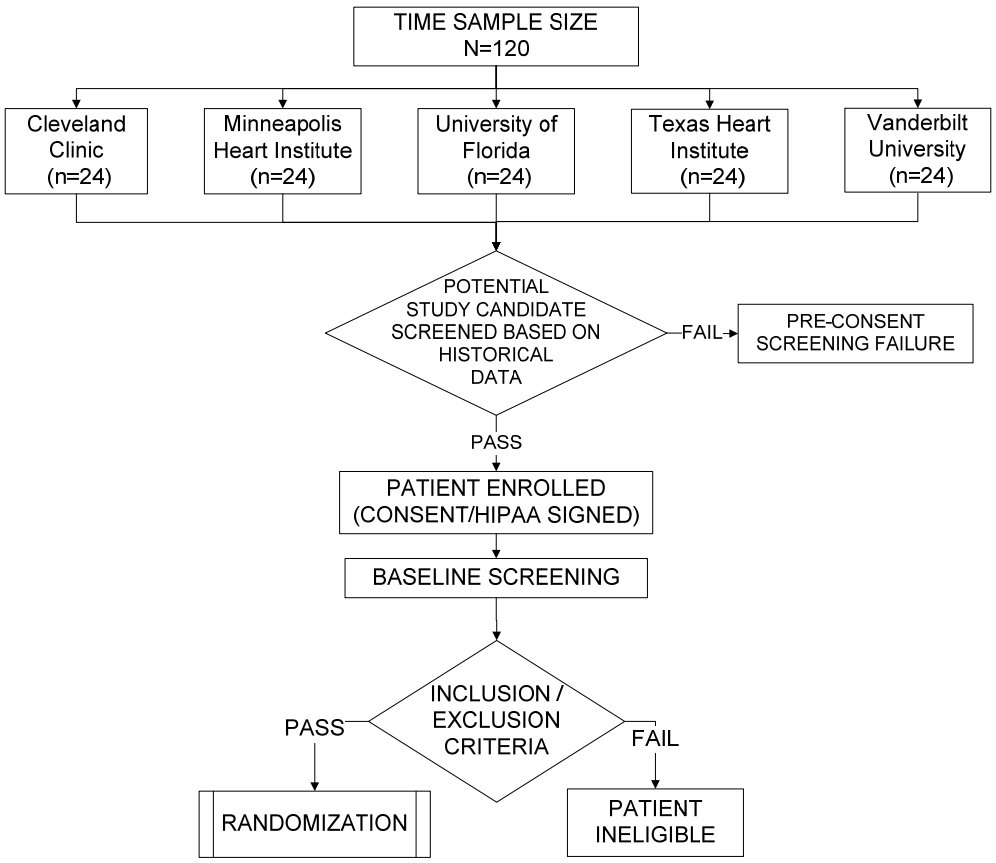
C. Baseline Testing: After obtaining a study ID, acrostic, and time-of-therapy assignment, the research coordinator collects a series of baseline assessments (within the allotted time) to determine whether the individual truly is a viable candidate for study product infusion.

D. Randomization to Study Product: Individuals who have successfully met eligibility criteria via initial screening, baseline assessments, final review of the Treatment Checklist, and whose bone marrow cells have met the cell processing release criteria, are then randomized to a study product assignment (cell therapy or placebo).

E. Intervention: Bone marrow aspiration, cell processing, and study product infusion follow in accordance with time-of-therapy assignment (3-day or 7-day post revascularization). The participant is monitored overnight and, with physician authorization, is discharged within 24 hours.

F. Follow up Visits: Participants are asked to return to the clinical center for follow up visits at 1-, 3-, 6-, 12-, and 24-months post intervention.

Enrollment Flowchart



1) Dr. Linda Piller: 1-713-500-9507; Linda.B.Pillar@uth.tmc.edu
2) Dr. Lem Moyé: 1-713-500-9518; Lemuel.A.Moye@uth.tmc.edu

A. Adverse Events and Serious Adverse Events

You must report all AE's and SAE's (from the time the participant signs consent through and including 30 calendar days after the subject completes the study) that occur regardless of whether you believe the cell therapy caused the event. **All SAE's must be followed until they resolve. Do not delay the initial reporting of a serious adverse event in order to obtain resolution or follow-up information.**

i. Report **adverse events** to the DCC via the database using **Form CNB041.** Please group all signs, symptoms, and abnormal diagnostic procedure results under one diagnosis.
ii. Report **severe adverse events** to the DCC via the database using **Form CNB042.** The investigator is required to report the event within 24 hours of learning of it. This information can also be communicated via phone, email, or fax if necessary (See Attachment 5 for Fax Cover).

B. Unanticipated Problems, Protocol Deviations/Violations, and Protocol Exemptions

Unanticipated Problem: An incident, experience, or outcome that specifically causes increased risk to the study or to its participants and may be of medical or non-medical etiology. The event is unexpected, probably or possibly related to the research, and places patients or others at greater risk of harm than was previously known (e.g. loss/theft of a laptop containing identifiable, sensitive subject information; device failures; incarceration of a study staff member).

Protocol Deviation: A departure from the IRB-approved research plan that does not constitute a threat to the health, safety, and welfare of a research participant, and has no substantive effect on the value of the data collected (e.g. follow up visits which take place outside the specified time outlined in the protocol or blood samples collected at times close to but not precisely at the times specified in the protocol).

Protocol Exemption: A *prospectively* approved deviation granted by the study sponsor that does not increase the risk to the participant (e.g., minor exceptions to the inclusion/exclusion criteria or an exception to the treatment schedule).

Protocol Violation: A departure from the IRB-approved research plan that jeopardizes the health, safety, welfare, or privacy of a research participant or the integrity of the study (e.g. knowingly or unknowingly delivering study product to the patient which does not meet release criteria or infusing study product into a vessel that was not patent at the time of delivery).

i. Report **unanticipated problems** to the DCC via the database using **Form CNB043** within 24 hours of PI or study staff awareness of event**.**

ii. Report **protocol deviation/violations** to the DCC via the database using **Form CNB044** within 7 days of the PI or staff's awareness of the event. If the departure from the protocol is required to protect the life or physical well being of a participant, the DCC must be notified within 24 hours.

- Fill out the hard copy Protocol Deviation workbook located either in your Manual of Operations binder or printable form from the CCTRN website (www.cctrn.org).
- Enter the information from the workbook into the CCTRN web application Protocol Deviation form **CNB044** which describes the event.
- Fax the complete and signed workbook form to a Project Manager at the DCC using the DCC Fax Coversheet.
    - If the protocol deviation is being completed to request an exemption, you should check the box labeled, "Event has not occurred (exemption request)"
    - If the protocol violation was submitted for an event that has already occurred, the receipt of information will be acknowledged (waiver granted).
- The DCC will complete the bottom portion of the form and enter if the exemption or waiver was granted.
- The DCC will fax the complete and signed workbook back to the site.
- Copies of all protocol deviation/exemption correspondence should be placed in the corresponding participant's research record for documentation purposes.

For the purposes of IRB and other local regulatory reporting, the DCC will provide each site with regular reports which include enrollment figures; general demographics; and number, frequency, and type of AEs, SAEs, and UPs for the site as well as the overall Network. Reports regarding frequency and type of protocol deviations will also be made available to each individual site.

V. Data Query Reports and Data Clarifications/Data Change Requests

A. Data Query Reports

- A form that has been submitted with entries that have created data queries will show up in CCTRN web application the top navigation menus with a "p" for pending. (Forms that are complete and have no pending queries will show as green with a check mark and will be automatically submitted for payment.)
- In order to resolve the data queries so that the forms can be completed and paid, follow the process below:
    - RCs run Data Query Reports each week for forms that have generated data queries. To run the report:
        1. From main CCTRN website, select Data Management
        2. Select "Reports and Invoices"
        3. Select "Generate a List of Unresolved Data Queries"

- Print the form and verify the queries with the source documents.
- Initial/date next to the correct entries.
- If the entry needs correction, fill in the value to be changed, initial and date.
- Sign the report and fax it to the DCC (please use the DCC Fax Coversheet Attachment 5).
- **All data queries should be faxed to the DCC by the 15th of each month for processing of payment.**
- An individual at the DCC will mark the fields for change in the web application. A batch process is run routinely to actually change the entries in the database and set the status code to "verified" for records that have had all data queries resolved. This process will also change the form in the top navigation bar to green with a check mark.
- The DCC will initial/date the changes were made, sign the form and fax a copy back to the site for your file.

Tips for Identifying forms on the Data Query Report:

- In the Data Query Report, a form name "Labs (Panels)" refers to the Baseline or Day After Infusion lab form while a form name of "Labs (Follow-up)" refers to one of the follow-up time points.
- In the CCTRN web application, select Patient Form Status from the "Other" menu. This form includes the statuses all forms for a given patient and will be displayed as follows:
    1. Incomplete
    2. Complete
    3. Pending (data queries exist and have not been corrected)
    4. Complete-verified (data queries existed and have been verified or corrected)
    5. Missing
- In the CCTRN web application, when you select a lab or ECG form from a drop down menu, you will see a list of all submitted lab or ECG forms and their form status will be displayed as one of the following:
    1. Incomplete
    2. Complete
    3. Verify errors (data queries exist and have not been corrected)
    4. Verified complete (data queries existed and have been verified or corrected)

B. Data Clarifications/Data Change Requests (DCCRs)

The DCCR form (see Attachment 10) will be accessible via the Research Coordinator Resources section of the CCTRN website. The DCCR form can be generated by the Sponsor, the Clinical Monitor, or a Site Research Coordinator. The DCCR process is the following:

1. Data Change Request:
    - The top half of the form is to be completed by a site RC when an eCRF previously submitted as complete requires a change.

    - Ex. A request indicating that on the Baseline Lab form, the blood sample was actually drawn on 2/13/08 and not on 2/3/08 as was indicated on the submitted eCRF.
  - The action is a request that requires the DCC to respond.
  - Print DCCR form, fill out, sign and fax to the DCC with a DCC fax cover sheet
  - The DCC makes the change in the database, initials the DCCR form and faxes it back to the site with signature.
  - The site maintains a copy and the DCC maintains a copy.
2. Data Clarification Request:
  - The bottom half of the request is typically completed by the DCC or Clinical Monitor (CRA) when there is a question about submitted or pending data.
  - The action is a question that requires the Site to respond.
    - Ex. RC's patient has completed all baseline eCRFs except the ECG. The DCC notices this form is missing and faxes a DCCR form to the site requesting clarification (did the subject complete the ECG procedure? RC would indicate the resolution (complete the ECG eCRF or complete a missing form eCRF).
  - The Site receives the form from the DCC or Monitor.
  - Complete the form, initials/date the clarification, sign and fax the form back to DCC with a DCC fax cover sheet.
  - The site maintains a copy and the DCC maintains a copy.
3. The CRA will verify all data change/data clarification requests with source documents during the monitoring visit.

VI. Transferring Participants Between Centers and Satellites

There may be occasions when participants transfer from center to center, center to satellite facility, or from one satellite facility to another. In order to activate a transfer, the coordinator at the subject's current facility must complete the CCTRN Transfer Request. The request form should be completed with the information of the effective date of transfer, the destination center/satellite facility, and signature of the principle investigator. Please note: All outstanding data entry and data queries must be completed, reviewed, and paid by the DCC prior to activating the transfer. Coordinators at both locations (transferring and receiving) will ensure the transfer of the patient's care and his/her medical and research records.

VII. Site and Monitoring Visits

To ensure the highest quality data collection, your site will undergo research monitoring periodically. These visits will take place at the outset of enrollment, at regularly scheduled intervals during the trial, and at the close of the study. These visits are to ensure that you, your Principal Investigator, and the Network are collecting the best available data while protecting

the participant's interest. All visits should be scheduled several weeks in advance to ensure that all required research team staff are available to meet with the monitor.
It is expected that the average duration of each visit will be 1 to 2 days per protocol (depending on the number of participants to be reviewed and any outstanding issues at that visit). The DCC clinical monitor or project manager(s) should be contacted with any questions concerning the amount of time to schedule for a particular monitoring visit. The visit duration may be adjusted as needed.

VIII. Device Accountability and Disposition Logs

The device used for study product delivery in this protocol is the Maverick over-the-wire PTCA catheter (Boston Scientific). The devices will be shipped from the Data Coordinating Center to the designated clinical center personnel. The clinical center is responsible for accounting for the receipt and use of each catheter. Such information will be logged (see MOP Binder Section 2 "Subject Screening and Catheter Accountability Log") and the logs will be made available to the CCTRN monitor during scheduled monitoring visits. Questions regarding device shipments or to request additional devices should be directed to the Data Coordinating Center. Requests for additional shipments should be made by contacting the DCC project managers or the DCC regulatory specialist.

Project Manager, Rachel Vojvodic:	713-500-9528 Rachel.W.Vojvodic@uth.tmc.edu
Project Manager, Shelly Sayre:	713-500-9529 Shelly.L.Sayre@uth.tmc.edu
Project Manager, Judy Bettencourt:	713-500-9527 Judith.L.Bettencourt@uth.tmc.edu

IX. Biorepository Peripheral Blood/Plasma Collection
This protocol includes peripheral blood/plasma collections for the biorepository at several time points during the trial. The research coordinators will be responsible for assuring the accurate collection, processing, storing, and shipment of these samples to the biorepository.
The standard operating procedure for the management of these samples is included in MOP Binder Section 3 "Peripheral Blood/Plasma Sample Procedures".

X. Payment

Payments are made on a per form basis. As eCRF forms are submitted in the CCTRN web application, they are checked for errors. When a form's data query process is complete, the form is marked for payment by the DCC. Submitted forms that meet payment criteria are paid automatically on a monthly basis. A check and a copy of detailed invoices are mailed to each center. The invoices will also be available for view by site personnel with a proper security role via the CCTRN website. This system for payment alleviates site billing departments' administrative burden of having to process monthly billings. Payment will be transparent as sites will receive a check every month along with a detailed invoice for services that have been submitted via the electronic CRFs in the web application. To view the invoices, follow the process below:

- From main CCTRN website, select Data Management
- Select “Reports and Invoices”
- Select “View Payment Vouchers”
- Select Invoice Date

Attachment 1-TIME Protocol Schedule Matrix

Randomized to Day 3

Day 0 (MI)	**Sunday**	**Monday**	**Tuesday**	**Wednesday ##**	**Thursday #**	**Friday ****	**Saturday**
Day 1	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Day 2 (consent*)	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday
Day 3	Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday
BMA/Therapy Administered	Wednesday	Thursday	Friday	Friday	Monday	Monday	Tuesday

*Could consent on day 1

**Unless you have someone "on call" over the weekend you would miss the Friday patients because they would not be consented in time to randomize.

Would need to consent on Day 1 in order to randomize these patients on time unless you have someone taking call over the weekend.

Would need to consent on Day 1 in order to randomize on day 1 for a possible day 2 BMA/Therapy administration.

Randomized to Day 7

Day 0 (MI)	**Sunday**	**Monday**	**Tuesday**	**Wednesday ##**	**Thursday #**	**Friday ****	**Saturday**
Day 1	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Day 2 (consent*)	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday
Day 3	Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday
Day 4	Thursday	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday
Day 5	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday
Day 6	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
Day 7	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
BMA/Therapy Administered	Monday	Monday	Tuesday	Wednesday	Thursday	Friday	Friday

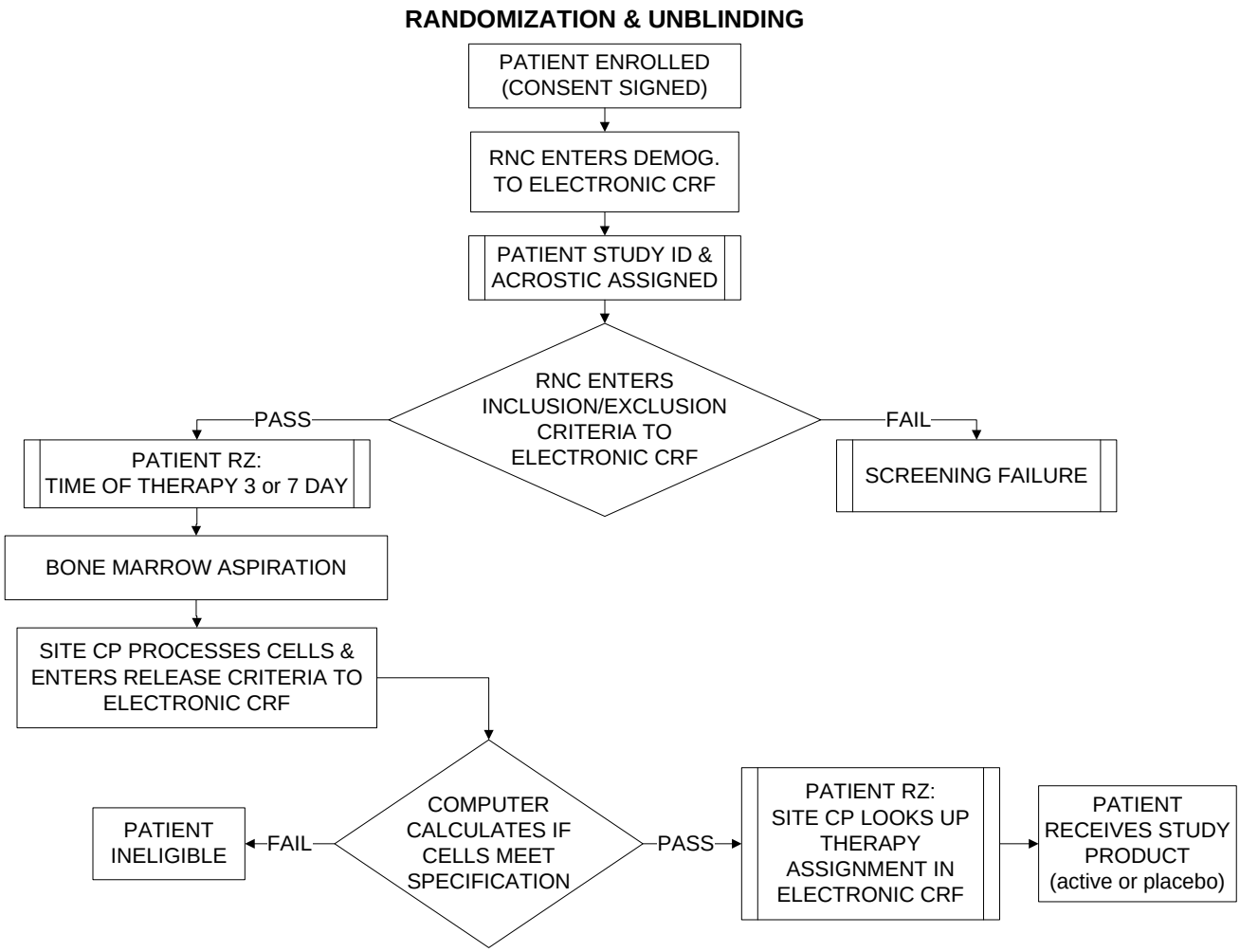
*Could consent on day 1

**Unless you have someone "on call" over the weekend you would miss the Friday patients because they would not be consented in time to randomize.

Would need to consent on Day 1 in order to randomize these patients on time unless you have someone taking call over the weekend.

Would need to consent on Day 1 in order to randomize on day 1 for a possible day 2 BMA/Therapy administration.

Attachment 2- Randomization



Attachment 3- CCTRN Bone Marrow Aspiration Standard Operating Procedure

The following standard operating procedure (SOP) is for carrying out bone marrow aspirations for patients recruited in the Cardiovascular Cell Therapy Research Network (CCTRN) protocols.

CCTRN patients will undergo one and only one bone marrow aspiration to harvest cells for a protocol.

Purpose:

Bone marrow aspiration is a scheduled procedure performed by a trained Physician (e.g., hematologist, pathologist, or hematopathologist). Only physicians with substantial experience in carrying out bone marrow harvesting procedures (more than forty previous successful procedures) will perform the procedure. Other medical personnel trained in bone marrow aspiration procedures (e.g. registered nurses, nurse practitioners, and medical technologists) will assist in the collection to ensure proper sample collection, preparation and processing of the specimen. The bone marrow aspiration is indicated for research regarding stem cell therapy for cardiovascular conditions.

Scope:

This SOP refers to bone marrow collections at the five stem cell therapy centers involved in the CCTRN. The five centers are as follows:

1. Texas Heart Institute Stem Cell Center
2. Minneapolis Heart Institute Foundation
3. University of Florida Department of Medicine
4. Cleveland Clinic Lerner College of Medicine
5. Vanderbilt University Medical Center

PROCEDURE

Supplies and transportation:

1. Bone marrow aspiration supplies will comply with the site-specific institutional procedures and practices.
2. All equipment, supplies, and reagents used in the process of bone marrow collection must be sterile with a lot number and date of expiration noted and able to be recorded on site-specific institutional data forms.
3. Study personnel will notify the site-specific cell processing lab at the following time points: 1)when a patient is enrolled and randomized, 2) when a patient's bone marrow aspiration has been scheduled, 3)when the bone marrow aspiration has begun.
4. Bone marrow aspiration specimen transportation to the cell processing laboratory will be treated as a STAT procedure.

Patient preparation and specimen collection performed by Physician:

1. Verify patient identification with the patient.
2. Explain the risks and benefits of bone marrow aspiration. Give patients an opportunity to ask questions

and be able to verbalize understanding.

3. A separate consent form specific for the bone marrow aspiration procedure is signed by patients to document the informed consent process and to permit the physician to perform the aspiration.
4. Medication of patients for the bone marrow aspiration will be left to the discretion of the performing or overseeing Physicians with the exception of general anesthesia which will not be covered by the study.
5. Patients on aspirin and Plavix (clopidogrel) at the time of consent should remain on aspirin and Plavix (clopidogrel) for the bone marrow aspiration procedure. Continuance or discontinuance of other medications at the time of bone marrow aspiration, (e.g. Coumadin) are left to the discretion of the Study Physician.
6. All collection procedures must be performed with universal precautions and sterile aseptic technique.

Bone marrow aspiration procedures:

1. The media container and/or heparin vials must be opened with sterile technique and media prepared with the appropriate amount of anticoagulant. The final concentration of heparin will be 10-25 units of heparin/ml of bone marrow.
2. After the administration of medication (sedatives and/or analgesics) and prior to collection, the donor will be evaluated while in the prone position to be safely positioned without pressure compromise on arms, brachial plexus, breasts, genitalia, knees, vascular structures or other body parts.
3. The donor shall be prepped and draped in the usual manner using alcohol, Betadine and sterile draping.
4. Prior to insertion of collecting needles, the landmarks and sites of aspiration shall be reviewed and confirmed by both the Physician and Assistant.
5. A total of 80-90 mls of bone marrow product will be obtained. So that the samples are comparable across the five centers, physicians will aspirate no more than 5 ml of product per needle puncture into the marrow space. Approximately 5 mls of marrow is aspirated with each aspirate. Although there are multiple needle punctures in the bone marrow spaces, there are generally 1-2 skin punctures on the iliac crest.
6. An incision is made in the iliac crest and a needle is advanced through the periosteum and into the marrow space. A minimum of one skin puncture and 16 needle punctures into the marrow space are required to aspirate 80 ml of bone marrow. The number of skin punctures or needle punctures must not be so frequent as to require general anesthesia.
7. Physicians will perform the aspiration on one side. The only time aspiration will takes place in the contralateral site is if the initial site produces a dry tap.
8. In the event that no marrow is aspirable, then pressure will be applied to the injection site until hemostasis is achieved. A dressing will then be applied.
9. Patients will be on anticoagulant medications, thus pressure will be applied to the injection site until hemostasis is achieved. A sterile dressing will be applied. A pressure dressing will be applied if persistent venous oozing is present.
10. All bone marrow collections will be sent to the site's cell processing laboratory using site-specific institutional transportation procedures. Bone marrow aspiration transportation to the cell processing laboratory will be treated as a STAT procedure and arrive at the cell processing lab as soon as possible following the bone marrow aspiration procedure.

Reporting requirements:

1. Label the CCTRN Study Product Infusion form and all specimens with the patient acrostic, study ID, date and time of collection, and label the form with the amount aspirated.
   Site-specific chain of custody forms must be used to document the chain of custody of the bone marrow aspirate from the site of the procedure to the cell processing laboratory to the study product infusion site.

Attachment 4- Participant Contact Log

Study ID	Acrostic	Date/Time of Contact	Type of Contact (mail/phone)	Purpose of Contact	Outcome
Example 01-1234-02	ACRPUE	03/31/2008 15:30	Phone	Schedule 3mos fu	Appt set

Attachment 6 – List of eCRF Form Names and Codes

FORM #	DESCRIPTION of TIME FORMS
CNB099	Screening/Demographics
CNB001	Eligibility
CNB003	Baseline Risk Factors & Other Cardiac Hx
CNB004	Baseline Non Cardio. Med. Hx
CNB005	Physical Exams
CNB006	Index Event (Revascularization)
CNB007	Treatment Checklist
CNB011	Medication List
CNB012	Medication Allergies
CNB021	Labs (Panels)
CNB022	Labs (F/U)
CNB023	Holter
CNB024	ECG
CNB026	Labs (Interim)
CNB029	Bone Marrow Aspiration
CNB031	Study Product Infusion
CNB041	Adverse Event
CNB042	Serious Adverse Event
CNB043	Unanticipated Problem
CNB044	Protocol Deviation
CNB045	Schedule of Procedures
CNB047	Data Glossary
CNB048	Missing Form
CNB051	End of Study

Attachment 7 – Schedule of Procedures TIME 3-Day Group

Schedule of Procedures TIME 3-Day Group	
Procedures	**Time Window**
Screening/Baseline	
Screen/Demographics Eligibility (Inclusion/Exclusion criteria) Revascularization/PCI Baseline PE Baseline Lab Panels Baseline Non-Cardiovascular History Baseline Risk Factors Baseline Allergies Baseline Medications Baseline EKG Baseline Echo (core)	
Aspiration/Infusion (SPI)	**PCI + 3 days +/- 1 day**
Day of Infusion PE Treatment Checklist Biorepository blood draws Bone Marrow Aspiration Baseline cMRI (core) Cell Processing Cell Processing - Post Release Study Product Infusion	
Day after Infusion	**SPI + 1**
Day after Infusion PE Biorepository blood draws Day after Infusion Lab Panels Day after Infusion EKG	
1 Month	**SPI + 30 days +/- 7 days**
PE Labs (F/U) Biorepository blood draws EKG Holter	
3 Month	**SPI + 90 days +/- 14 days**
PE Labs (F/U) Biorepository blood draws	
6 Month	**SPI + 180 days +/- 30 days**
PE Labs (F/U) EKG Biorepository blood draws Echo (core) cMRI (core)	
12 Month	**SPI + 360 days +/- 30 days**
PE Labs (F/U) cMRI	
24 Month	**SPI + 720 days +/- 30 days**
PE Labs (F/U) cMRI End of Study	

Attachment 8 – Schedule of Procedures TIME 7-Day Group

Schedule of Procedures TIME 7-Day Group	
Procedures	**Time Window**
Screening/Baseline	
Screen/Demographics Eligibility (Inclusion/Exclusion criteria) Revascularization/PCI Baseline PE Baseline Lab Panels Baseline Non-Cardiovascular History Baseline Risk Factors Baseline Allergies Baseline Medications Baseline EKG Baseline Echo (core)	
Day 3	**PCI + 3 days +/- 1 day**
Baseline cMRI (core)	
Aspiration/Infusion (SPI)	**PCI + 7 days +/- 1 day**
Day of Infusion PE Treatment Checklist Biorepository blood draws Bone Marrow Aspiration cMRI Cell Processing Cell Processing - Post Release Study Product Infusion	
Day after Infusion	**SPI + 1**
Day after Infusion PE Biorepository blood draws Day after Infusion Lab Panels Day after Infusion EKG	
1 Month	**SPI + 30 days +/- 7 days**
PE Labs (F/U) Biorepository blood draws EKG Holter	
3 Month	**SPI + 90 days +/- 14 days**
PE Labs (F/U) Biorepository blood draws	
6 Month	**SPI + 180 days +/- 30 days**
PE Labs (F/U) EKG Biorepository blood draws Echo (core) cMRI (core)	
12 Month	**SPI + 360 days +/- 30 days**
PE Labs (F/U) cMRI	
24 Month	**SPI + 720 days +/- 30 days**
PE Labs (F/U) cMRI End of Study	

Attachment 9 – Clarification for Infectious Disease Testing

As per the requirement of Infectious Disease Testing at baseline for each patient that will participate in the TIME and Late TIME protocols, the sponsor (CCTRN) has clarified at each of the five CCTRN clinical sites listed below, where this function is performed and by whom.

This testing will consist of the following standard tests for infectious diseases; assays for the detection of HIV and HCV (by nucleic acid testing), anti-HIV I/II, anti-HTLV I/II, anti-HBc antibody (Ab), HBsAg, anti-HCV, and Treponema palladium (by serology).

Blood samples should be drawn prior to study product infusion according to local institutional policy (see below). To reduce discomfort to the patient, these samples can be drawn at the same time as the initial peripheral bloods for the Biorepository (immediately preceding bone marrow aspiration).

1) **Texas Heart Institute- Texas Heart Institute Stem Cell Center**

   The blood tubes are transported for Infectious Disease testing (baseline) to the cell processing lab and the cell processing laboratory will send this out with other samples for testing

2) **Cleveland Clinic- Cleveland Clinic Lerner College of Medicine**

   a) Anti HIV I/II will be done in the microbiology lab
   b) The HTLV I/II are sent to our lab then are sent out to a lab in California called Specialty Labs
   c) The Hepatitis screening Anti HBc, HBsAg, Anti HCV and Treponema Palladium IgG are done in the immunology lab

3) **Minneapolis Heart Institute Foundation**

   At the time that the marrow is harvested, the blood samples are collected and sent to the MHIF. The Coordinators send the samples to Memorial Blood Center in Minneapolis who does the testing and sends reports to the cell processing lab.

4) **University of Florida Department of Medicine-SHANDs**

   All of the infectious disease tests are conducted by the local community blood center, (which uses FDA approved kits, CLIA licensed). The patient's blood is drawn by the RN and delivered to the Stem Cell Processing Lab. Couriers transport the blood to the blood center for testing.

5) **Vanderbilt University Medical Center**

   For autologous donors, the nurses send the blood to the Diagnostic Clinical Laboratory at Vanderbilt University Medical Center

Attachment 10- **CCTRN- Data Change/Clarification Request**

Site:	**Patient ID:**
Date of request:	**Patient Acrostic:**

Request initiated by: **Sponsor** ☐ **Monitor** ☐ **Site** ☐

Change Request (complete this portion if requesting a change to previously submitted data)

Form	Field Name/Description	Change Action	Change Complete Sponsor initials/date

Clarification Request (complete this portion if requesting clarification on submitted or pending data)

Form	Field Name/Description	Clarification (note: if response results in change, complete change action above)	Resolution	Clarification Complete Site initials/date

Signature for File:

Sponsor representative signature & date: _____ **Site representative signature & date: _____**