes		Other: specify	Mmm-dd-yyyy	Mild	Single	Change in Parameters/ specify	No	Related		No	Recovered/ Mmm-dd-yyyy
xxxxx	KCI	Yes		Chills	Mmm-dd-yyyy	Severe	Cont	Interrupted	Yes	Unlikely Related	Related	Yes/ Death	Continuing

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
AEs=adverse event
Listing Status: DRAFT; SAS Program: Listing 16.10.1.sas

Listing 16.10.2
Listing of MedDRA Coded Adverse Events During Procedure
All Subjects Enrolled (N=xx)

Subject ID	Study Site	Adverse Event Number	Description of Event	MedDRA Term			
				System Organ Class	Preferred Term	High Level Term	Low Level Term
xxxxx	BCW		Nausea				
xxxxx	BCW		Chills				
xxxxx	BCW		Other: specify				
xxxxx			Chills				

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Listing Status: DRAFT; SAS Program: Listing 16.10.2.sas

Listing 16.11
Listing of Adverse Events Post-Procedure Assessment
All Subjects Enrolled (N=xx)

Subject ID	Study Site	Was the subject contacted on 1st attempt?	Date and time of 1st contact[1,2]	Was the subject contacted on 2nd attempt?	Date and time of 2nd contact[1,2]	If subject was not contacted by telephone, was a certified letter sent to the subject?	Was there AE during procedure with Outcome of Continuing?	AE Number	Current Outcome of the Continuing Adverse Event				Did subject experience any AE post-procedure?
									Recovered (End Date)	Recovered with Sequela(e) (End Date)	Continuing	Death (Date of Death)	
xxxxx	02	Yes	Mmm-dd-yyyy hh:mm	No	Mmm-dd-yyyy hh:mm	No	Yes		Mmm-dd-yyyy	Mmm-dd-yyyy	Yes	Mmm-dd-yyyy	Yes
xxxxx	15	Yes	Mmm-dd-yyyy hh:mm	No	Mmm-dd-yyyy hh:mm	Yes	No		Mmm-dd-yyyy	Mmm-dd-yyyy	No	Mmm-dd-yyyy	Yes
xxxxx	16	No	Mmm-dd-yyyy hh:mm	Yes	Mmm-dd-yyyy hh:mm	Yes	No		Mmm-dd-yyyy	Mmm-dd-yyyy	No	Mmm-dd-yyyy	No

Clinical Study Protocol: AMIC-003-CMD
[1]Time is 24 Hour clock
[2]Refers to either contact or attempt date and time
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Listing Status: DRAFT; SAS Program: Listing 16.11.sas

Listing 16.12.1
Listing of Adverse Events Post Procedure
All Subjects Enrolled (N=xx)

Subject ID	Study Site	Any AEs?	AE Number	Description of Event	Start Date	Severity	Episode Pattern	Action Taken (Procedure)	Action Taken (Subject)	Relationship to Procedure	Relationship to Device	Serious/ Reason	Outcome /End date
xxxxx	BCW	Yes		Nausea	Mmm-dd-yyyy	Mild	Single	No Change	No	Possibly Related	Not Related	No	Recovered/ Mmm-dd-yyyy
xxxxx	BCW	Yes		Chills	Mmm-dd-yyyy	Severe	Cont	Interrupted	Yes	Not Related	Possibly Related	Yes/ Hospitalization	Cont
xxxxx	BCW	Yes		Other: specify	Mmm-dd-yyyy	Mild	Single	Change in Parameters/ specify	No	Related	Unlikely Related	No	Recovered/ Mmm-dd-yyyy
xxxxx	KCI	Yes		Chills	Mmm-dd-yyyy	Severe	Con	Interrupted	Yes	Unlikely Related	Related	Yes/ Hospitalization	Cont

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
AEs=adverse event
Listing Status: DRAFT; SAS Program: Listing 16.12.1.sas

Listing 16.12.2
Listing of MedDRA Coded Adverse Events Post-Procedure
All Subjects Enrolled (N=xx)

Subject ID	Study Site	Adverse Event Number	Description of Event	MedDRA Term			
				System Organ Class	Preferred Term	High Level Term	Low Level Term
xxxxx	BCW		Nausea				
xxxxx	BCW		Chills				
xxxxx	BCW		Other: specify				
xxxxx			Chills				

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Listing Status: DRAFT; SAS Program: Listing 16.12.2.sas

Listing 16.13.1
Listing of Input Parameters - Pre-Procedure
All Subjects Enrolled (N=xx)

Subject ID	FCR (%)	End Hct (%)	Depletion Hct[1] (%)	Replacement Volume (mL)	Fluid Balance (mL)	AC Ratio (X:1)	Start Prime Hct (%)	End Prime Hct (%)
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Applicable for Depletion/Exchange Procedures
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
FCR=fraction of cells remaining, AC=anticoagulant; Hct=hematocrit
Listing Status: DRAFT; SAS Program: Listing 16.13.1.sas

Listing 16.13.2
Listing of Estimator Parameters Pre-Procedure
All Subjects Enrolled (N=xx)

Subject ID	Whole Blood Flow Rate (mL/min)	Procedure Time (minutes)	AC to Subject (mL)	AC Used (mL)	Other Replacement Fluid (mL)	Depletion Red Cell Volume[1] (mL)
xxxxx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Applicable for Depletion/Exchange Procedures
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
AC=anticoagulant; Hct=hematocrit
Listing Status: DRAFT; SAS Program: Listing 16.13.1.sas

Listing 16.13.3
Listing of Input Procedure Parameters
All Subjects Enrolled (N=xx)

Subject ID	Subject Hct (%)	Was Value changed during procedure ? If Yes, Final value	Average Replacement Fluid Hct (%)	Was Value changed during procedure ? If Yes, Final Value	Total Blood Volume (mL)	Was Value changed during procedure ? If Yes, Final Value	Max Whole Blood Flow Rate (mL/min)	Was Value changed during procedure ? If Yes, Final Value	Citrate Infusion Rate (mg/kg/min)	Was Value changed during procedure ? If Yes, Final Value
xxxxx	xx	Yes, xx	xx	Yes, xx	xxx	Yes ,xx	xx	Yes, xx	xx	Yes, xx
xxxxx	xx	Yes, xx	xx	Yes, xx	xxx	Yes, xx	xx	Yes ,xx	xx	Yes, xx
xxxxx	xx	No	xx	No	xxx	No	xx	No	xx	No

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Hct=hematocrit; Max=maximum; RBC=red blood cell; WB=whole Blood
Listing Status: DRAFT; SAS Program: Listing 16.13.2.sas

Listing 16.14
Listing of End of Depletion Phase Parameters[1]
All Subjects (N=xx)

Subject ID	Fluid Balance (mL)	Depletion Hct (%)	WB Processed (mL)	Replacement Fluid Albumin Returned (mL)	Replacement Fluid Saline Returned (mL)	Custom Replacement Fluid Returned (mL)	Plasma Returned (mL)	Procedure Time (minutes)	AC Used (mL)	AC to Subject (mL)	Saline to Subject (mL)
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Applicable for Depletion/Exchange Procedures
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
AC=anticoagulant; Hct=hematocrit; WB=whole blood
Listing Status: DRAFT; SAS Program: Listing 16.14.sas

Listing 16.15.1
Listing of Procedure Results
All Subjects Enrolled (N=xx)

Subject ID	Procedure Time (minutes)	End Hct (%)	Fluid Balance (mL)	WB Processed (mL)	Replacement Fluid to Subject (mL)	AC to Subject (mL)	AC Used (mL)	Red Blood Cell Mass Balance (mL) [1] Theoretical	Red Blood Cell Mass Balance (mL)[1] Empirical
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
AC=anticoagulant; Hct=hematocrit; WB=whole blood
Listing Status: DRAFT; SAS Program: Listing 16.15.1.sas

Listing 16.15.2
Listing of Procedure Results
All Subjects Enrolled (N=xx)

Subject ID	Saline to Subject (mL)	Replacement Fluid Albumin Returned (mL)	Replacement Fluid RBC Returned (mL)	Replacement Fluid Saline Returned (mL)[1]	Custom Replacement Fluid Returned (mL)[1]
xxxx	xx	xx	xx	xx	xx
xxxx	xx	xx	xx	xx	xx
xxxx	xx	xx	xx	xx	xx
xxxx	xx	xx	xx	xx	xx

Clinical Study Protocol: AMIC-003-CMD
[1]Applicable for Depletion/Exchange procedures
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
RBC=red blood cell
Listing Status: DRAFT; SAS Program: Listing 16.15.2.sas

Listing 16.16
Listing of Primary Endpoint
All Subjects Enrolled (N=xx)

Subject ID	Pre-Procedure Hemoglobin S (%)	Post-Procedure Hemoglobin S (%)	FCR[1] (%)	Actual FCR[2] (%)	Calculated A:T FCR Ratio[2]
xxxxx	xx.xx	xx.xx	xx.xx	xx.xx	x.xx
xxxxx	xx.xx	xx.xx	xx.xx	xx.xx	x.xx
xxxxx	xx.xx	xx.xx	xx.xx	xx.xx	x.xx

Clinical Study Protocol: AMIC-003-CMD
[1]Fraction of Cells Remaining reported by AMICUS at end of procedure.
[2]For calculated parameters refer to algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
FCR=fraction of cells remaining
Listing Status: DRAFT; SAS Program: Listing 16.16.sas

Listing 16.17.1
Listing of Secondary Endpoints[1]
All Subjects Enrolled (N=xx)

Subject ID	**Depletion Hct Accuracy[2] (%)**	**Subject Depletion WBC Percent Loss[2] (%)**	**Subject Depletion RBC Percent Loss[2] (%)**	**Subject Depletion Platelet Percent Loss[2] (%)**	**Subject Depletion Plasma Hb Delta[2] (mg/dL)**	**Target End Hct Accuracy (%)**	**Subject WBC Percent Loss (%)**	**Subject RBC Percent Loss (%)**	**Subject Platelet Percent Loss (%)**	**Subject Plasma Hb Delta (mg/dL)**
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.xx	xx.xx	xx.xx	xx.xx
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.xx	xx.xx	xx.xx	xx.xx
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.xx	xx.xx	xx.xx	xx.xx
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.xx	xx.xx	xx.xx	xx.xx
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.xx	xx.xx	xx.xx	xx.xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to algorithm document (AD)
[2]Applicable for Depletion/Exchange procedures
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Hct=hematocrit; RBC=red blood cell; WBC=white blood cell
Listing Status: DRAFT; SAS Program: Listing 16.17.1.sas

Listing 16.17.2
Listing of Waste Material for Secondary Endpoints[1]
All Subjects Enrolled (N=xx)

	Depletion/Exchange Procedures						Exchange Procedures		
Subject ID	**Depletion Phase Waste Material Volume (mL)**	**Exchange Phase Waste Material Volume (mL)**	**Depletion Phase Waste WBC Count ($x10^{10}$)**	**Exchange Phase Waste WBC Count ($x10^{10}$)**	**Depletion Phase Waste Platelet Count ($x10^{11}$)**	**Exchange Phase Waste Platelet Count ($x10^{11}$)**	**Waste Material Volume (mL)**	**Waste WBC Count ($x10^{10}$)**	**Waste Platelet Count ($x10^{11}$)**
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xxx.x	xx.x	xx.x	xxx.x
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xxx.x	xx.x	xx.x	xxx.x
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xxx.x	xx.x	xx.x	xxx.x
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xxx.x	xx.x	xx.x	xxx.x
xxxxx	xx.x	xx.x	xx.x	xx.x	xx.x	xxx.x	xx.x	xx.x	xxx.x

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
WBC=white blood cell
Listing Status: DRAFT; SAS Program: Listing 16.17.2.sas

Listing 16.17.3
Listing of End Hematocrit
All Subjects Enrolled (N=xx)

Subject ID	Target Depletion Hct[1] (%)	Subject Post-Depletion Phase Hct[2] (%)	Delta End of Depletion Phase Hct[5] (%)	Target Exchange End Hct[3] (%)	Procedure Results End Hct[4] (%)	Subject Post-Procedure Hct[2] (%)	Delta End of Exchange Hct[5] (%)
xxxxx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx
xxxxx	xx	xx	xx	xx	xx	xx	xx

Clinical Study Protocol: AMIC-003-CMD
[1]End Hct (%) results reported Post-Depletion Phase.
[2]Subject laboratory measured values
[3]Target Hct entered Pre-Procedure
[4]End Hct (%) results reported Post-Procedure
[5]For calculated parameters refer to the algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done; Hct=hematocrit;
Listing Status: DRAFT; SAS Program: Listing 16.17.3.sas

Listing 16.18
Listing of Replacement RBC Unit Parameters
All Subjects Enrolled (N=xx)

Subject ID	Type of RBC Unit	Unit ID Number	Date Sample Drawn	Time Sample Drawn	Hct (%)	Volume (mL)	Total Volume (mL)	ABO Type/ Rh Factor	Expiration Date	Plasma Hb (mg/dL)	Confirmation of Sickle Trait Negative	Confirmation of Leukoreduction	Confirmation of RH (D) Compatibility
xxxxx	CPD RBCs	xx	Mmm-dd-yyyy	hh:mm	xx	xx	xx	xx	Mmm-dd-yyyy	xx	Yes	Yes	Yes
xxxxx	Other	xx	Mmm-dd-yyyy	hh:mm	xx	xx	xx	xx	Mmm-dd-yyyy	xx	No	No	Yes
xxxxx	Washed RBCs	xx	Mmm-dd-yyyy	hh:mm	xx	xx	xx	xx	Mmm-dd-yyyy	xx	No	Yes	No

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Hb=hemoglobin; Hct=hematocrit; RBC=red blood cell
Listing Status: DRAFT; SAS Program: Listing 16.18.sas

Listing 16.19
Listing of Device Alarms
All Subjects Enrolled (N=xx)

Subject ID	Did alarm(s) occur during the procedure?	If yes, record all alarms that occurred	Frequency (Occurrence per procedure) x
xxxxx	Yes	ACD Flow Problem	4
xxxxx	No		
xxxxx	Yes	Blood Warmer Prime Flow Problem	2
xxxxx	Yes	Empty Saline	3

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Listing Status: DRAFT; SAS Program: Listing 16.19.sas

Listing 16.20
Listing of Waste Material - RBC Depletion/Exchange Procedures
All Subjects Enrolled (N=xx)

	RBC Depletion Phase								RBC Exchange Phase							
Subject ID	**Gross Weight (g)**	**Tare Weight (g)**	**Volume(mL)[1]**	**WBC Count ($x10^3/\mu L$)**	**Total WBC Count ($x10^{10}$)[1]**	**Platelet Count ($x10^3/\mu L$)**	**Total Platelet Count ($x10^{11}$)[1]**	**Hct (%)**	**Gross Weight (g)**	**Tare Weight (g)**	**Volume(mL)[1]**	**WBC Count ($x10^3/\mu L$)**	**Total WBC Count ($x10^{10}$)[1]**	**Platelet Count ($x10^3/\mu L$)**	**Total Platelet Count ($x10^{11}$)[1]**	**Hct (%)**
xxxxx	xxx	xx	xx	xx.x	xx.x	xx	xx.x	xx	xxx	xxx	xx	xx.x	xx.x	xx	xx.x	xx
xxxxx	xxx	xx	xx	xx.x	xx.x	xx	xx.x	xx	xxx	xxx	xx	xx.x	xx.x	xx	xx.x	xx
xxxxx	xxx	xx	xx	xx.x	xx.x	xx	xx.x	xx	xxx	xxx	xx	xx.x	xx.x	xx	xx.x	xx
xxxxx	xxx	xx	xx	xx.x	xx.x	xx	xx.x	xx	xxx	xxx	xx	xx.x	xx.x	xx	xx.x	xx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Hct=hematocrit; RBC=red blood cell; WBC=white blood cell
Listing Status: DRAFT; SAS Program: Listing 16.20.sas

Listing 16.21
Listing of Waste Material - RBC Exchange
All Subjects Enrolled (N=xx)

Subject ID	Gross Weight (g)	Tare Weight (g)	Volume (mL)[1]	WBC Count ($x10^3/\mu L$)	Total WBC Count ($x10^{10}$)[1]	Platelet Count ($x10^3/\mu L$)	Total Platelet Count ($x10^{11}$)[1]	Hct (%)
xxxxx	xx	xx.x	xx	xx	xx.x	xx	xx.x	xxx
xxxxx	xx	xx.x	xx	xx	xx.x	xx	xx.x	xxx
xxxxx	xx	xx.x	xx	xx	xx.x	xx	xx.x	xxx
xxxxx	xx	xx.x	xx	xx	xx.x	xx	xx.x	xxx

Clinical Study Protocol: AMIC-003-CMD
[1]For calculated parameters refer to algorithm document (AD)
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Hct=hematocrit; WBC=white blood cell
Listing Status: DRAFT; SAS Program: Listing 16.21.sas

Listing 16.22
Listing of Protocol Deviation
All Subjects Enrolled (N=xx)

Subject ID	Was there a deviation?	Date of Deviation	Protocol Deviation	Specify
xxxxx	Yes	Mmm-dd-yyyy	Inclusion Criteria	Subject ≥ 6 years old
xxxxx	No	Mmm-dd-yyyy	Exclusion Criteria	Subjects who are pregnant
xxxxx	Yes	Mmm-dd-yyyy	Sampling/ Testing Issues	Sample Lost/Broken/Mislabeled
xxxxx	No	Mmm-dd-yyyy	Procedure Related Issues	Incorrect Use
xxxxx	Yes	Mmm-dd-yyyy	Subject receives the wrong treatment or incorrect dose	Randomization
xxxxx	Yes	Mmm-dd-yyyy	Informed consent issues (specify)	
xxxxx	No	Mmm-dd-yyyy	Follow-Up not performed	
xxxxx	Yes	Mmm-dd-yyyy	Follow-Up outside of window	
xxxxx	No	Mmm-dd-yyyy	Other	

Clinical Study Protocol: AMIC-003-CMD
Note: NA=Not Applicable; UNK=Unknown; ND=Not Done
Listing Status: DRAFT; SAS Program: Listing 16.22.sas