TERUMO BLOOD AND CELL TECHNOLOGIES

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CLINICAL INVESTIGATION PLAN

Study Title:	An In Vivo 24-Hour Recovery Study of Leukoreduced RBCs After Automated Separation of Whole Blood by the Reveos System and Storage for 42 Days
Study Number:	CTS-5085
Study Device:	The Reveos® Automated Blood Processing System (Reveos System)
Legal Manufacturer:	Terumo Blood and Cell Technologies 10811 West Collins Avenue; Lakewood, CO 80215; USA Phone: +1 303-231-4832
Sponsor:	Terumo Blood and Cell Technologies 10811 West Collins Avenue; Lakewood, CO 80215; USA Phone: +1 303-231-4832
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Funded By:	Terumo Blood and Cell Technologies

Version/Date:	Version 3.0: 11 March 2022

Confidentiality Statement

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DOCUMENT REVISION HISTORY

Study Title:	An In Vivo 24-Hour Recovery Study of Leukoreduced RBCs After Automated Separation of Whole Blood by the Reveos System and Storage for 42 Days	
Study Number:	CTS-5085	
CIP Amendment Version and Date:	Version 3.0 11 March 2022	
Replaces CIP Version and Date:	Version 2.0: 11 August 2022	
Rationale:	Typographical copy and paste errors were noted and corrected to align with FDA criteria for in vitro RBC quality metrics per Vostal presentation criteria (Reference # 7). This change is reflected in sections 13.2, 13.3 and are detailed in the table below.	
Section(s)	**Used to Read:**	**Now Reads (new wording bolded):**
Section 13 .2. Visit 2 - Day 0, third last sentence in the section.	Should LR-RBC Mass Recovery after filtration not meet recovery >85% or Leukoreduction not meet required FDA limit (< 5 x 106 WBC/per unit) LR-RBC unit will be discarded and the participant will be withdrawn from the study.	Should LR-RBC Mass Recovery after filtration not meet recovery **≥ 85%** or Leukoreduction not meet required FDA limit (< 5 x 10^6 WBC/per unit) LR-RBC unit will be discarded and the participant will be withdrawn from the study.
Section 13.3 Visit 3 (Day 42), REINFUSION -fifth paragraph	Should LR-RBC not meet hemolysis requirement of < 1 % after storage, the units will not to be further processed and will be discarded. The participant will be withdrawn from the study before reinfusion	Should LR-RBC not meet hemolysis requirement of **≤ 1 %** after storage, the units will not to be further processed and will be discarded. The participant will be withdrawn from the study before reinfusion
Section 13.3: Visit 3 (Day 42): Procedures and data recorded from visit 3 (Day 42) Bullet 4	Confirm of continued eligibility prior to reinfusion of radiolabeled cells (record current health status, current medications, negative RBC bacterial testing and/ or visual inspection, donor viral screen, hemolysis <1% of stored LR-RBC)	Confirm of continued eligibility prior to reinfusion of radiolabeled cells (record current health status, current medications, negative RBC bacterial testing and/ or visual inspection, donor viral screen, hemolysis **≤1%** of stored LR-RBC)

SYNOPSIS

Sponsor:	Terumo Blood and Cell Technologies
Study Title:	An In Vivo 24-Hour Recovery Study of Leukoreduced RBCs After Automated Separation of Whole Blood by the Reveos System and Storage for 42 Days
Study Number:	CTS-5085
Device Description:	The Reveos® Automated Blood Processing System (Reveos system) is an automated whole blood processing system, not cleared for use in the United States. The Reveos System has been available outside the United States since 2012 and is seeking United States Food and Drug Administration (FDA) 510(k) clearance as an automated whole blood processor. The Reveos System is an integrated manufacturing system that processes whole blood (WB) units into blood components and designed to minimize manual blood processing variables resulting from processing time, product and procedural variability. The Reveos System consists of the primary device (equipment) that uses centrifugal force to separate whole blood into its components, a disposable blood bag set to collect and store separated components, and a software program to manage the operations. The Reveos disposable blood bag set contains CPD (citrate phosphate dextrose) anticoagulant, additive solution formula 5 (AS-5), and a red blood cell (RBC) leukoreduction filter. The Reveos System can simultaneously process up to 4 whole blood units into 4 RBC units, 4 leukoreduced plasma units, and 4 interim platelet units (IPU). The CPD/AS-5 RBC product is leukoreduced and may be stored up to 42 days.
Intended Use:	**Intended Use of the Reveos Device** The Reveos device is intended to automatically separate units of whole blood into blood components. **Intended Use and Description of the Reveos Blood Bag Set** The Reveos Blood Bag Set is intended to collect a unit of whole blood and to process the unit on the Reveos device, producing blood components. **Intended Use of the Reveos System Manager Software** The Reveos System Manager is a software application that manages Reveos procedures and processing data.
Objectives:	The primary objective of this study is to evaluate whether the LR-RBCs derived from whole blood and processed with the Reveos System meet FDA criteria for 24-hour recovery after 42-day storage.
Primary Endpoint:	The primary endpoint is the 24-hour in vivo RBC recovery after 42-day storage.

Study Design:	This is a prospective, open-label, multicenter study to evaluate whole blood derived red blood cells processed using the Reveos System. The main objective is autologous in-vivo recovery of radiolabeled leukoreduced RBCs derived from whole blood processed using the Reveos System and stored for 42 days. **DAY -14- 0** Screening for all participants. **DAY 0** One (1) unit of whole blood (500mL +/- 10%) will be collected, and the whole blood unit will be processed with the Reveos System within 8 hours. The whole blood will be separated into three blood components: red blood cells, plasma and platelets. RBCs will be leukoreduced with red blood cell (RBC) leukoreduction filter integrated into the Reveos Blood Bag Set. RBC mass recovery and leukoreduction post filtration will be measured. LR-RBC units will be stored at 1-6°C for 42 days. Plasma and platelet products will be discarded per site policy. **DAY 42:** Stored RBCs will be tested for hemolysis, in addition visual inspection and /or bacterial testing, and donor viral screens will be confirmed negative. Radiolabeling: An aliquot of 42-day stored autologous LR-RBCs will be radiolabeled with chromium-51 (^{51}Cr). An aliquot of freshly collected and prepared RBCs will be radiolabeled with technetium-99m (^{99m}Tc). The labeled aliquots will then be combined and infused to the autologous donor. Blood samples will be collected approximately at 5, 7.5, 10, 12.5, 15, 20, and 30 minutes post infusion. **DAY 43:** Blood sample for 24-hour RBC recovery will be drawn. This visit concludes the study.
Study Sites Planned:	Hoxworth Blood Center, Cincinnati, OH and Bloodworks Northwest, Seattle, WA
Study Duration:	Approximately 57 days per participant
Target Population:	Healthy adult participant
Number of Subjects Planned:	24 evaluable participants (up to 50 enrolled).
Inclusion Criteria:	1. Healthy volunteers., of either gender 2. Age 18 years or older. 3. Normal health status as per AABB criteria for healthy donor. 4. Able to commit to the study schedule. 5. Meets the inclusion criteria defined by the Blood Center for whole blood donor. These criteria are based on FDA Regulations and AABB standards. Note: Participants who are deferred from volunteer community donations because of travel restrictions, piercings, tattoos or other reasons by PI approval may participate in the study, as products are re-transfused to the autologous donor. 6. Participants of childbearing potential (either male or female) must agree to use medically acceptable method of contraception throughout of the study. 7. Females of childbearing potential must be willing to take a pregnancy test prior to WB donation and infusion of radiolabeled RBCs. 8. Signed and dated informed consent form.
Exclusion Criteria:	1. Pregnant or nursing females. 2. Serum ferritin <12 ng/mL 3. Has previously completed this study with evaluable data points.

	4. Participation currently, or within the past 30 days, in another investigational trial that would potentially interfere with the analysis of this investigation (eg, pharmaceutical). 5. As determined by the Investigator a. Has been diagnosed with a blood disorder(s) affecting RBC characteristics (eg, G-6PD). b. Reported history of RBC autoantibodies/autoimmune hemolytic anemia, RBC alloantibodies. c. Clinically significant acute or chronic disease d. Reported history of known hypersensitivity to technetium or chromium. e. Treatment with any medication as specified in site deferral list (based on AABB medication deferral list for blood donors). 6. Other unspecified reasons that, in the opinion of the investigator make the subject unsuitable for enrollment.
Statistical Methodology:	Based on FDA criteria for in vivo RBC quality, the following criteria will be assessed: The mean 24-hour, post-transfusion, in vivo red cell recovery of at least 75% with a standard deviation of ≤ 9%, and the lower limit of a one-sided 95% confidence interval for the population proportion of successes is ≥ 70% where an individual success is defined to be a recovery of at least 75%. If there are no more than 3 failures (ie, 3 recoveries <75%), in an N of 24 or no more than 2 failures in an N of 20, than the lower limit of a 95% one-sided will be at least 70%.

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

AABB	American Association of Blood Banks
ADE	Adverse Device Effect
AE	Adverse Event
AS-5	Additive Solution 5
AUC	Area Under the Curve
BK080010	510(k) Approval Number for Atreus
CRF	Case Report Form
CDRH	Center for Devices and Radiological Health
CFR	US Code of Federal Regulations
CIP	Clinical Investigation Plan
CPD	Citrate Phosphate Dextrose
CPM	Counts per Minute
Cr-51	Sodium Chromate 51
CTA	Clinical Trial Agreement
CTS-5085	Protocol Number
DMC	Data Monitoring Committee
EC	Ethics Committee
EDC	Electronic Data Capture
FDA	US Food and Drug Administration
G-6PD	Glucose 6 Phosphate Dehydrogenase Deficiency
GCP	Good Clinical Practice
Hgb	Hemoglobin
Hct	Hematocrit
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	Helsinki, International Conference of Harmonization
ICSH	International Committee for Standardization in Hematology
IDE	Investigational Device Exemption
IPU	Interim Platelet Unit
IRB	Institutional Review Board
ISO	International Organization for Standardization
LTFU	Lost to Follow-up
MDR	EU Medical Device Regulation
mL	Milliliter
MOP	Manual of Procedures
ng	Nanogram(s)
PE	Procedure Emergent

PEAE	Treatment Emergent Adverse Event
PI	Principal Investigator
PVC	Polyvinyl Chloride
RBC	Red Blood Cell
LR	Leukoreduced Red Blood Cell
SAE	Serious Adverse Event
SD	Standard Deviation
SOP	Standard Operating Procedure
Tc-99m	Technetium-99m pertechnetate
TMF	Trial Master File
UADE	Unanticipated Adverse Device Effect
US	United States
USID	Unique Study Identification Number
WB	Whole Blood

1 STATEMENT OF COMPLIANCE

This study will be conducted according to this Clinical Investigation Plan (CIP), Good Clinical Practice (GCP) as described in the International Council for Harmonization Guidance for Industry E6(R2), and, as applicable, United States Code of Federal Regulations (CFR) concerning clinical studies (45 CFR Part 46; 21 CFR Parts 50, 56, 312 and 812), International Organization for Standardization (ISO) 14155:2020, European Union Medical Device Regulation (EU MDR) 2017/745, and other regulatory requirements of the region(s) where the study is conducted. The study will not begin until the required approvals or favorable opinions from the Ethics Committee (EC) and regulatory authority have been obtained, as applicable. As directed, any additional requirements imposed by the EC or regulatory authority will be followed. All individuals responsible for the design and conduct of this trial have completed Human Subjects Protection Training. Any applicable information required per above regulations that is not contained in this CIP may be submitted in separate documentation and will be attached to the CIP as an appendix. All essential documents will be archived together in the Trial Master File (TMF).

2 INTRODUCTION

Terumo Blood and Cell Technologies is a corporation that continuously develops medical devices for blood manufacturing and cell therapies. These devices include products for whole blood (WB) collection and processing, apheresis, therapeutic apheresis, pathogen reduction, and cell expansion. The focus in this study is whole blood processing with the Reveos® Automated Blood Processing System (Reveos System).

Blood transfusions have been widely used in medical practice since the early 20th century.[1] Blood transfusion is the most common procedure during hospital stays in the United States.[2] In 2017 over 12 million WB and apheresis red blood cell (RBC) units were collected in the US and approximately 85% of these units were WB collections.[3] Patients may receive a unit of WB or individual blood components to treat any particular condition and the Global Database on Blood Safety reports that in high income countries 97% of WB donations are processed into blood components.[4]

Whole blood consists of blood components with cellular elements, colloids, and crystalloids. Having different relative densities, sedimentation rate, and size, blood components can be separated when centrifugal force is applied. This separation is controlled in part by the specific gravities of these components including, in increasing order, plasma, platelets, leukocytes, and RBCs.[5] WB units are currently separated into RBC, plasma, and platelet components through a labor intensive, largely manual processes, often including multiple steps. The first fully automated system for WB unit processing developed by Terumo Blood and Cell Technologies was Atreus (BK080010), which could process one unit of WB into blood components in one run.[6]

The Reveos System can process up to four (4) WB units in one run. It combines balancing, centrifugation, component separation, and sealing into one platform.

As an automated blood processor, the Reveos System is beneficial in reducing manual blood processing drawbacks including processing time, and variability in the procedures and end product leading to standardized blood component yield and quality.

The aim of this study is to evaluate the in-vivo 24-hour recovery of autologous RBCs produced with the Reveos System and stored for 42 days, in order to meet the FDA's criteria for manufactured RBCs.

3 DEVICE DESCRIPTION

The Reveos® Automated Blood Processing System is an automated WB processing system. Within the protocol it will be referred as Reveos System. The Reveos System has been released for sale in certain regions accepting the CE mark since 2013, Terumo Blood and Cell

Technologies is seeking US Food and Drug Administration (FDA) 510(k) clearance of the Reveos System as an automated whole blood processor.

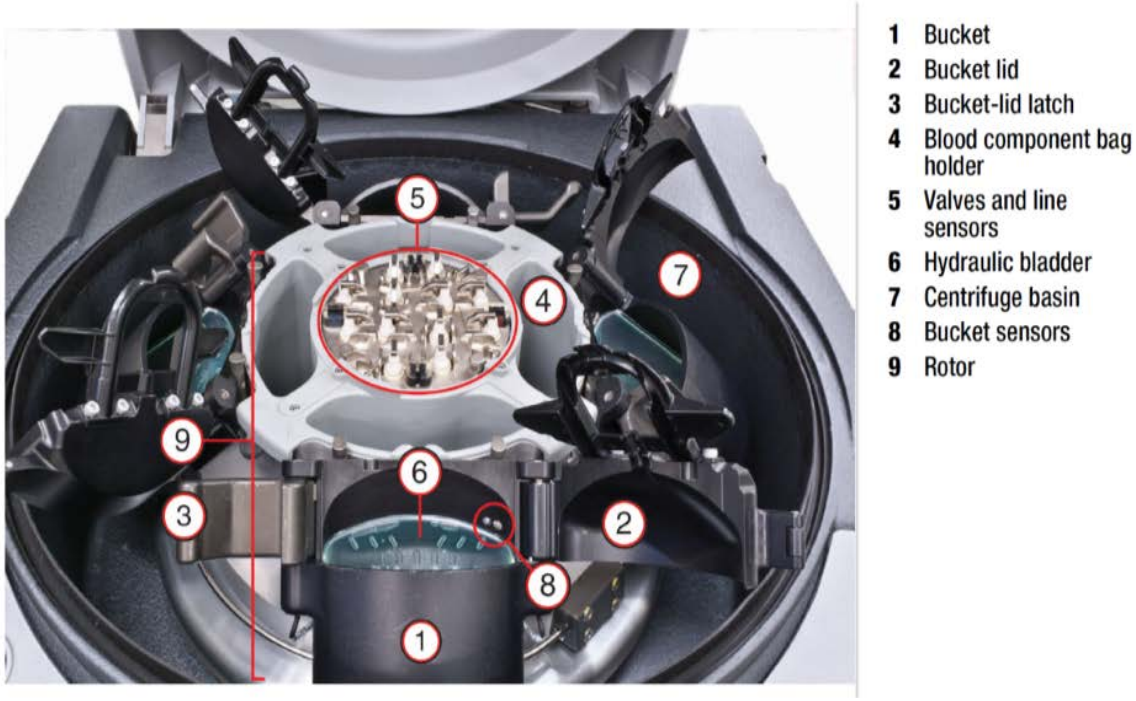
The Reveos System consists of the Reveos device (processing equipment) that uses centrifugal force to separate WB into its components, a disposable Reveos blood bag set intended to collect and store separated components, and a software program to manage the operations.

Reveos Device

The Reveos System (Figure 3-1) is an easy-to-use platform that automates and integrates the manual steps involved in WB processing. The system processes up to 4 units of WB to produce RBCs, leukoreduced plasma, platelets, and residual leukocytes with a single centrifugation step. The Reveos System (Figure 3-2) consists of a computer-controlled centrifuge equipped with a rotor with 4 fixed buckets, in which the Reveos blood bag set can be placed. Each bucket contains a hydraulic-driven expressor to press the different fractions of the centrifuged blood from the top to the satellite bags.

Figure 3-1 Reveos Equipment

Figure 3-2 Reveos Device Rotor Compartment



The Reveos System produces three components from each unit of whole blood processed: a plasma unit, an RBC unit, and an interim platelet unit (IPU) Interim Platelet Unit (IPU). The IPU is pooled with other IPUs to create a therapeutic platelet dose. A residual leukocytes unit is also produced as a by-product. All buckets must contain a loaded blood bag set or counterbalance bag before beginning a procedure.

Reveos System Manager

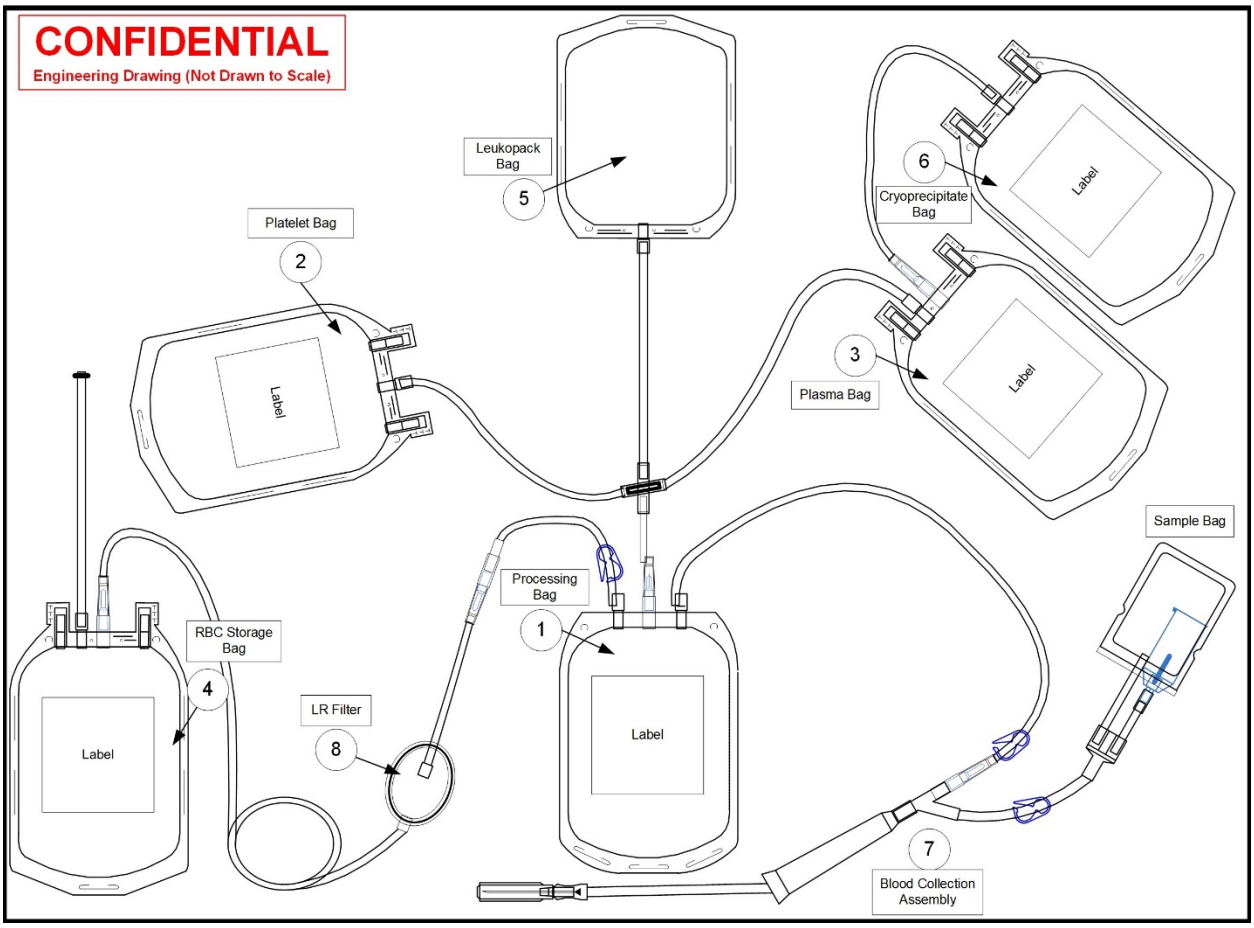
Reveos System Manager is a software application that manages procedures and product data. This data is automatically transferred from the Reveos device to the Reveos System Manager. The Reveos System Manager lets users perform the following tasks:

- Configure Reveos devices
- Define users and assign permissions
- Configure barcodes and procedures
- Record and output process and product data
- Track information entered into the Reveos System Manager
- Standardization of workflows
- Report generation

Reveos Blood Bag Set

The Reveos blood bag set (Figure 3-3) consists of medical grade Polyvinyl Chloride (PVC) container closures (i.e. blood component bags and tubing). The blood bag set is steam sterilized, single use disposable set consisting of a needle connected to a sampling bag and a WB collection bag used to collect and process 500 mL ±10% WB. The WB bag has 70 ml of anticoagulant (CPD-citrate phosphate dextrose), and the RBC component bag has 111 mL of additive solution formula AS-5 (Optisol), and an integrated RBC leukoreduction filter.

Figure 3-3 The Reveos blood bag set configuration



A general overview of the investigational Reveos blood bag set with: 1) WB bag (processing bag) containing CPD anticoagulant, 2) Platelet bag, 3) Plasma bag, 4) RBC bag containing red cell additive solution (AS-5), 5) Residual leukocyte bag, 6) Cryoprecipitate bag 7) Blood collection assembly (needle, needle injury protector, sample/diversion bag) 8) RBC leukoreduction filter.

The Reveos System primary equipment (processing device) does not come into contact with the study participants. After Reveos System processing, RBC units are diluted with AS-5 additive solution and transferred through an integrated leukoreduction filter to the RBC bag for storage.

CPD and AS-5

(Optisol) solutions used in the disposable sets were approved for use with TERUFLEX (or IMUFLEX) blood bag Systems in 1988 (NDA: BN880217).

Citrate Phosphate Dextrose (CPD) (Table 3-1)

The WB bag has 70 ml of anticoagulant CPD.

Table 3-1 The composition of CPD

CPD Solution		
Description	**Concentration (1000ml)**	**Reveos Blood Bag Set (70ml)**
Dextrose Anhydrous	23.2 g	1.624 g
Sodium Citrate	26.3 g	1.841 g
Citric Acid	3.27 g	0.229 g
Sodium Dihydrogen Phosphate Dihydrate	2.51 g	0.176 g
Water for Injection	977 ml	up to 70 ml

Additive solution, AS-5 (Table 3-2)

The RBC component bag has 111 mL of additive solution formula AS-5.

Table 3-2 The composition of AS-5

AS-5 Solution		
Description	**Concentration (1000ml)**	**Reveos Blood Bag Set (111ml)**
Dextrose Anhydrous	8.18 g	0.908 g
Sodium Chloride	8.77 g	0.973 g
Mannitol	5.25 g	0.583 g
Adenine	0.315 g	0.035 g
Water for Injection	984 ml	up to 110 ml

Relevant research personnel will be trained on the use of the Reveos System. Device accountability will be tracked throughout the study.

The investigational products will be labeled per 812.5 (a) *"Caution- Investigational Device. Limited by Federal (or United States) law to investigational use."*

4 INTENDED USE STATEMENT

Intended Use of the Reveos Device

The Reveos device is intended to automatically separate units of whole blood into blood components.

Intended Use and Description of the Reveos Blood Bag Set

The Reveos Blood Bag Set is intended to collect a unit of whole blood and to process the unit on the Reveos device, producing blood components.

Intended Use of the Reveos System Manager Software

The Reveos System Manager is a software application that manages Reveos procedures and processing data.

5 NONCLINICAL STUDIES

Nonclinical studies for verification and validation are ongoing for the Reveos System.

To date a feasibility, in vitro study for Reveos System processed RBCs has been done. The study evaluated hemolysis on Reveos System processed and LR RBC units (n=52). The units were stored in CPD/AS-5 for 42 days. The mean hemolysis ± SD was 0.18% ± 0.09% with range of 0.08% - 0.55%, meeting FDA defined criteria for hemolysis.

6 CLINICAL TRIAL EXPERIENCE

The investigational Reveos System intended for US market does not have clinical trial experience.

7 RATIONALE FOR THE CURRENT STUDY

Terumo Blood and Cell Technologies is seeking 510(k) clearance from FDA/CBER for the Reveos® Automated Blood Processing System (Reveos System).

The proposed study will provide validation on the in vivo performance of LR-RBC units derived from WB processed with the Reveos System. The results will provide data as to whether the Reveos System produced LR-RBC can maintain required levels of 24-hour in vivo recovery that meet FDA criteria for RBC.[7]

8 OBJECTIVES

8.1 Primary Objective

The primary objective of this study is to evaluate whether the LR-RBC derived from WB processed with the Reveos System meet FDA criteria for in vivo 24-hour recovery.

Based on FDA criteria for in vivo RBC quality, the following criteria will be assessed:

LR-RBC mean 24-hour recovery ≥ 75% with SD ≤9 % and one-sided lower confidence limit for population proportion of RBC in vivo recovery 70%†. Success is >75%.

†Allows for low recoveries (<75%) in 2/20 or 3/24 volunteers.

If all three criteria are met, the Reveos System will be deemed to have met the FDA criteria for 24-hour in vivo RBC recovery.

Performance criteria will be evaluated in healthy adult participants, who receive radiolabeled, autologous infusions of LR-RBC components after being stored for 42 days at 1-6°C.

9 ENDPOINTS

9.1 Primary Endpoint

The primary endpoint is the 24-hour in vivo RBC recovery.

LR-RBC mean 24-hour recovery ≥ 75% with SD ≤9 % and one-sided lower confidence limit for population proportion of RBC in vivo recovery 70%†. Success is >75%.

†Allows for low recoveries (<75%) in 2/20 or 3/24 volunteers.

10 INVESTIGATIONAL PLAN

10.1 Study Design

Prospective:

- Evaluation of LR- RBC recovery
- Healthy adult volunteers
- 24 total evaluable participants enrolled (i.e., approximately 12 participants at each site)
- Single arm - autologus reinfusion of radiolabelled RBCs
- Double radiolabel with ^{51}Cr (LR-RBCs for recovery) and ^{99m}Tc (Fresh RBCs for RBC volume/mass determination)

Multi- Center:

- Hoxworth Blood Center
- Bloodworks Northwest

This study evaluates Day 42 RBC recovery. After donation and processing of WB with the Reveos System, the RBCs are leukoreduced (LR) and stored for 42 days. An autologous aliquot of stored LR-RBCs and fresh RBCs will be radiolabeled with ^{51}Cr and ^{99m}Tc, respectively, and reinfused to the donor. RBC recovery testing will be performed at 24-hour post-infusion.

All procedures related to labeling, infusion, sampling and recovery/mass determination will follow site common standardized procedures and standard operating procedures (SOPs).

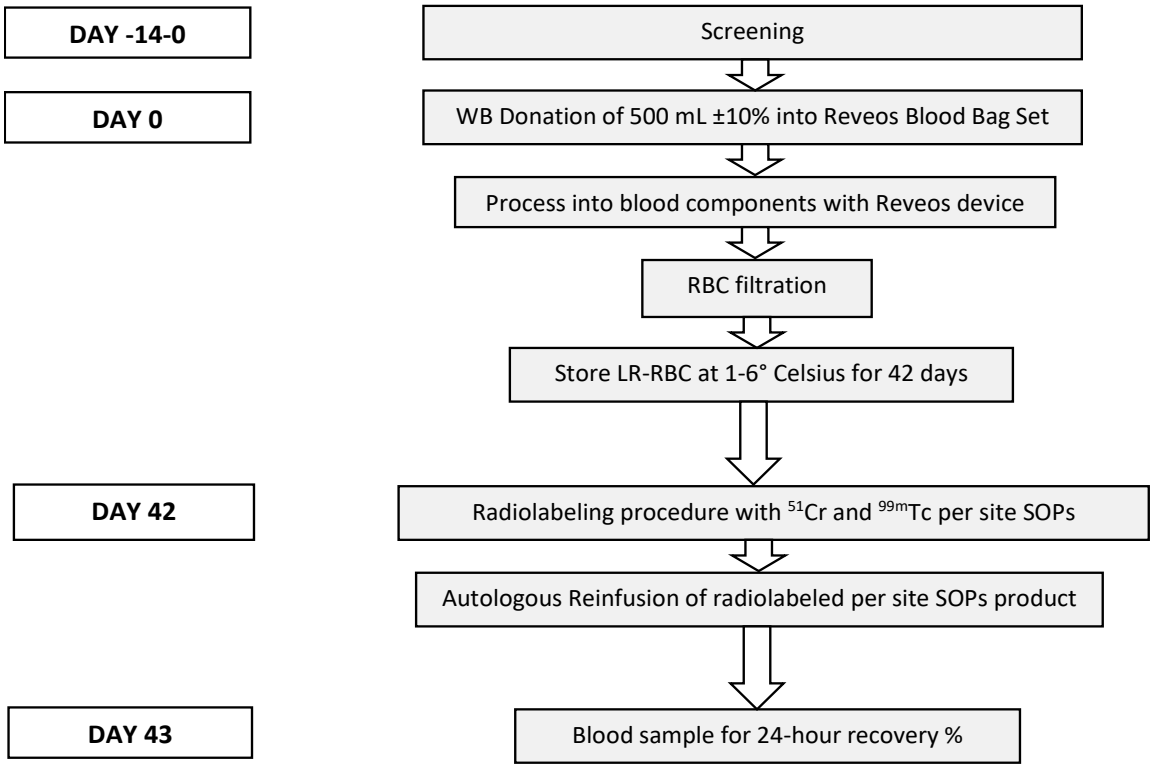
The procedures for radiolabeling of RBCs to evaluate RBC recovery are based and adapted from methods recommended by International Committee of Standardization in Haematology (ICSH) *Recommended Methods for Radioisotope Red-Cell Survival Studies* 1980[8] and previously published literature by Moroff and colleagues *Proposed Standardization of Methods for Determining the 24-Hour Survival of Stored Red Cells,* 1984[9]. The method of calculating the blood volume with ^{99m}Tc is based on the ICSH *Recommended Methods for measurement of Red-Cell And Plasma Volume* 1980[10].

10.2 Study Duration

The total study duration is expected to last 6 months from first participant enrollment. Each study participant will have a total of 4 study visits (Figure 10-1) including screening within a time span of 57 days (1.9 months). Visit details are described in section 13.

- Study visit 1(Screening 0-14 days)
- Study visits 2 to 4 (over approximately 43 days)

Figure 10-1 Study Flow



11 STUDY POPULATION

11.1 Number of Participants and Selection

It is estimated that up to 50 volunteers will be enrolled to allow targeted twenty-four (24) evaluable recovery endpoints. Healthy adult volunteer study participants will be enrolled at two (2) centers; approximately 12 at each study center. Study participants will come from the general population. Eligible WB donors exhibiting normal health status and vital signs as determined by standard American Association of Blood Banks (AABB) blood donation criteria.

Volunteers who cannot commit to completing all study requirements should not be considered for enrollment. No medical records are accessed during inclusion exclusion determination, all medical history is based on known or self-reported history of the prospective participants. A participant can screen multiple times but participate only once for the study. The Informed Consent process described below will be undertaken following determination of initial eligibility.

11.2 Inclusion Criteria

Inclusion criteria for participant selection:

1. Healthy volunteers, of either gender
2. Age 18 years or older.
3. Normal health status as per AABB criteria for healthy donor.
4. Able to commit to the study schedule.
5. Meets the inclusion criteria defined by the Blood Center for whole blood donor. These criteria are based on FDA Regulations and AABB standards. Note: Participants who are deferred from volunteer community donations because of travel restrictions, piercings, tattoos or other reasons by PI approval may participate in the study, as products are re-transfused to the autologous donor.
6. Participants of childbearing potential (either male or female) must agree to use medically acceptable method of contraception throughout of the study.
7. Females of childbearing potential must be willing to take a pregnancy test prior to WB donation and infusion of radiolabeled RBCs.
8. Signed and dated informed consent form.

11.3 Exclusion Criteria

Exclusion criteria for participant selection:

1. Pregnant or nursing females.
2. Serum ferritin <12 ng/mL
3. Has previously completed this study with evaluable data points.
4. Participation currently, or within the past 30 days, in another investigational trial that would potentially interfere with the analysis of this investigation (eg, pharmaceutical).
5. As determined by the Investigator
    a. Has been diagnosed with a blood disorder(s) affecting RBC characteristics (eg, G-6PD).
    b. Reported history of RBC autoantibodies/autoimmune hemolytic anemia, RBC alloantibodies.
    c. Clinically significant acute or chronic disease
    d. Reported history of known hypersensitivity to technetium or chromium.
    e. Treatment with any medication as specified in site deferral list (based on AABB medication deferral list for blood donors).
6. Other unspecified reasons that, in the opinion of the investigator make the subject unsuitable for enrollment.

12 ENROLLMENT

12.1 Recruitment and Pre-Screening

Recruitment and pre-screening activities to identify appropriate candidates for study inclusion will be conducted prior to obtaining informed consent. These pre-screening measures will be in accordance with Institutional Review Board (IRB) guidelines and approvals. Because this period precedes informed consent, study documentation (eg, AE reporting) will not be required during this period.

Specific activities may include:

1. Conducting pre-screening measures to identify appropriate candidates from blood center donor lists include:
   a. Reviewing for qualified donor status
   b. Reviewing donor demographics and phlebotomy history
2. Introducing study and suggesting possibility of entry to potential participants.
3. Providing information about the study to include informed consent process, required study schedule, specific study procedures, risks, benefits and compensation.
4. Providing a copy of the informed consent forms (ICFs) to potential participants for review.

12.2 Informed Consent Process

Prior to participant involvement in this study, the Investigator must obtain written IRB approval for the Clinical Investigation Plan (CIP) and ICF. A copy of the site-specific ICF must be provided to the Sponsor for review and approval prior to submission to the IRB for approval. The approved ICF will clearly reflect the IRB approval date. Once approved, the ICF must be provided to the Sponsor prior to implementation in this study. All study participants must provide written informed consent using the Sponsor and IRB approved ICF.

Once the participants initial suitability for study participation has been determined per pre-screening measures, the Investigator or person designated by the Investigator who has been trained on the CIP, will explain the nature and scope of the study, potential risks and benefits of participation, answer questions for the donor, and ask the donor to participate in the study. The study will be explained to the donor in lay terms, in English language in a quiet, non-disruptive setting. Potential participants will be given as much time and privacy as necessary to review the informed consent prior to agreeing to participate in the study. Additionally, if the donor requests, they can take a copy of the consent with them so that they can discuss potential participation with others outside the study team. If the donor agrees to participate, has read the ICF, and has had all of their questions answered, then the ICF must be signed and dated by the donor and the

person completing the consent process. A copy of the signed and dated ICF will be provided to the study participant and the original is placed in the study file.

Failure to obtain a signed ICF prior to participant involvement in the study constitutes noncompliance with the Declaration of Helsinki, International Conference of Harmonization (ICH) Good Clinical Practice (GCP), US Code of Federal Regulations (21 CFR 812), and International Organization for Standardization (ISO) 14155.

12.3 Participant Enrollment

A donor is considered an enrolled participant upon giving informed consent for study participation; this timepoint represents the beginning of a participant's involvement in the study. After informed consent has been obtained, participants will receive a unique subject identification number (USID) to de-identify participants. The USID number will use the following convention: XX-YYY, where XX is the pre-assigned site number and YYY will be a sequential number starting with 001. The USID number will be recorded on the Case Report Form (CRF). Participant identifiers such as initials or names will not be used, for example:

First participant enrolled at Site #01: John Doe = 01-001

First participant enrolled at Site #02: Jane Doe = 02-001

It is expected that some proportion of enrolled participants will not qualify for study inclusion per the screening and eligibility criteria, and some who are deemed eligible will not initiate the WB collection procedure. Participants will be considered study procedure discontinuations or study terminations if, following initiation of the WB collection, they do not complete the study procedures, as applicable and as described further in Section 13.

13 STUDY PROCEDURES

The study procedures are to be performed following the WB collection day (Day 0), and are therefore referenced as days post WB collection (e.g. the reinfusion of autologous LR-RBC will take place 42 days after the WB collection day). A study procedure schedule of events is provided in Table 13-1 Schedule of Procedures.

13.1 Visit 1 – (Day -14-0)

SCREENING

Visit 1 can take place within 14 days before WB Collection.

Screening will consist of:

1. Review and signing informed consent prior to initiating any protocol-required procedure that is not considered standard of care
2. Assign USID number

3. Review of relevant health history and medications (relevant to RBC viability and study procedures)
4. Record – Height, weight, and vital signs
5. Demographics (date of birth, gender, race, ethnic origin,)
6. Confirm subject eligibility.
7. Blood draw for Serum ferritin (ABO/Rh, standard viral screen, CBC per site SOP)

13.2 Visit 2 – Day 0

WB COLLECTION

After enrolling the participant into the study, the following baseline activities will be done for the participant and will be recorded:

1. Re-confirm eligibility
2. Physical assessment
    a. Record vital signs (pulse rate, blood pressure, temperature) and skin integrity prior WB collection
3. Female participant will have a serum or urine pregnancy test. No test is needed if participant has history of bilateral oophorectomy, hysterectomy, postmenopausal for 1 year, or PI confirmed justification
4. Collect WB into the Reveos Blood Bag Set
5. Laboratory(ies):
    a. Select complete blood count (Hgb, Hct)
    b. ABO/Rh of participant
    c. Donor laboratory tests (standard viral screen, if not done at screening)
6. Record Adverse Events (AEs)

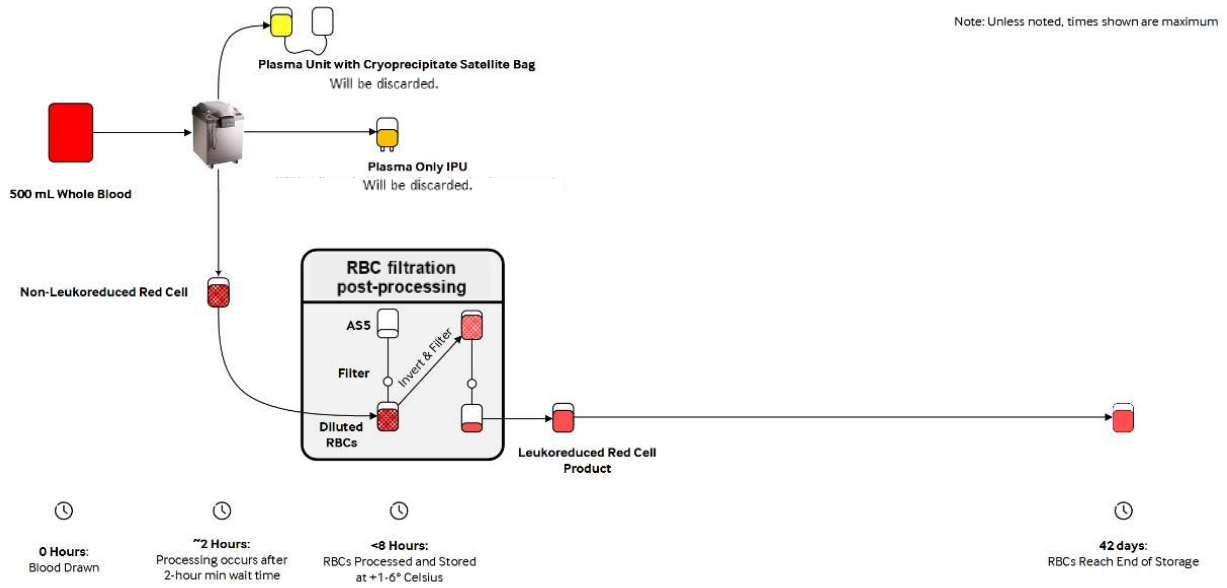
The WB collection as well as sample testing will be performed in accordance with the study site SOPs. A target final volume of 500 mL +/- 10% of WB will be collected. Thereafter, at least 2 hours after collection it will be maintained in an ambient temperature environment of 18 – 24° C until processing. Leukoreduced (LR) RBCs will be stored in < 8 hours.

Reveos System Whole Blood Processing

"Whole blood processing" in this study refers to the Reveos System separation of a WB product into its platelet, plasma and RBC components. Study staff will be trained for the use of the Reveos System. Study staff will refer to Manual of Procedures, Reveos Blood Bag Set with RBC Leukoreduction Filter Instructions For Use (Package Insert) and the Reveos® Automated Blood Processing System Operator's Manual on how to use the Reveos System.

In short summary, the Reveos Blood Bag Set with the collected WB will be placed into the Reveos System for WB processing. At the end of the separation procedure, the separated products are removed from the Reveos System device. The residual leukocyte bag, the plasma bag and the platelet bag are discarded. Figure 13-1 below shows a schematic of WB processing and RBC processing and storage.

Figure 13-1 Study RBC Processing and Storage



RBC Product Sampling and Storage

Additive Storage solution AS-5, enclosed in the bag set, will be used to prime the leukoreduction filter and RBCs will be then LR by gravitational filtration (Figure 13-1).

RBC products from the collections will be sampled pre-and post-leukoreduction for yield assessment and leukoreduction for red cell quality assessments on Day 0 (beginning of storage). The LR-RBC product will then stored for 42 days at 1-6°C.

Data recorded on Visit 2 (Day 0) from processes and products:

1. WB collection date, start and end time
2. WB weight or volume
3. Reveos System processing start and end time
4. RBC Filtration start and end time
5. RBC bag weight pre-and post-filtration
6. Select CBC pre- and post-filtration units (Hct)

7. LR-RBC Mass recovery %
8. Residual WBC content per LR-RBC unit post-filtration
9. Time of placement into refrigerated storage
10. Reveos System device serial number
11. Reveos System disposable serial/LOT number
12. Device /procedure deficiencies

Should LR-RBC Mass Recovery after filtration not meet recovery ≥ 85% or Leukoreduction not meet required FDA limit (< 5 x 10^6 WBC/per unit) LR-RBC unit will be discarded and the participant will be withdrawn from the study.

Any participants with positive viral screens will be withdrawn from the study.

Bacterial testing and/or visual inspection for RBC screening is done according to the site's research SOPs.

13.3 Visit 3 (Day 42)

REINFUSION

Visit 3 is day 42 after WB collection and marks the end of storage of LR-RBCs.

The procedures during this visit will follow site procedures for labeling, infusion, sampling and RBC recovery/mass determination (Study design 10.1).

Ensure participants viral screening results are negative prior re-infusion.

Bacterial testing and /or visual inspection for signs of unusual hemolysis or discoloration indicative of bacterial growth will be done per sites research SOP's. Affected units will not to be further processed and will be discarded.

Should LR-RBC not meet hemolysis requirement of ≤ 1 % after storage, the units will not to be further processed and will be discarded. The participant will be withdrawn from the study before reinfusion.

Female participant will have a serum or urine pregnancy test per specific procedures. Pregnancy test results must be available before re-infusion and have to be negative for the subject to continue in the study.

Measures to ensure the study donor receives his or her own (autologous) radiolabeled RBCs begin at donation when the study donor's name, birth date and unique study identifying number will be recorded on the donor registration form. Clinical sites must have a standard labeling and handling process intended to eliminate errors in linking packed RBC units with the correct study donor.

Qualified RBCs will be radiolabeled with ^{51}Cr (LR-RBC) and ^{99m}Tc (fresh blood), and then reinfused back to the original participant. Radiolabeling will be done per site procedures and SOPs (Study Design 10.1).

Procedures and data recorded from visit 3 (Day 42)

Preinfusion

1. Pregnancy test result, if applicable
2. Vital signs: Blood Pressure (BP), Pulse Rate (PR), and temperature
3. Draw blood for select CBC (Hct, Hgb), background radiation determination and for radiolabeling
4. Confirm of continued eligibility prior to reinfusion of radiolabeled cells (record current health status, current medications, negative RBC bacterial test and/ or visual inspection, donor viral screen, hemolysis ≤1% of stored LR-RBC)

Post infusion

5. Record reinfusion start and end time
6. Record vital signs: Blood Pressure (BP), Pulse Rate (PR), and temperature within 1 hour (±15 minutes) post-start reinfusion of the radiolabeled aliquots
7. Draw blood for post-infusion samples per site SOP at approximately:
    - 5 min
    - 7.5 min
    - 10 min
    - 12.5 min
    - 15 min
    - 20 min
    - 30 min
8. Complete post-infusion worksheet including, but not limited to (refer to Manual of Procedures for full detailed data collection):
    a. Exact time in minutes and seconds of post- infusion blood samples
    b. CPM for ^{51}Cr and ^{99m}Tc for post-infusion blood samples in duplicate or as many samples as per site SOPs, background and empty counting tube CPM, weight of counting tubes and infusate, CPM at time 0
    c. Hematocrit of each post-infusion sample
9. Record AEs
10. Record device/product deficiencies

13.4 Follow-Up Visits

13.4.1 Visit 4 (Day 43)

Visit 4 is 43 days after WB donation. The visit follows site SOP for determining 24-hour recovery.

A blood sample (6-10 mL) will be drawn 24 (± 2) hours post-infusion

Data recorded from visit 4

1. Complete worksheet including, but not limited to (refer to Manual of Procedures for detailed data collection):
    a. Exact time of the blood draw
    b. CPM readings from blood sample in duplicate or as many samples as per site SOPs, net CPM, corrected CPM
    c. Hematocrit(s) of the blood sample
2. 24-hour RBC recovery (%)
3. AEs

Visit 4 will conclude the participants study participation.

Primary endpoint, 24-hour RBC recovery, will be calculated from the data of this visit according to the sites's standardized in vivo RBC recovery procedure.

Data collection will be completed by both sites for RBC % recovery. Calculations for this will be conducted for enrolled participants by both sites.

Table 13-1 Schedule of Procedures

Study Procedures	Visit 1	Visit 2	Visit 3		Visit 4
	Days (-14-0) Screening	Day 0 WB collection	Day 42 Infusion		Day 43 24-hr Post-infusion
			Pre-Infusion	Post-Infusion	
Obtain informed consent	X				
Confirm eligibility	X	X			
Collect demographics (date of birth, gender, race, ethnic origin), height, and weight	X				
Record relevant medical history	X				
Blood sample for Ferritin (approximately 3.5ml)	X				
Confirm participant is healthy		X	X		

Study Procedures	Visit 1	Visit 2	Visit 3		Visit 4
	Days (-14-0) Screening	Day 0 WB collection	Day 42 Infusion		Day 43 24-hr Post-infusion
			Pre-Infusion	Post-Infusion	
Pregnancy test for women of childbearing potential[a]		X	X		
Blood sample for donor eligibility (approximately 35 ml) (Hgb or Hct, ABO, viral screen[b])	X	(X)			
WB donation 500 ml ± 10%		X			
Record serial numbers[c], LOT#, and expiry dates of equipment and disposables		X			
Label LR-RBC product with USID number		X			
Confirm LR-RBC product meets mass recovery and leukoreduction requirements		X			
Store LR-RBCs at 1°C−6°C		X			
Bacterial testing and/or visual inspection on stored LR-RBCs per site SOP [d]			X*		
Radiolabeling of blood [e]			X		
Infusion of radiolabeled sample (^{51}Cr & ^{99m}TC) [f]			X		
Blood samples Pre-infusion and post-infusion			Total of approximately 80 ml blood collected during visit 3		X 10 ml
			Pre-infusion sample	Post-infusion samples approximately at 5, 7.5, 10, 12.5, 15, 20, 30 minutes [g]	
Total blood volume drawn during the clinical investigation	Approximately 678.5 ml				
Counts per minute [h]			X	X	X
Record vital signs (PR, BP, t°)	X	X	X	X	
Record AEs, SAEs, and UADEs	X	X	X		X
Record current medications	X	X	X		X
Record Device Deficiencies		X	X		

[a] Pregnancy test is done by serum or urine test per site SOP
[b] Part of AABB criteria. If not determined within 14 days prior to planned blood collection date, then as part of standard blood bank donor screening process (all viral screen results have to be negative for infections).
[c] Record Reveos machine serial number and lot number and expiration date of the disposable set used
[d, e, f, g, h] Prescribed tasks will be done per site SOP
*Timeframe per site SOP

Abbreviations: AE = adverse event; CBC = complete blood count; HCT = hematocrit; Hgb = hemoglobin; SAE = serious adverse event; UADE = unanticipated adverse device effect; USID = Unique Subject Identification number; PR = Pulse rate; BP = Blood pressure; t° = temperature; LOT# = control number for disposable products (combination of letters, numbers, or symbols)

13.5 Long-Term Follow-Up

All Adverse Events(AEs) will be reported. AEs related to the study device or procedure will be followed until resolution, except the expected AE of mild hematoma (bruise) and/or mild infiltration, which are not followed to resolution as described in Section 16.7 otherwise there is no long term follow-up.

13.6 Participant Discontinuation/Termination

All subjects are free to withdraw from participation in this study at any time, for any reason, specified and unspecified, and without prejudice. Participants may be discontinued by the PI or study sponsor if it is in the best interest of the subject's health, the study is placed on hold or other factors. Should this occur, the reason for discontinuation must be recorded in the source documentation, and the Study Exit CRF. Factors leading to participant discontinuation may include, but are not limited to the following:

Screen failures: Participants will be considered screen failures if they fail to meet any of the eligibility criteria after signing informed consent.

Participant withdrawal: Participant participation in a clinical trial is voluntary and the participant may discontinue participation (refuse all subsequent testing and follow-up) or withdraw their consent from the study at any time without affecting their future relationship with blood center.

Participant withdrawn: Participants who test positive for infectious diseases will be notified of these results per the study site's SOPs. Results of positive infectious disease testing will be reported to state and/or local health authorities as required in each site's geography. Participant who do not return to visit 3 or 4. The collected blood fails quality checks, the blood will be considered non-evaluable for the primary endpoint analysis, the participant will not undergo reinfusion or recovery evaluations, and the participant will be discontinued from the study.

Investigator /Sponsor Decision: The investigator /may terminate the participant's participation without regard to the participant's consent if, in the judgment of the investigator, the participant is unable to continue in the study for medical or other pertinent reasons.

Lost to Follow-up (LTFU): A participant will be considered as LTFU only after three unsuccessful, documented attempts to contact the participant have been made.

Death: Upon learning of the death of the participant, the study site will be responsible for notifying the sponsor, recording the information in the source documentation and in the appropriate study CRFs, and obtaining a copy of the autopsy report and death certificate, if available.

14 LABORATORY TESTS

Laboratory tests will be performed at each study site at the timepoints outlined in Table 14-1. Copies of the current laboratory certifications and/or calibrations and normal ranges will be provided to the Sponsor prior to start of the study and upon every renewal throughout the duration of the study. Some samples may be shipped to designated central laboratory facilities.

Table 14-1 In vitro Tests

Test type	Visit 1 (Screening)	Visit 2 (Day 0)	Visit 2 (Day 0) RBC Unit:		During storage LR-RBC Unit or day 42	Visit 3 (Day 42): LR-RBC Pre-infusion	Visit 3 (Day 42): Post-infusion	Visits 40 (Day 43):
			RBC Unit pre-filtration	LR-RBC Unit post-filtration				
Ferritin	X							
Select CBC (Hct, Hgb)	X	(X)[a]	X	X		X	X[b]	X
ABO/Rh	X	(X)[a]						
Viral screen	X	(X)[a]						
LR-RBC unit Residual WBC concentration				X				
LR-RBC unit Mass recovery post filtration				X				
LR-RBC unit Free hemoglobin						X		
LR-RBC unit % Hemolysis						X		
Bacterial testing and/or visual inspection on stored LR-RBCs per site SOP					X[c]			

[a] Tests are done at screening and/or at visit 2, [b] Multiple blood samples will be drawn from participants during pre-and post-infusion, [c] Timeframe per site SOP.

15 CONCOMITANT MEDICATIONS, TREATMENTS, AND PROCEDURES

Current medications and/or treatment administered to treat AEs will be recorded.

16 ADVERSE EVENTS/EFFECTS

16.1 Potential Risks

Risks of Venipuncture, Whole Blood Collection and Radiolabel Infusion

The general common risks of venipuncture are apprehension, pain, discomfort, extravasation of blood into the tissue causing a bruising or hematoma and presyncope, including pallor, lightheadedness, dizziness, nausea, diaphoresis. Other, less common and rare side effects are fainting, nerve irritation, infection, arterial puncture, allergy(skin), neuropathic pain, phlebitis and deep vein thrombosis (DVT). Occurrence rates of venipuncture AEs are summarized in Table 16-1 below.

Table 16-1 Venipuncture Adverse Event Frequency

Location	Very Common ≥ 1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1,000 to < 1/100	Rare ≥ 1/10,000 to < 1/1,000	Very rare < 1/10,000	Not known Sporadic case reports
General[11,12,13,14]	Apprehension	Presyncope[a]	Faint[b]			
At puncture site [11,12,14,15]		Hematoma		Nerve irritation	Arterial puncture	
		Pain		Infection		
Distant of puncture site[11,14,16,17]		Discomfort			Skin allergy	Phlebitis
					Neuropathic pain	DVT

Abbreviations: DVT = deep venous thrombosis
[a] Presyncope includes symptoms such as pallor, lightheadedness, dizziness, nausea, diaphoresis.
[b] Faint defined as a brief loss of consciousness, usually less than 30 seconds.

Since participants will be re-infused with small amount of their own, radiolabeled RBCs, the risk of a transfusion reaction is minimal, however, in very rare cases, a reaction may occur, causing severe illness or death.

The amount of radiation exposure from radioisotopes, ^{51}Cr and ^{99m}Tc, used in this study and received by the participant is low and is not considered to be harmful. However, women who are pregnant or who are nursing will be excluded from the study, as the risks of radiation exposure to a fetus or infant are unknown. All enrolled women of childbearing potential will have a pregnancy test performed during the screening process, and prior to her reinfusion as an added precaution. Any participant with a positive pregnancy test will not be given radiolabeled LR-RBCs and will be withdrawn from the study.

There is a possibility of bacterial overgrowth if bacteria have inadvertently entered the blood bag collection system. The stored LR-RBCs will undergo bacterial testing and/or visual inspection, per site's SOP. The results from this testing or inspection will be reviewed prior to the infusion of cells. Any participant with positive results will not be re-infused with their RBC. Total volume of blood drawn from subjects completing the study will be approximately 670 mL over 57 days. The standard blood center eligibility criteria for donating blood products includes tracking RBC loss. A standard single unit WB collection (211 ml of RBC loss) is between 450-550 mL. After a WB collection the body replaces the plasma in about 24 hours, RBCs are restored in two to four weeks, and platelets are replenished in about 72 hours.

16.2 Risk Mitigation

The Reveos Blood Bag Sets are manufactured according to good manufacturing practices (GMP) and are sterile. The systems instructional labeling will be provided for the disposables blood bag sets and the hardware/software and the site will be trained for correct use of the system. Site SOPs will be used for technical aspects of blood collection.

Risks for the subject can be minimized by:

- Ensuring that all Investigators are properly qualified and meet pre-specified criteria for Investigator selection and that they and their study teams successfully complete the following training: site-specific training, Human Subject Protection, Good Clinical Practice (GCP), and CIP training to include device and procedure training.
- Ensuring that participants who are enrolled meet all eligibility criteria
- Ensuring universal precautions are used for handling all study blood products in accordance with each site's SOPs.
- With the collection of health data associated with this research study, there is a small risk of violation of privacy and loss of confidentiality. The source data and CRFs will only use de-identified subject USID number as participant identifiers, to ensure confidentiality.
- Participants will be monitored for adverse experiences throughout the study. Suspected adverse events will be treated according to study sites' SOPs and documented as described in Section 16.5.

16.3 Potential Benefits

There is no direct benefit to the study subject. Real benefits are altruistic in nature: subjects participating in this study will assist in gathering important information for safety and performance, to assess The Reveos® Automated Blood Processing System (Reveos System) to obtain required regulatory clearance for future use in the USA.

16.4 Adverse Event/Effect Definitions

16.4.1 Adverse Event

An AE is defined (ISO 14155 Section 3.2) as any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated. This definition includes events related to the investigational medical device or the comparator and events related to the procedures involved. For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.

16.4.2 Procedure Related Adverse Event

Procedure-emergent adverse events (PEAEs) are defined as any AE that occurs upon or after the exposure to Reveos Blood Bag set. As described in Section 16.5 AEs occurring after signing of the ICF and until participant study completion will be recorded and require follow-up; however, only PEAEs will be included in the safety analysis. Study timepoints (eg, start of study procedure, participant study completion) are defined in Section 13.

16.4.3 Serious Adverse Event

A serious adverse event (SAE) is defined (21 CFR 312.32 and ISO 14155 Section 3.45) as an AE which meets any of the following criteria:

1. Results in death
2. Leads to serious deterioration in the health of the subject, users, or other persons that either results in:
    a. A life-threatening illness or injury, or
    b. A permanent impairment of a body structure or a body function including chronic diseases, or
    c. In-patient or prolonged hospitalization, or
    d. Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
3. Leads to fetal distress, fetal death or a congenital abnormality or birth defect including physical or mental impairment.

NOTE: The following are not considered SAEs:

Planned hospitalization for a pre-existing condition or a planned procedure required by the CIP, without serious deterioration in health.

Anticipated day-to-day fluctuations of pre-existing disease(s)/condition(s) present or detected at screening that do not worsen.

16.4.4 Adverse Device Effect

An ADE (adverse device effect) is defined (ISO 14155 Section 3.1) as any AE related to the use of an investigational medical device. This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. This definition also includes any event resulting from use error or from intentional misuse of the investigational medical device.

An AE is considered related to the use of the study medical device if the attribution is probably, possibly or definitely related, whereas the definition of "not related" is considered to be unrelated to the use of the study medical device.

16.4.5 Unanticipated Adverse Device Effect

An unanticipated adverse device effect (UADE) is defined (21 CFR 812.3[s]) as any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Whether an UADE is anticipated or not will be analyzed and determined by the Sponsor.

16.5 Adverse Event Recording

Safety oversight and reporting during the course of this study will be per ICH GCP guidelines, US Code of Federal Regulations [CFR] part 812. The Investigator will monitor the occurrence of AEs for each subject during the course of the study. All AEs reported by the subject, observed by the Investigator, or documented in medical records will be listed on the AE CRF, assessed by the Investigator to be not related, possibly related, probably related or definitely related to the investigational product. Only procedure emergent AEs (PEAEs) will be included to the safety evaluation. Collection of PEAEs will begin at the time of the first exposure to Reveos Blood Bag set per Section 13.2 and continue throughout the entire study until study exit or observed related AEs are resolved. All AE's will be classified by the site investigators for its relation to procedure per 16.6.2. Starting with the first baseline procedure, any new event/experience that was not present at baseline, or worsening of an event present at baseline, will be considered an AE.

During reinfusion of RBC, the subject will be monitored for AEs; e.g., fever, chills, dyspnea, urticaria, or pain (infusion site, chest pain or other). AEs will be recorded in the source and CRFs, and reported to the study investigator with the following conditions:

- At each visit, AEs since the last visit will be actively assessed via subject interview, and if necessary, via physical exam, and will be documented.
- Ongoing and/or recurrent conditions that were documented on Day 0 will be recorded as AEs only if their severity or frequency increases.

16.6 Adverse Event Classification

16.6.1 Severity

The Principal Investigator (PI) at each site will review and document his/her opinion of the severity of the adverse events to the study and/or procedure(s) according to as follows:

Grade 1 – Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated

Grade 2 – Moderate; minimal, local or noninvasive intervention indicated.

Grade 3 – Severe; medically significant but not immediately life-threatening hospitalization or prolongation of hospitalization indicated.

Grade 4 – Life-threatening consequences; urgent intervention indicated.

Grade 5 – Death related to AE.

16.6.2 Relationship

The PI at each site will document his/her opinion of the relationship of the event to the study procedure(s) as follows:

Not Related:

The event is clearly related to factors other than the study device and/or procedure(s), such as the participant's clinical state or the relationship in time suggests that a causal relationship is impossible.

Possibly Related:

The event follows a reasonable temporal sequence from the time of study treatment administration/procedure, and/or follows a known response pattern to study device/procedure(s) but could have been produced by other factors, such as the participant's clinical state or other therapeutic interventions.

Probably Related:

The event follows a reasonable temporal sequence from the time of study device/procedure(s) and cannot be reasonable explained by other factors, such as the participant's clinical state or therapeutic interventions.

Definitely Related:

The event follows a reasonable temporal sequence from the time of study device/procedure(s), and follows a known response pattern, and cannot be reasonably explained by other factors. In addition, the event occurs immediately following study procedure(s), and/or improves on stopping the study procedure, and/or reappears on resumption of study procedure(s).

These criteria, in addition to good clinical judgment, should be used as a guide for determining the causal assessment.

16.7 Adverse Event Follow-up

All study-related AEs must be followed at a minimum through to study completion and until return to baseline, resolution or until the Investigator deems the event to be chronic, the participant is stable, or the participant is lost to follow-up in accordance with the ICH GCP guidelines, and other applicable regulatory requirements (eg, 21 CFR 812). The Investigator should make a preliminary judgement regarding the relationship of each AE with the study device, the procedure, and the medical history.

Targeted treatment to all AEs should be provided as needed.

The Investigator should provide targeted treatment to AEs. All AEs must be followed at a minimum through to study completion and until return to baseline, resolution or until the Investigator deems the event to be chronic, the participant stable, or the participant is lost to follow-up in accordance with the ICH GCP guidelines.

The expected AE of mild hematoma (bruise) and/or mild infiltration are not followed to resolution.

16.8 Serious Adverse Event Reporting Requirements

In the interest of subject care and to allow the Sponsor to fulfill all regulatory requirements, any SAE, regardless of causal relationship to study treatment/procedure(s), and all UADEs must be reported to the Sponsor within 24 hours of knowledge of the event at the following email address: ClinicalAffairs@TerumoBCT.com.

Additionally, an SAE/UADE Form must be submitted to the Sponsor within 24 hours of knowledge of the event to:

Terumo Blood and Cell Technologies
Email: ClinicalAffairs@TerumoBCT.com

Additionally, the SAE/UADE must be entered on the AE page(s) of the CRF. Follow-up SAE/UADE reports need to be submitted to the Sponsor as soon as additional information regarding the event becomes available.

The Sponsor may request additional information from the Investigator to ensure the timely completion of accurate safety reports.

The Sponsor is responsible for reporting SAE/UADEs to the regulatory authorities in accordance with applicable regulatory reporting guidelines. The Investigator is responsible for submitting SAE/UADEs to his/her IRB as required by local policy.

16.9 Medical Monitoring

It is the responsibility of the PI to oversee the safety of the study at his/her site. The Sponsor/designee will review the patient data, SAEs, UADEs, and device deficiency reports to oversee the safety throughout the study.

Terumo Blood and Cell Technologies will monitor the safety of the study on an ongoing basis.

17 DATA MONITORING COMMITTEE

A Data Monitoring Committee will not be utilized for this study.

18 STUDY DEVICE DEFICIENCY

18.1 Device Deficiencies

A Device Deficiency is defined (ISO 14155 Section 3.19) as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance, and includes malfunctions, use errors and inadequate labeling. All device deficiencies involving any device component must be reported and a Device Deficiency Form must be submitted to the Sponsor within 24 hours of knowledge of the event to:

Terumo Blood and Cell Technologies
Email: ClinicalAffairs@TerumoBCT.com

Every attempt should be made by the Site to save or collect the defective device, and if appropriate, the packaging, for return to the Sponsor. If the deficiency occurs with the device, a service technician from the Sponsor will evaluate and determine whether service or replacement is necessary. A qualified company representative will investigate and determine root cause and corrective actions as applicable, and directives will be provided to the site if warranted. If unable to retain the device, photographs should be taken to assist in the root cause investigation.

If a device deficiency is associated with an AE, refer to Section 16 to assess severity criteria and for reporting requirements in the event of an SAE or UADE.

18.2 Device Accountability

18.2.1 Receipt of Study Device

The contents should be examined upon receipt to ensure packaging and labeling is intact and the devices have not been damaged. Any damage should be immediately reported to the Sponsor.

18.2.2 Storage

The Reveos System device, and the disposables should be stored in a dry place at room temperature. Proper care should be taken to ensure that the study inventory will not be damaged.

18.2.3 Accountability

The investigator shall maintain adequate records of the receipt and disposition of the investigational devices. This includes all investigational devices received, used, or returned, and includes those that malfunctioned and/or were discarded for any reason. Device accountability logs supplied by the sponsor must be completed for all investigational devices. The disposition of all devices must be documented, including those that have been discarded and those returned to the sponsor. During the course of the study, device accountability logs will be monitored on a regular basis. When the enrollment phase of the study is complete, the investigator will return to the sponsor any unused devices and a copy of the completed device accountability logs. Any use of a device outside of this study protocol is strictly forbidden and will constitute immediate grounds for removal of the investigator and/or institution from the study.

All investigational devices that are not used must be returned to the sponsor.

These devices may include the following:

- All unused investigational devices when enrollment is complete.
- All expired study devices.
- All investigational devices associated with a device malfunction or failure.
- All opened but unused devices that may be contaminated, have a defect in the sterile barrier prior to use, or have some other potential defect identified.

Devices that were opened in error, prepared incorrectly, or contaminated in the lab (e.g., dropped on the floor), do not need to be returned to the sponsor.

19 STATISTICAL PLAN

The following section summarizes the statistical methods that will be used in the analysis of the clinical data from this study. Please see Statistical Analysis Plan for full details.

General Considerations for Data Analysis

Inferential statistical tests will be identified in the post-text tables as being either one or two sided, and the construct of the confidence limits will be defined (e.g. 90% or 95%). Asymptotic confidence limits will be presented based on the normal approximation to the binomial distribution for the proportion of subjects classified as a treatment success. Exact confidence intervals will be used for all other presentations. Continuous demographic parameters, such as the subject's age at the time of enrollment, will be summarized using descriptive statistics (N, mean, median, standard deviation, minimum and maximum value, and 95% 2-sided confidence limits).

In addition to examining the demographic and baseline parameters for establishing the pool-ability of subject data across the 2 clinical sites participating in the study, adherence to the sampling preparation and reinfusion procedure will also be examined and presented as evidence of compliance. The examination for compliance to the study protocol will be performed both on a site-level and a subject-level within sites. Failing to follow the sample handling and preparation procedures could have a demonstrative effect on the results. Including information from reinfusion where the sample was not properly prepared could dampen the results and significantly contribute to the variability and challenge the normality of the distribution of values used for calculating the average recovery values.

The following general conventions will be applied to all data presentations and analyses.

- Summary statistics will consist of the number and percentage of responses in each level for categorical variables, and the sample size (n), mean, median, standard deviation (SD), range, and 95% 2-sided confidence limits for continuous variables.
- All mean and median values will be formatted to one more decimal place than the measured value. Standard deviation values will be formatted to two more decimal places than the measured value. Minimum and maximum values will be presented with the same number of decimal places as the measured value.
- The number and percentage of responses will be presented in the form XX (XX %) where the percentage is in the parentheses.
- All summary tables will include the analysis population sample size (i.e., number of subjects enrolled in the study).

19.1 Sample Size Rationale

The sample size in this study will be 24 evaluable subjects.[7] In order to reach the total target number of evaluable subjects, additional subjects will be enrolled to replace subjects for whom the primary endpoints are not evaluable (i.e., those subjects who are lost-to-follow-up or withdrawn; those subjects whose health status has changed prior to their reinfusion, thereby potentially affecting their safety after receiving a reinfusion or potentially confounding study results; or those subjects for whom recovery calculations cannot be made due to missing value). It is anticipated that up to 50 donors may need to be enrolled to accrue 24 evaluable subjects to the primary endpoint analysis. All subjects, regardless of the availability of their endpoint data, will be included in evaluations of In vitro data (where samples are available) and in evaluations of AEs.

Sample Size Estimates for LR-RBC Evaluation

The 3 parts of FDA's RBC recovery criteria that must be met are presented below. The derivation of the sample size was based on the level of precision attained with 24 subjects relative to the 1st part of the criteria.

1. The one-sided 95% lower confidence limit for the population proportion of success is greater than 70% where success of a unit is defined as the RBC in vivo 24-hour percentage recovery ≥ 75%*,
2. The sample mean of percent recovery ≥ 75%, and
3. The sample standard deviation of in vivo 24-hour RBC recovery ≤ 9%.

*Allows for low recoveries (<75%) in 2/20 or 3/24 volunteers.

Estimates were prepared based on the 1st criterion (i) with 24 subjects, examining the one-sided lower 95% confidence limit relative to the a priori value of 70%. Results are presented in the table presented below. If the observed proportion of treatment successes is 21/24 (87.50%) or higher, the one-sided lower 95% binomial confidence interval will exceed 70% (lower confidence limit = 70.77%).

Table 19-1 Statistical Scenarios 1-5 Estimation of LR-RBC Evaluation Sample Size.

Scenario Number	1	2	3	4	5	6
Number of Treatment Successes	17/24	18/24	19/24	20/24	21/24	22/24
Percentage of Treatment Success	70.83	75.00	79.17	83.33	87.50	91.67
One-Sided Lower 95% Confidence Limit	52.13	56.53	61.09	65.82	70.77	76.02

19.2 Endpoints

19.2.1 Primary Endpoint

The analysis of the primary endpoint will be conducted using the evaluable population. Evaluable population is defined in section 19.3.3.

In vivo RBC viability has been assessed for decades using radiolabeled autologous RBCs to assess the proportion of RBCs remaining in the circulation 24 hours after autologous infusion (24-hr RBC recovery). Radiolabeling methods and reporting of recovery have been standardized [8,9,10] allowing comparison of data between studies. Calculation of the proportion of RBCs surviving at 24-hr post infusion requires that RBC mass be accurately measured. This can be performed by extrapolating the early disappearance of cells to the midpoint of the infusion.

Additional exploratory analyses may be performed on estimates of RBC recovery using RBC mass derived from ^{99m}Tc radiolabeling.

RBC recovery 24 hours after infusion will be reported using the single label method recommended by Moroff et al.[9] The ^{51}Cr value at time = 0 (T zero, T0) is obtained by doing a regression analysis of the values obtained for ^{51}Cr labeled samples drawn at different time-points post-infusion. The T0 is used to calculate the percent recovery at 24 hours. The calculated T0 may be falsely low if the labeled RBCs are removed by the reticulo-endothelial (RE) system in large numbers prior to the first blood being drawn at 5 minutes post injection. This would result in a falsely higher 24-hour recovery. Recovery at 24 hours will be calculated using the following equation:

% recovery = (Adjusted RBC CPM at 24 hours/ Adjusted RBC CPM at time 0) x 100

Radiolabeled samples will be drawn at different time-points post-infusion. The counts will be adjusted for background counts and corrected for loss of label (elution) over time.[8]

The primary endpoint of RBC recovery at 24 hours post-infusion will be used to assess each of the three criteria specified by FDA. The % recovery for analysis will be provided by the site(s), and not derived during analysis. To assess the criteria associated with the percent of samples with at least a 75% recovery, a success or failure for each observed value will be determined. RBC recovery of at least 75% will be deemed a success, and failure otherwise. A one-sided confidence interval for the proportion of successes will be determined using an exact 95% confidence interval. If the one-sided 95% lower confidence limit is greater than 70% the study will have met its primary endpoint, which will be met if no more than 3/24 data points have less than 75% recovery.

Summary statistics and 2-sided confidence intervals will be presented to assess the actual RBC recovery values and to evaluate the remaining criteria specified by FDA.

19.3 Analysis Populations

19.3.1 Full Analysis Population

The Full Analysis Population will include all participants enrolled in the trial.

19.3.2 Safety Analysis Population

The Safety Analysis Population will include all participants enrolled in the trial who are exposed to Reveos Blood Bag Set and experience adverse event that is related to the device or study procedure as determined per 16.6.2; accordingly, the safety analysis will be limited to PEAEs (defined in Section 16.5). The Safety Analysis Population will be utilized to assess safety of the device and procedure.

19.3.3 Evaluable Analysis Population

The analysis of the primary endpoint in the evaluable population will be based on all recorded data. Subjects are considered evaluable for the primary endpoints if they have:

- Met all of the inclusion and none of the exclusion criteria at enrollment,
- Were not found, after being enrolled in good faith, to be in fact, non-compliant with one or more of the inclusion/exclusion criteria,
- The subject has not had a change in health status which would cause them to fail the inclusion/exclusion criteria at the time of infusion of radiolabeled cells
- Have not met any other protocol exclusion criteria as defined in Section 19.4.

The Evaluable Analysis Population will be included in the analysis of the primary endpoint. Within the enrolled population, all attempts will be made to obtain complete recovery data from all subjects for the analysis of the primary endpoint.

19.4 Protocol Analysis Exclusions

There may be situations wherein the data will be considered non-evaluable and will not be included in the Evaluable Analysis Population.

Data will be excluded from the Evaluable Analysis Population in the following situations:

1. Incomplete or incorrect procedure that affects the primary endpoint due to:
    a. Equipment failure or malfunction (e.g. filter plugs)
    b. Unanticipated processing failure
    c. Results of primary endpoint tests are not available

2. Protocol deviations that affect the primary endpoint due to:
    a. Failure to follow collection procedures outlined in the device Operator's Manual, Instructions for Use (IFU) (Package Insert), Manual of Procedure(s), and site SOPs
3. Product non-reinfusbale due to:
    a. Product does not pass quality check for reinfusion (residual WBC, LR-RBC mass recovery, visual inspection, hemolysis, bacterial growth)
4. Subject issues
    a. Participant lost to follow-up or withdrawn from study
    b. Other participant issues (e.g. inadequate access, reaction, needle abort)

19.5 Missing, Unused, and/or Spurious Data

Please see Statistical Analysis Plan (SAP) for the handling of Missing, Unused and/or Spurious Data.

19.6 Interim Analysis

There will be no interim analysis for the study.

20 STUDY MANAGEMENT

20.1 Ethics

This CIP will be submitted and reviewed by FDA(CBER) IDE committee and Institutional Review Board (IRB). The study will not begin until approvals for the study is received from the FDA and IRB.

20.2 Investigator Responsibilities

20.2.1 Investigator Agreement

Each Investigator will provide the Sponsor a copy of his/her current curriculum vitae and a signed Investigator Agreement, prior to initiation of the study.

20.2.2 Institutional Review Board

The Investigator/study staff is responsible for knowing and adhering to their IRB requirements.

The institution's IRB, or other committee functioning in a similar capacity, will review and approve the CIP, initial and revised ICFs, and CIP amendments. After approval by the IRB, documentation of approval and the approved ICF will be sent to Terumo Blood and Cell Technologies before any subject is enrolled into this study.

20.2.3 Informed Consent

The Investigator is responsible for preparing the written ICF for this study. Terumo Blood and Cell Technologies will provide the Investigator an ICF template. The Investigator may rearrange or reword the contents of this template, or may add other elements or language, provided the meaning and content are not changed or deleted.

Prior to subject participation in this study, the Investigator must obtain written IRB approval for the CIP and the ICF. The approved ICF will clearly reflect the IRB approval date.

All subjects are free to withdraw from participation in this study at any time, for any reasons, specified or unspecified, and without prejudice. The reason for the subject discontinuing or terminating from the study must be recorded on the CRF.

20.2.4 Study Files and Record Retention

The Investigator must retain all study records until notified by the Sponsor that they are no longer needed. The Investigator will also notify the Sponsor in the event he/she relocates, or for any reason desires to dispose of the records.

20.3 Sponsor Responsibilities

20.3.1 General Responsibilities

As per 21 CFR 812, Terumo Blood and Cell Technologies is responsible for selecting qualified investigators and providing them with the information they need to conduct the investigation properly, ensuring quality study conduct and proper monitoring of the investigation, ensuring required approvals are obtained and that significant new information about an investigation is promptly reported to reviewing IRB/EC and government authorities as well as annual reports as required.

20.3.2 Amendments to the Clinical Investigation Plan

Any amendment to the CIP, as deemed appropriate by Terumo Blood and Cell Technologies, will be implemented as the study progresses. Amendments will be submitted to the IRB/EC and /or regulatory bodies as needed/FDA for written approval before implementation.

20.4 Joint Investigator-Sponsor Responsibilities

20.4.1 Access to Information for Monitoring and Auditing

The Investigator and investigative sites will permit trial-related monitoring, audits, IRB/EC review, and regulatory inspections, providing direct access to source data/documents.

In accordance with ICH GCP guidelines, the Sponsor/auditor must have direct access to the subject's source documentation to verify the data recorded in the CRF. The Sponsor is responsible for routine review of the CRFs at regular intervals throughout the study and to verify adherence to the CIP, as well as the completeness, consistency, and accuracy of the data being recorded. The Sponsor/auditor must have access to any subject records needed to verify the entries in the CRFs. The Investigator agrees to cooperate with the Sponsor/auditor to ensure that any problems detected in the course of these monitoring/auditing visits are resolved. This study will be source document verified by the Sponsor as per the criteria outlined in the study management and monitoring plan.

20.4.2 Training

The Sponsor will train applicable study team members as to the device, protocol, and study procedures and will provide updated information as it becomes available during the course of the study, if applicable. The Investigator is responsible for ensuring that additional site personnel that were not trained by the Sponsor receive applicable documents and training.

20.5 Collecting and Recording Data

The Investigator will maintain complete, accurate, legible, and easily retrievable data, and will allow personnel authorized by Terumo Blood and Cell Technologies access to all study data at any time. Such data will also be secured to prevent loss of data. All required data for this study will be recorded from the source documentation onto standardized CRFs.

20.5.1 Source Documents

Source data is all information, original records of clinical observations, or other activities in a clinical study necessary for the reconstruction and evaluation of that trial. Examples of these original documents and data records include study site records, evaluation checklists, and laboratory results.

20.5.2 Case Report Forms

Case report forms will be in electronic data capture (EDC) or paper format.

All data must be recorded in English. Any missing data must be explained.

Completed CRFs will be reviewed and signed by the Investigator. The Clinical Research Associate (CRA) will verify the CRF data with the participant's source data, evaluate the data for accuracy, consistency, and completeness, and will ensure that all forms with missing data and/or errors are ultimately addressed. Accurate and complete CRFs for a participant must be completed in a timely manner.

20.5.3 Data Queries

Data Queries may be used by Terumo Blood and Cell Technologies staff or designee to attempt to correct or clarify missing, incomplete, or illogical data. Queries must be reviewed and signed off by the Investigator or his/her designee.

20.6 Clinical Investigation Plan Compliance

The Investigator is responsible for ensuring the study is conducted in accordance with the procedures and evaluations described in this CIP. A protocol (CIP) deviation is defined as any event where the Investigator or site personnel deviate from the study CIP or study procedures for any reason.

CIP deviations are prohibited during this study, except as described per ISO 14155 Section 5.6.4(c) "Deviations from the CIP to protect the rights, safety and well-being of human subjects under emergency circumstances may proceed without prior approval of the sponsor and the EC – such deviations shall be documented and reported to the sponsor and the EC as soon as possible."

All deviations must be addressed in study source documents and reported to the Sponsor. Requests for deviations, and reports of deviations (if the deviation affects subject's rights, safety and wellbeing, or the scientific integrity of the clinical investigation), will be provided to the IRB/EC per their guidelines. Further details about the handling of CIP deviations will be included in the MOP.

20.7 Suspension or Termination of the Study

For reasonable cause, either the Investigator or the Sponsor may terminate the Investigator's participation in this study, provided a written notice is submitted within the time period provided for in the Clinical Trial Agreement (CTA). In addition, Terumo Blood and Cell Technologies may terminate the study at any time upon immediate notice for any reason, including but not limited to, Terumo Blood and Cell Technologies belief that termination is necessary for the safety of subjects.

20.8 Publication Policy

Terumo Blood and Cell Technologies recognizes the importance of communication of medical study data and encourages the publication of such data in reputable scientific journals and the presentation of such data at scientific seminars and conferences. Any proposed publication or presentation of the data generated from the study must be provided to Terumo Blood and Cell Technologies for timely review in accordance with the terms of the CTA between the Investigator, the Institution, and Terumo Blood and Cell Technologies. Terumo Blood and Cell

Technologies will not, in its scientific publications or promotional material, quote from publications by Investigators without full acknowledgment of the source. For multi-site trials, all Investigators agree not to publish individual site data. All trial data will be published as one or more manuscripts based on the accumulated data from all trial sites.

21 INVESTIGATOR SIGNATURE

Study Title: An In Vivo 24-Hour Recovery Study of Leukoreduced RBCs After Automated Separation of Whole Blood by the Reveos System and Storage for 42 Days

Study Number: CTS-5085

Version/Date: Version 3.0: 01 MAR 2022

I have read this Clinical Investigation Plan (CIP), including all appendices, and I agree that the CIP contains the necessary details for carrying out the clinical investigation as described. I will conduct this study in compliance with the CIP, Good Clinical Practices, and all applicable regulations. I will make every reasonable effort to complete the study within the time designated.

I will provide copies of the CIP and access to appropriate information furnished by the Sponsor to study personnel under my supervision who are involved in carrying out the study. I will discuss this material with them to ensure they are fully informed about the investigational device and the study.

I understand that under circumstances where an adverse event is likely to affect the safety of the subjects, appropriate urgent safety measures will be taken to protect the subjects against any immediate hazard. I understand that if it becomes necessary to protect the best interests of the subjects, they may be withdrawn from the clinical investigation, enrollment of the clinical investigation may be suspended, or the clinical investigation may be terminated as described in the CIP. I will give prompt notice to the Sponsor of any such event. The Sponsor may terminate the clinical investigation at any time, with or without cause.

I have read the Confidentiality Statement of this CIP. The contents of this CIP may not be used in any other clinical investigation and may not be disclosed to any other person or entity without the prior written permission of the Sponsor. The foregoing shall not apply to disclosure required by law or regulation (eg, submission to an Ethics Committee); however, I will give prompt notice to the Sponsor of any such disclosure.

Name: Principal Investigator Name, Credentials

Title: Principal Investigator

Signature: *See Attached for Signature Pages* **Date:** _____

21 INVESTIGATOR SIGNATURE

Study Title: An In Vivo 24-Hour Recovery Study of Leukoreduced RBCs After Automated Separation of Whole Blood by the Reveos System and Storage for 42 Days

Study Number: CTS-5085

Version/Date: Version 3.0: 01 MAR 2022

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Name: Jose A. Cancelas, MD, PhD

Title: Principal Investigator

Signature: Jose A Cancelas Digitally signed by Jose A Cancelas DN: cn=Jose A Cancelas, o, ou, email=jose.cancelas@uc.edu, c=US Date: 2022.03.03 07:59:17 -05'00' **Date:** 3/3/2022

21 INVESTIGATOR SIGNATURE

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I have read the Confidentiality Statement of this CIP. The contents of this CIP may not be used in any other clinical investigation and may not be disclosed to any other person or entity without the prior written permission of the Sponsor. The foregoing shall not apply to disclosure required by law or regulation (eg, submission to an Ethics Committee); however, I will give prompt notice to the Sponsor of any such disclosure.

Name: Moritz Stolla, MD, PhD

Title: Principal Investigator

Signature:  **Date:** 8 MAR 2022

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TERUMO BLOOD AND CELL TECHNOLOGIES

Where Used

Number	Version	Name	Context

Uses

Number	Version	Name	Context

References Documents

Number	Version	Name	Context	State	Last Modified

Referenced By Documents

Number	Version	Name	Context	State	Last Modified

Describes Parts

Number	Version	Name	Context	State	Last Modified

Referenced By Parts

Number	Version	Name	Context	State	Last Modified

Revision History Table

Revision	Date Approved	Change Notice / PR Number
Rev A	2022-03-15 20:41 GMT	TBCT Record Document Workflow