TRANSFUSION TRIGGER TRIAL FOR FUNCTIONAL OUTCOMES IN CARDIOVASCULAR PATIENTS UNDERGOING SURGICAL HIP FRACTURE REPAIR (FOCUS)

PROCEDURES MANUAL

FOR

FOCUS CLINICAL SITES

10/24/06

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CHAPTER 1

INTRODUCTION

The purpose of this Procedures Manual is to provide a detailed explanation of study procedures and instructions for requesting treatment allocations (transfusion group assignment), use of the FOCUS Web Site, and general instructions for completing study forms. The method for transmitting the study data to the Data Coordinating Center (DCC) via E-mail is described. Several definitions that are common to all study forms are provided in this manual. Each of the study forms also has detailed instructions for completing each item on the form. These specific instructions are included in the section for Study Forms in the FOCUS Binder. This binder contains the FOCUS Protocol, Procedures Manual, study forms and instructions. The FOCUS Binder should be retained for reference and updated as revised materials are distributed.

CHAPTER 2

START-UP PROCEDURES

A. Documents

Each Clinical Site must provide to the Clinical Coordinating Center (CCC) the following documents before patient recruitment may be initiated.

1. Institutional Review Board (Ethics Committee) approval and stamped copied of Informed Consent
2. Clinical Site Director's Financial Disclosure Form
3. Human Subjects Protection in Research certificate.
   This must be completed by the Clinical Site Director and Clinical Site Coordinator and any other individuals involved in patient contact for FOCUS.
4. Signed contract
5. Form 310 Protection of Human Subjects (Appendix B)
6. FOCUS ITTRS Application Form H (Hospital Application)

Each site must send the completed Form H (hospital application form) to the DCC as directed at the bottom of the form. This form identifies the individual(s) who are authorized to request treatment allocations (randomize patients using the Interactive Touch Tone-Randomization System (ITTRS)). If a Clinical Site has more than one hospital, a separate form is submitted for each hospital.

B. Training Start-up Requirements

1. Attend training session

   The Clinical Site Coordinator from each Clinical Site must attend a FOCUS training session or receive training via telephone.

2. Test E-mail submission of data forms

   Each site must submit a test form via E-mail to assure that E-mail submission of forms is working satisfactorily (see Chapter 7, Procedures for Data Entry).

3. Sample Chart Review

Prior to patient recruitment, the CCC will send each site a sample medical record of a hip fracture repair patient. Each Clinical Site Coordinator will review the sample chart and record the study data on a paper copy of the data forms. Each site is to mail the completed sample data forms to the CCC. The data abstracted by each site will be compared to the data abstracted by the CCC for the same medical record. This is to ensure that all data is collected in a uniform and consistent manner. If there are many discrepancies in the abstracted data, the CCC will review

data definitions and the data sources in the medical record with the individual site. The CCC will then send the site a second sample chart and again compare the abstracted data.

4. Certification Test

Each Clinical Site Director, Clinical Site Coordinator and staff member who will be obtaining consent, randomizing patients, or entering data on study forms must complete a Certification Test to demonstrate an understanding of the fundamental design and requirements in performance of the trial. Once individuals who will be randomizing patients or entering data have completed the test, it should be faxed to Dr. Michael Terrin at the DCC following directions at the end of the test. For individuals whose activities in FOCUS are restricted to obtaining informed consent, copies of the completed certification test may be kept on file in the Clinical Site office and need not be submitted for central review.

5. Assign Certification Number

Once certification test is completed, Dr. Terrin will assign a certification number and send a copy back to the Clinical Site Coordinator.

C. Start-up Materials

DCC staff will send Clinical Sites FOCUS materials that include the following:

FOCUS Binder (current edition)
Master set of Forms and Form Instructions
List of Patient IDs and letter codes
Site Information Sheet with certified staff and staff ID numbers
Patient ID Number labels, Chart labels (Country specific) and ECG labels
Cryo vials and cryo vial labels (from SeraCare)

All numbered memos issued prior to the date of Clinical Coordinating Center approval will be provided.

D. Preparation for Start of Study

Careful preparation for the study will improve recruitment rates and reduce protocol violations.

1. Training of Study Personnel

It is the responsibility of the Study Chairman and Data Coordinating Center to train study personnel at each Clinical Site. This will involve training session and conference calls to review the procedures manual with careful examination of each phase of the study: recruitment; pre-randomization; randomization; in-hospital follow-up; 30 and 60 day follow-up telephone calls. It is critical that the Clinical Site Director and Clinical Site Coordinator completely understand

the study protocol and procedures so they can teach other members of the medical and nursing staff at their hospital(s).

2. Training of Orthopaedic Attendings and Residents

Prior to the start of the study, the trial should be presented at a Departmental meeting. Each Orthopaedic Surgeon in the hospital will be personally contacted (e.g., by letter) by the Clinical Site Director from that hospital. A brief written description of the trial will be provided. Permission will be sought from each Orthopaedic Surgeon to recruit his/her hip fracture patients. A sample letter with study description to be sent to the Orthopaedic Surgeons is included in Appendix G (and on disk/website). Three lists of Orthopaedic Surgeons will be compiled: 1) Surgeons for whom every hip fracture patient may be recruited, 2) Surgeons for whom permission must be sought for each individual patient prior to recruitment, 3) Surgeons who do not want to participate in the trial.

The Clinical Site Director must provide a detailed review of procedures to any Orthopaedic resident who will be recruiting patients and/or involved in the care of recruited patients and writing orders for transfusion. This should be done in a separate meeting with the residents. The residency program director and/or Chief of Orthopaedic Surgery must emphasize the need for cooperation with the study and in following the protocol. All residents and attendings participating in FOCUS recruitment must have a certificate of human subjects training and a completed FOCUS certification test on file at the Clinical Site.

3. Informing and Training of Nursing Personnel

Prior to the start of the study, the trial should be presented at a Department of Nursing meeting. Each nurse who works on the Orthopaedic wards and recovery room should be personally contacted by the Clinical Site Coordinator from that hospital. He/she should emphasize the need for the nurses to remind the Orthopaedic Surgeons and residents to follow the transfusion protocol and to identify patients in whom protocol violations may occur and to contact the Clinical Site Coordinator. Consent forms and materials describing the protocol (these materials are available from the Clinical Coordinating Center – contact Dr. Jeffrey Carson or Ms. Helaine Noveck) must be available on the orthopaedic ward, emergency room, and the recovery room for review.

4. Informing Other Clinicians at Study Hospitals

It is especially important, that consultants who are frequently involved with the care of hip fracture patients be identified and contacted about the rationale for the study and the transfusion protocol. Presentation at Medical Grand Rounds prior to the initiation of the study protocol may be helpful in providing a detailed rationale for the study and to justify the transfusion protocol that is tested.

The study should be publicized in the hospital newsletter and through posters placed in the emergency room, recovery room, Orthopaedic wards, operating room changing room, and medical and nursing staff lounges.

5. Obtaining Assistance from the Blood Bank

Prior to the start of the study, cooperation should be sought from the blood bank. The Clinical Site Director and Clinical Site Coordinator should meet with the Director and Administrator of the blood bank. The protocol should be summarized and the need to minimize protocol violations emphasized. The Clinical Site Director should request that the blood bank notify the Clinical Site Coordinator every time a request for transfusion is received for a study patient. A presentation should be organized for blood bank staff to explain the study and seek their cooperation.

At the time of randomization, the Clinical Site Coordinator will notify the blood bank of patient's participation in the study and treatment group assignment. When an order for blood transfusion is received by the blood bank, the Clinical Site Coordinator should be paged to confirm that the transfusion protocol is properly implemented. If the blood transfusion could be a protocol violation (Hgb > 8g/dL in the Symptomatic Group, or > 10 g/dL in the 10g/dL Group), the Orthopaedic Surgeon or ordering physician will be contacted to determine if the patient has symptoms (blood should immediately be released) or if this represents a protocol violation. If the order for a blood transfusion is a protocol violation, the protocol should be explained to the surgeon/ordering physician and a request be made not to transfuse the patient. If the physician agrees not to transfuse the patient, then the blood bank should be notified not to release the blood. If the physician affirms that blood transfusion should be given, the blood bank should be instructed to release the blood. The final decision on the transfusion is ALWAYS the attending surgeon's and cooperation with the study protocol is voluntary. Patients of surgeons unwilling to cooperate with the protocol should not be entered into the study.

E. Quality Assessment

For the first two patients randomized in FOCUS in each Clinical Site, in addition to sending the forms to the DCC, hard copies of the completed data forms (00, 01, 02, 03, 04, 4A, 05, 06, 07, 08, 8A, and 09, 12, 13, 15) should be sent to the Clinical Coordinating Center for review. The Clinical Coordinating Center will also need a copy of the entire medical record (excluding the face sheet) to support the data on these forms. The copied medical record is to be confidentialized and each page is to be labeled with the patient identification number and letter code (patient ID labels will be provided by the DCC upon request). A confidentialized copy of the informed consent should also be included. These materials should cover the period from the date the hospital admission for the hip fracture to hospital discharge. The CCC will supply preprinted FedEx shipping labels to each Clinical Site. The CCC will provide a FOCUS FedEx account number which will pay shipping costs.

After the first two patients, we will request this same procedure be followed for a random sample of 10% of patient medical records at each site. The DCC will generate a listing of the study identification numbers and letter codes for the charts to be reviewed. This will be sent to the Clinical Site Coordinator who will then copy and confidentialize the medical charts and send all relevant materials to the CCC.

CHAPTER 3

IDENTIFICATION OF PATIENTS AND OBTAINING INFORMED CONSENT

A. Identification of Eligible Patients

A system must be developed at each hospital to identify hip fracture patients when they are admitted to the hospital. Options include telephoning one or more of the following people each morning or requesting they telephone the Clinical Site Coordinator when a patient comes to the hospital: 1) Emergency room personnel, contact Clinical Site Coordinator, 2) Nurses or ward clerk working on the Orthopaedic ward, call Clinical Site Coordinator, 3) Admissions office personnel, call Clinical Site Coordinator, 4) Orthopaedic residents call Clinical Site Coordinator, 5) Operating room scheduler, or 6) Orthopaedic attending call study Clinical Site Coordinator (not very likely to occur). Regardless of what system is used, the Clinical Site Coordinator will telephone the orthopaedic ward admissions office or other appropriate place each morning to learn if any hip fracture patients have been admitted during the prior evening. Since most patients do not go to surgery until sometime later in the day, there is time to recruit the patient. Positive feedback is provided to the people contacting the Clinical Site Coordinator by sending a thank you letter which is copied to the Chief of Orthopaedic Surgery and their immediate supervisors.

B. Suggested Recruitment Protocol

The exact method of patient recruitment will vary among the sites and must be approved by the local IRB (Ethics Committee). Below is the suggested recruitment protocol, which is consistent with Health Insurance Portability and Accountability Act (HIPAA) guidelines for patient confidentiality.

All Orthopaedic surgeons who agree to participate, are to sign a copy of the Letter to Recruit Hip Fracture Patients (Appendix G, which will be printed on letter-head stationary). The study staff will maintain copies of these letters.

Study staff will identify new admissions (above) and obtain the name of the orthopaedic surgeon. If the orthopaedic surgeon has not signed the Letter to Recruit Hip Fracture Patients no further information will be given and there will be not attempt to contact the patients. If there is a signed Letter to Recruit Hip Fracture Patients, the resident/hospital staff will provide the name of the patient. Study staff will review medical records for information pertaining to basic eligibility criteria (age, fracture type, cardiovascular disease, and ambulatory status). The eligible fracture types include femoral neck, intertrochanteric, revise oblique and subtrochanteric (below the lesser trochanter) if the fracture does not extend beyond the proximal 1/3 of the femur (check the extent with the operating surgeon if there is uncertainty). Eligibility status (yes/no) will be recorded. If the patient is not eligible, any notation of the patient name and admission will be immediately destroyed. The only study record maintained for these subjects will be a unique sequential number and letter code (see below), date of screening, and notation of ineligibility. All eligible subjects will be approached for informed consent. Research staff will introduce themselves and provide each subject a copy of the Letter to Recruit Hip Fracture Patients signed by his/her physician.

C. Assignment of Unique Patient Identifier

Every hip fracture patient who comes to the hospital will be assigned a unique number and letter code generated by the DCC. The number will include the three digit number designation for hospital and the four-digit sequence number (e.g. 101-0002; 101 represents the hospital number and 0002 the sequence number from that hospital). A unique three-letter code will also be assigned that does not relate to the patients initials. A sequential list of patient identifiers (sequential number codes plus 3 letter code) will be provided to each of the Clinical Sites prior to the start of the study (see sample sequential listing of patient ID Numbers and Letter Code in Appendix J). A Screening Log (FCS 00) will be kept for each patient admitted with a hip fracture requiring surgical repair. This form will be used to characterize the proportion of patients entered into the trial and reasons for exclusion.

D. Obtaining Informed Consent

Informed consent will be obtained prior to the patient going to the operating room for surgery by properly trained (certified in human subjects research and FOCUS certification test) orthopaedic residents, hospital nurses, or Clinical Site Coordinators. If needed, the attending orthopaedic surgeon or medical collaborators could also obtain consent. The patient will be told about the purpose of the study, the transfusion protocol in the two arms of the study, chart review at the time of discharge from the hospital, and the telephone follow-up by the Clinical Coordinating Center nurses at 30 and 60 days following randomization. If consent is not obtained prior to surgery, consent will be sought postoperatively. In patients who sign informed consent, a label will be placed on the cover of their chart or if not acceptable under HIPPA(Patient Privacy Act) place inside chart cover (sample chart label in Appendix K) and a note written in the progress note that identifies the patient as willing to participate in the trial. Patients will always have the option of withdrawing from the study. It is also suggested that the patient/family member be asked the patient's height and weight at the time consent is obtained (collected on Patient History and Clinical Data – see specific information for study forms). All patients who sign informed consent will be provided with a copy of the signed consent, which includes the name and phone number of the Clinical Site Director or other study personnel and instructed to call if there are any study-related concerns.

Some patients may be too sick or not competent to give permission to enter the study. Patients in this study will often be confused from the recent injury, or may suffer from dementia. In these cases, if the treating physicians believe that the cognitive impairment is a reason not to surgically repair the hip fracture, do not recruit the patients into the study. If the patient will undergo surgical repair of the hip fracture, attempt to recruit the patient by seeking permission of a responsible third party. The responsible third party will be identified through inquiry with the patient's physician, hospital administration, and, if necessary, family. On making these inquiries, if an individual is identified as holding power of attorney or medical power of attorney for the patient, informed consent and permission to enroll the patient in the study will be sought from that individual. If there is no individual with power of attorney or medical power of attorney, we will identify and contact the patient's closest, responsible relative ("next of kin"). If there is no responsible next of kin, we will contact the relative or responsible party whose consent allows the hip fracture repair surgery. If no individual who can be responsible for enrolling or declining to enroll the patient in FOCUS can be identified, that patient cannot be enrolled in FOCUS.

If a patient who is not competent to give consent indicates that he/she does not wish to enroll in FOCUS, no effort will be made to obtain third-party consent. A copy of the FOCUS consent form will be offered to all patients approached for recruitment whether or not enrolling or competent.

We will determine each potential study subject's competency to sign consent by means of a direct evaluation.

E. Evaluation to Sign Consent

To evaluate a patient's competency to give informed consent, start by making a subjective judgment regarding item 1 below. If a patient is alert and able to communicate answer question 2. If the patient is responsible for consent for hip fracture surgery, ask the patient questions 3-6. The evaluator may select the language to use in asking the questions in order to help the patient understand them. This is not a test but a tool to determine if the patient understands the study. If the patient does not answer the question correctly, then review the issue again until the evaluator is convinced that the patient understands the study. Record the exact responses provided by the study subject. The completed copy of the evaluation to sign consent is to be kept by the Clinical Site in the patient's FOCUS study file.

Items:

1. Is the patient alert and able to communicate with the examiner?
   _____yes _____no
   If NO, patient will not be allowed to give consent. A proxy for the patient must be interviewed for consent. If YES,

2. Is the patient responsible for consent for hip fracture surgery?
   _____yes _____no
   If NO, the patient will not be allowed to give consent. A proxy for the patient must be interviewed for consent.

3. Ask the patient to briefly describe the transfusion protocol in the study.
   Answer expected: two alternatives, one with blood transfusion to higher levels and one for symptoms or transfusion if needed to sustain lower levels.

4. Ask the patient to describe follow-up after discharge from the hospital.
   Answer expected: telephone call at 30 days and 60 days.

5. Ask the patient to explain what he/she would do if he/she decides that he/she no longer wishes to participate in the study.
   Answer expected: tell the study nurse, study doctor, personal doctor, or a hospital official that he/she does not wish to participate.

6. Ask the patient to name a potential risk of participation in the study.
   Answer expected: complications of blood transfusion or loss of privacy.

Signatures:

I hereby certify that the above patient is alert, able to communicate and able to give acceptable answers to items 3, 4, 5, and 6 above.

Evaluator	Date	Witness	Date

If a study subject is not alert or unable to provide correct responses to all the questions, the subject will be judged as not competent to give consent. Permission to participate for these individuals will be obtained from the appropriate third party.

F. Preliminary Completion of the Registration and Randomization Forms

After the patient signs the consent form, all available information on the Patient Registration form and the ITTRS Voice Response Worksheet should be filled in. These forms can then be set aside until the time the target hemoglobin is reached. At that time the Patient Registration form and the Worksheet should be completed. If the patient's postoperative hemoglobin level is < 10 g/dL (100g/L) during the immediate postoperative time period (end of anesthesia to 3rd postoperative day), the patient is entered into the study. PRIOR to telephoning the randomization system, the ITTRS Voice Response Worksheet must be completed.

G. Patient Follow-up Prior to Randomization

If consent has been obtained preoperatively, the Clinical Site Coordinator will also have the preoperative blood sample for troponin analysis drawn, processed, and stored by the hospital laboratory (see Chapter 8 B.2 - Blood Specimens for Central Troponin Analysis).

For each consented patient, the Clinical Site Coordinator will insure that a preoperative hemoglobin level is obtained. Post-operative hemoglobin measurements are to be obtained in the recovery room and for 3 days or until the measurement falls below 10 g/dL (100g/L) during the first three days after surgery (whichever occurs first). If the hemoglobin does fall below the entry level threshold, permission must be confirmed from the surgeon (or resident) to randomize the patient. It is possible the clinical situation has changed in way that leads the surgeon NOT to want to randomize the patient or follow the transfusion protocol. It may also be advisable to confirm that the internal medicine/cardiology consultants are agreeable to follow the transfusion protocol. It is extremely important the physicians will be comfortable following the transfusion protocol in each randomized patient.

Some otherwise eligible patient may suffer from end stage cancer or other debilitating disease. The Clinical Site Coordinator should always consult the Clinical Site Director concerning these patients. The final decision as to whether a patient is a suitable candidate for randomization is left to the discretion of the Clinical Site Director.

After it has been confirmed that the surgeon is willing to randomize the patient, the Clinical Site Coordinator will have the pre-randomization blood sample for troponin analysis drawn (see Chapter 8 B.2 - Blood Specimens for Central Troponin Analysis).

If a consenting patient is not randomized into the trial, the Clinical Site Coordinator is to notify the hospital laboratory and request that the preoperative blood sample drawn for troponin analysis be destroyed. Document the collection and destruction of the preoperative blood specimen on the sequential list of identification numbers and letter codes supplied by the DCC (see the sample sequential list of patient identification numbers and letter codes in Appendix J).

CHAPTER 4

REQUESTING TREATMENT ALLOCATIONS

A. Introduction

The DCC staff maintain an Interactive Touch-Tone Randomization System (ITTRS) for Clinical Site staff to use to request treatment allocations at the time consented patients become eligible for entry into the study. The (ITTRS) system is accessible only to study personnel who enter the Hospital Password and identification number (PIN) for the Clinical Site (a separate pin number for each staff member will be assigned by DCC after the hospital application is submitted). Authorized staff at a Clinical Site can request treatment allocations for eligible patients after they have completed a practice randomization using the ITTRS and the Clinical Coordinating Center has notified the Clinical Site that recruitment can be initiated.

Access to the ITTRS is obtained by calling a toll-free telephone number at the DCC (see ITTRS Worksheet). The ITTRS prompts authorized users by asking prerecorded questions; users respond by pressing keys on a touch-tone telephone. The prerecorded questions include confirmation that the patient meets all inclusion criteria and has no exclusion criteria and that the patient and the patient's physician have given informed consent for enrollment. Depending on the answers to these items, the next available treatment allocation is issued. The treatment allocation is given over the telephone by a prerecorded voice message and confirmed by fax transmission to the Clinical Site; a copy of the latter is sent to the Study Chair. The date and time of the completion of the call is the time of study entry for each patient. A computer record is maintained for each attempt to enroll a patient using the ITTRS. If the Clinical Site fax machine is found to be inoperative after the call is completed, the investigator can call the ITTRS again to request a second transmission of the allocation to the preprogrammed fax number. At the time of the second phone call, patient identifying information must be entered before the treatment allocation is transmitted. The ITTRS also announces the treatment allocation at the end of the second call.

The steps required for a Clinical Site to be authorized to use the ITTRS are:

1. Submit completed ITTRS Hospital Application to the DCC.

2. DCC staff assign a Clinical Site number (3-digit identifier), a Personal Identification Number (PIN) to each individual who randomizes patients and a Hospital Password for each hospital in which patient will be recruited. Each site will receive PIN cards with this information for the ITTRS (see Appendix A for sample PIN card). The PIN cards are sent to the Clinical Site with the instructions for a practice randomization using the ITTRS.

3. Patients at each hospital can be randomized by a staff member after that staff member has completed a practice randomization for the hospital (see below).

B. Practice Randomization for the Interactive Touch-Tone Randomization System (Required)

DCC staff have designed a system to allow authorized personnel to practice a few allocations without actually entering a patient. All study staff who have received a FOCUS randomization card from University of Maryland/Perry Point VA can perform a test randomization.

1. Use the script below to perform each test randomization:

Perry Point Cooperative Studies
Interactive Touch-Tone Randomization System (ITTRS)
(888) 831-3325

Randomizing a Subject

ITTRS:	Welcome to Perry Point Cooperative Studies Randomization System.
ITTRS:	Please enter your Study Number followed by the pound sign.
Caller:	Enter on telephone keypad 36287#
ITTRS:	Please enter the three-digit study password. *(Study PW(password) off of randomization card)*
Caller:	Enter on telephone keypad _ _ _
ITTRS:	Please enter your three-digit site number followed by the pound sign.
Caller:	Enter on the telephone keypad _ _ _# *(Site # off of randomization card)*
ITTRS:	Please enter your site password.
Caller:	Enter on the telephone keypad 9999 *(For testing purposes use site password 9999 otherwise Hospital Password off card)*
ITTRS:	Please enter the five-digit PIN number. *(This PIN number off of the randomization card are individually assigned, and identifies the caller. The chairman then gets a report of PIN numbers that have successfully completed their test call.)*
Caller:	Enter on the telephone keypad (As assigned)
ITTRS:	To randomize a subject, press 1. To request re-transmission of a verification fax, press 2.

Caller: Enter on the telephone keypad 1 or 2

ITTRS: Please enter this subject's seven-digit ID number.

Caller: Enter on the telephone keypad 999 9999
(For test call purposes use seven nines. This will help avoid mix up between real and test calls)

ITTRS: The subject ID number you entered was 999 9999. If this is correct press 1, if this is incorrect press 2, to hear your response again press 3.

Caller: Enter on the telephone keypad 1 or 2 or 3

ITTRS: Please enter this subject's letter code.

Caller: Enter on the telephone keypad 41 73 82 (Ex: GRU)

ITTRS: The letter code you entered was GRU. If this is correct press 1, if this is incorrect press 2, to hear your response again, press 3. For assistance in entering letters using the keypad, press 4.

Caller: Enter on the telephone keypad 1or 2 or 3 or 4

ITTRS: If the Patient Registration Form has been completed, press 1, if not press 2.

Caller: Enter on the telephone keypad 1 or 2

ITTRS: If the subject has met all eligibility criteria including informed consent requirements, press 1, if not press 2.

Caller: Enter on the telephone keypad 1 or 2

ITTRS: Please enter this subject's gender. If male, press 1; if female, press 2.

Caller: Enter on the telephone keypad 1 or 2

ITTRS: Is this subject of Hispanic or Latino origin? If yes, press 1, if no, press 2, if not specified, press 3.

Caller: Enter on the telephone keypad 1 or 2 or 3

ITTRS: Please enter the total number of race codes from the ITTRS Voice Response Worksheet you will be entering for this subject. To hear a listing of the codes, press 8. (For example, Patient may be Alaskan Native and Asian; Total # Race Codes to enter is 2)

Caller: Enter on the telephone keypad 1 or 2 or 3 or 4 or 5 or 8

ITTRS: Please enter the first code. (For example, First Code is #1(Alaskan Native and Second Code is #2 (Asian). (The system will prompt you to enter any additional codes).

Caller: Enter on the telephone keypad 1 or 2 or 3 or 4 or 5 or 6

ITTRS: The race you entered was **_ _.** If this is correct press 1, if this is incorrect press 2, to hear your response again press 3.

Caller: Enter on the telephone keypad 1 or 2 or 3

ITTRS: Subject Number **_ _ _ _ _ _ _,** Letter Code **_ _ _,** has been randomized into the FOCUS trial. The randomization date for this subject is **mm/dd/yyyy**. The treatment assigned to this subject is Symptomatic Transfusion Strategy.

ITTRS: For verification purposes, please enter the treatment assigned. For (US) 10 g/dL Threshold Transfusion or (CAN) 100 g/L Threshold Transfusion, press 1; for Symptomatic Transfusion Strategy, press 2.

Caller: Enter on the telephone keypad 2

ITTRS: To repeat the randomization information, press 1, to randomize another subject, press 2, to end this call, press 9. If you need additional assistance with this randomization, please call (410) 642-2411, extension 5331.

2. Follow the ITTRS voice instructions as if a patient were actually being randomized. The practice session should be performed during working hours at the DCC, weekdays 9:00 a.m. - 4:00 p.m. (EDT or EST) so that problems can be resolved if they occur.

3. At the end of the practice session, the system sends you a treatment allocation confirmation by FAX indicating the practice session came to a successful end. The FAX confirmation for the practice session clearly indicates that a patient has not been randomized. The receipt of this FAX shows that the accurate FAX number for your site is in the ITTRS system.

4. The practice system will remain in place for the duration of the trial. If your staff periodically think that they need some practice using the system, or if new personnel have been assigned to request allocations, the practice system can be used for this purpose.

5. Each authorized individual must perform a practice session prior to randomizing patients in the study. If an individual is authorized to enroll at more than one hospital, a separate practice using the appropriate site and PIN assigned to the staff member for that hospital must be performed.

C. How to Resolve Problems with the ITTRS

If there is no answer when you call the toll-free number, make at least two more attempts. Authorized users unable to connect with the ITTRS, please call…(The phone number 410-642-2411 x 5331, at the bottom of the ITTRS worksheet is incorrect--The correct number is 410-642-2411, x 5354 or 5329).

After entering your five-digit PIN number, if the system responds: “That is not a valid number,” check the small laminated PIN card to confirm that you used the correct PIN number. Dial the ITTRS and try the PIN number again. If the second attempt is not successful, contact DCC staff at the main number (410-706-4567) or if after hours, use cell phone contact for Jeffrey Carson (908-616-3421) or Michael Terrin (410-262-7841).

If after entering your hospital password the system responds: “The personal ID number you entered has not been approved to randomize patients. To complete this requirement you must successfully complete the test procedure,” you have not performed a practice randomization. Perform a practice as described above in Section B using your personal PIN number and the special practice hospital password “9999”.

If after entering your hospital password the system responds “Our records indicate that your center does not have approval for randomization,” your Clinical Site has not been authorized by the Clinical Coordinating Center to initiate patient recruitment. In this situation you should contact the Clinical Coordinating Center to determine what documents have not been received.

CHAPTER 5

GENERAL INSTRUCTIONS FOR COMPLETING FORMS

A. Types of Study Forms

There are four types of FOCUS Forms: (1) forms which are completed and retained at the Clinical Site; (2) forms which are submitted to the Clinical Coordinating Center by web based entry; (3) forms which are submitted to the Data Coordinating Center by E-mail and (4) Serious and Unexpected Adverse Event (SAE) documents which are sent by FAX to the Data Coordinating Center at two locations (Baltimore, MD and Perry Point, MD). This chapter addresses forms kept at the Clinical Site and forms entered by E-mail. Processing of ECGs and accompanying forms for shipment to the ECG Core Laboratory are described in Chapter 8. The list of study forms is given in the Section for Study Forms in the FOCUS Binder. The schedule of measurements and data collection is given in Appendix C. The windows for submission of all forms to the DCC are given in Appendix D.

The forms which are to be completed for each patient enrolled in the study and which are not to be submitted are the Inclusion and Exclusion Worksheets (FOCUS Forms D and E), the ITTRS (Interactive Touch-Tone Randomization System) Voice Response Worksheet, and the Evaluation to Sign Consent. These completed forms are to be kept by the Clinical Site in the patient's FOCUS study file.

The Patient Demographic Information will be recorded via web entry system. See Chapter 7 for web entry instructions.

The Serious or Unexpected Adverse Event Form is to be sent to both the DCC (by E-mail) and the narrative summary (which is a Microsoft Word file) by facsimile transmission to the DCC (See Chapter 10).

FOCUS Forms 00 – 16 are designed to be sent to the Data Coordinating Center (DCC) by E-mail Data Entry.

The underlying principle in processing information in the DCC is to process the information as submitted without interpretation or second guessing what the recorder had intended. The providers of the data are requested to complete the forms as clearly and as legibly as possible, but also to follow certain conventions in reporting data to reduce the possibility of errors in processing the data collection forms. The procedures for E-mail Data Entry are described in Chapter 7.

Before submitting the forms to the DCC, each form should be reviewed for completeness and accuracy. The person who collected the information is responsible for its accuracy, and he/she documents this by signing the form and providing his/her staff certification number (assigned by DCC). Hard copy of all completed forms should be filed in the patient's FOCUS records at the Clinical Site.

B. Obtaining Study Forms

Copies of FOCUS Study Forms can be obtained by several different methods. Each Clinical Site should use the procedure that is most efficient based on available resources. The two methods of obtaining current FOCUS forms are:

1. Use the FOCUS Web Site to download the forms.

2. Clinical Sites may obtain PDF files of study forms from the Data Coordinating Center.

CHAPTER 6

DEFINITIONS FOR FORM COMPLETION

A. Identifying Information

Each form has certain key items at the top, which uniquely identify a specific record in the study database. These items are called "Header Information" and must be filled in on all forms. "Header Information" includes the Patient Identification (ID) Number, Letter Code and Visit Number. It is vital that this information is **accurate** and **complete**. If this information is not completed correctly, the form cannot be processed in the DCC.

A.1 Patient Identification (ID) Number

A list of valid Patient ID Numbers and Letter Codes is provided to the Clinical Site in the start-up packet (see sample sequential listing of patient ID Numbers and Letter Code in Appendix J). Clinical Sites recruiting patients from more than one hospital will receive a separate list for each hospital.

Each screened patient is assigned an Identification Number from the list provided by the DCC. This Identification Number consists of seven digits; the first three digits represent the hospital number (assigned by the DCC before patient enrollment begins) and the next four digits specify the individual screenee.

A.2 Patient's Letter Code

The patient's Letter Code is three letters assigned to specify the patient and has no relationship to the patient's initials. The letter code is assigned from the list provided by the DCC.

Once the Letter Code and ID Number are assigned to a patient they are not changed.

The same Letter Code and ID Number must be used on all of the patient's FOCUS Forms and correspondence about the patient's data. If the Letter Code is entered into the ITTRS incorrectly, a note should be entered in the source document(s) explaining the discrepancy.

B. Dates

All dates on FOCUS Forms are to be recorded as a two-digit day (a leading zero is to be used for days 1-9; 01, 09), a three-letter abbreviation of the month (first three letters), and the complete four-digit year. The following letters are to be used for each month: January = JAN, February = FEB, March = MAR, April = APR, May = MAY, June = JUN, July = JUL, August = AUG, September = SEP, October = OCT, November = NOV, December = DEC. Thus, June 1, 1999 would be 01 JUN 1999 and November 10, 2000 would be 10 NOV 2000.

C. Randomization Date (Study Entry Date)

The study entry date for each patient is the date when the Clinical Site makes the call to the ITTRS to request the treatment assignment. This date is displayed on the Treatment Allocation Form (the randomization confirmation sent by fax).

D. Military Time

Times are to be recorded in local time at the site of data collection and recorded based on a 24-hour clock, which is referred to as military time. For example: 12 Noon = 12:00; 12 Midnight = 00:00; 12:01 am = 00:01; 10:15 am = 10:15; for pm time other than the period 12 Noon to 12:59 pm add 12 to convert to 24-hour recording, e.g., 2:30 pm = 14:30.

E. Leading Zeros

As for dates and military time, enter leading zeros for all numerical data items, e.g., a hemoglobin level of 9.8 g/dL in Form 01 (Patient Registration) item 5A, should be entered as 009.8.

F. Period from Hip Fracture to Hospital Discharge

If patient is discharged $\leq$ 30 days from randomization, complete Form 09 and record date of discharge. If patient is in the hospital >30 days, complete Form 09 at day 30. Indicate all events and procedures from the hospital admission for the hip fracture through hospital discharge/day 30 (whichever comes first).

G. Missing Data

Questions on a majority of data collection forms have choices for responses that are "unknown" or are "not available". Please refer to the Variable Reference Guide (VRG) for valid responses relative to all questions on the data collection forms. All items must be answered unless there is a conditional skip (e.g., if "NO", then skip to…). These instructions will appear on the data collection forms.

Exception: Form 02 (Patient History and Clinical Data): If response for Q7U, "Estimated Blood Loss" (BLDLOSS) is "unknown" or "not available", use the appropriate code; i.e., 9998 for "unknown" or 9999 for "not available".

CHAPTER 7

PROCEDURES FOR DATA ENTRY

The Data Coordinating Center (DCC) provides administrative, data processing and statistical support for the study. This support is provided by DCC staff at two locations: the DCC in Baltimore, Maryland and the DCC in Perry Point, Maryland. Please refer any questions you may have concerning this chapter to the staff at the DCC in Baltimore, Maryland.

A. Introduction

E-mail entry will be used to enter all information in this study (with two exceptions – web-based entry is to be used for the Demographic and Patient Information and fax submission is to be used for the Serious or Unexpected Adverse Event supporting documents even though E-mail is used for the narrative and Form 13). The E-mail system requires that designated staff complete a short training session to become familiar with the program and to test that all required components of the system are working before patient data are keyed. The training session for the keying and transmission of a test form should require no more than 15 minutes for the E-mail Data Entry. The E-mail Data Entry avoids the difficulties of poor quality images that are occasionally encountered with the facsimile transmission system. Keying the form may take a few minutes, but no form should require five minutes per page.

Clinical Site staff may print copies of the E-MAIL ENTRY forms to use as source documents or worksheets to record the information for each item. Copies of these hand-completed forms should be retained in the patient's FOCUS files (along with the printed hard copy of the E-mail submission).

B. Requirements for E-Mail Data Entry

To use E-mail Data Entry you must have the following:

1. An E-mail address to send and receive forms and messages.

2. Ability to check messages on a daily basis or more frequently.

3. Full version of Abode Acrobat Standard Program 6.0 (not just the Reader which is free). If you do not have the Adobe Acrobat Standard Program 6.0, the Data Coordinating Center will provide you with a license for the Adobe Acrobat Standard Program 6.0 and will loan you a CD-ROM so that you may load the program on the appropriate computer. The CD-ROM is to be returned to the DCC as soon as you have completed the test of the system.

4. A laser jet printer or ink jet printer is recommended to print hard copy of each form after the data have been entered using the system.

C. Web-Based Entry

The Demographic and Patient Information form is to be completed using web based computer entry. This requires a computer with Internet access. The Demographic and Patient Information form will be available on a secure server. Access will be limited to certified clinical site staff members who have been assigned a username and password and designated as a Center User. FOCUS study staff collecting the information captured on this form who have provided the Clinical Coordinating Center with a Human Subjects Protection in Research certificate and who have received a Staff ID Number from the DCC (assigned upon completion of the FOCUS Certification test) will be authorized as a Center User.

D. Microsoft Word File

Narrative summaries are required in patients with Serious Adverse Events (FCS 13) and Acute Coronary Events (FCS 15). A Microsoft Word template for the narrative summary will be provided by the DCC and will be available on the website (a copy is included in Appendix M). When completed, the summary is to be sent by E-mail or by fax to Connie Glassman, Computer Assistant at the DCC in Perry Point.

E. Start-Up Procedures and Test of Program

DCC staff will send each Clinical Site a CD-ROM which contains a copy of the full Adobe Acrobat Standard Program 6.0. This is the full Adobe Acrobat Standard Program, not just the Reader, and is necessary for keying the study forms. The license number for the program is listed in the memorandum accompanying the CD-ROM. After you have installed the CD ROM, follow the instructions below for regular data entry sessions to key a test form. You can select any FOCUS form as a test. Open the form in Adobe Acrobat (see instructions below), create any patient identification number and letter code you wish, then select a response for each of the questions. Code all 0's for the staff identification number. Then submit the form and send Tamar Pair an E-mail (tpair@som.umaryland.edu) telling her which form you submitted and the identification number and letter code on the form. She will then confirm that the transmission was received. This is necessary to assure that all components of the system are working properly.

PDF files for each study form for the data entry program are sent to you via email or can be downloaded from the FOCUS website. A specific directory should be created on your computer hard drive for these PDF files. Use this directory to open forms for data entry. If you are going to enter multiple forms at one sitting, it is helpful to minimize the directory; each time you wish to enter a new form all you need to do is open the directory and click on the appropriate form. If there is a problem and a new PDF file is required, request DCC staff to send a new PDF file to you. Send a test (practice) form to the DCC.

F. Regular Data Entry Session

See Appendix F for instructions for file directory set-up prior to data entry.

F.1 Open Adobe Acrobat

Begin the data entry session by opening up the Adobe Acrobat Program. Open up the appropriate form page that you plan to data enter. The names reflect the form and revision date, i.e., FCS 09 (Hospital Outcome) 11-24-04.

F.2 Field Entry

1. Use the mouse to click on the field you want to key.

2. The date item is one field, the day (2 numbers), the month (3 letters), and the year (4 numbers). Key the full date and hit enter.

3. Be sure to enter leading zeros and decimal points for numbers.

4. Clicking on a bubble will select that bubble and fill it.

When entering an item that will accept only one answer, click with the mouse on the answer. If you click on the "Yes" bubble, it will darken the bubble; if you click on the "No" bubble, the "No" bubble will darken and the "Yes" bubble will clear.

F.3 Comment Items

1. When typing into a comment or specify field, fill in the spaces provided and hit the Enter or Tab key to leave the field.

2. The Comment fields will not allow you to enter more letters than the 20 boxes available.

F.4 Date Items

1. The dates are entered as a two-digit number for the day, a three-letter abbreviation for each month, and a four-digit number for the year. For example, September 2, 2000 should be entered as shown below.

0	2
dd	

S	E	P
mmm		

2	0	0	0
yyyy			

F.5 Completing and Sending the Data

1. After completing all data on a form, review the header information (the patient's ID number and letter code) on page 1. Header information will not be re-entered on following pages of multipage forms) for accuracy. The standard method is sending directly to the DCC using the "Submit" button. Occasionally a Clinical Site has

problems with this method. This will be detected via the test form submission. If absolutely necessary, CCC and DCC staff will establish an alternate method of submitting forms.

2. Click on the button at the bottom of the page called "submit". The page will be forwarded either automatically to the DCC or forwarded to your outbox. If during the test of the system you determined that this step did not work for your site, contact the CCC and DCC for assistance starting the FOCUS E-mail Entry.

3. Print and sign the form for your hard copy file; a copy of each completed form is to be kept in the patient's file at the Clinical Site. You may use this copy or the hand-completed original as the primary document for site visit audits.

4. You may save forms as separate PDF files by going to file and clicking "Save As" (see Section F.6 below and Appendix F). Give the saved file the name of the patient ID number and form number (e.g., 010-0011Form03.pdf would be patient 010-0011, Form 03). My Documents is a good place to save these files. You may save a form by clicking on "Save" to the right of the file name entry. Close the saved form by closing the inner "x".

   WARNING: Once a form is saved, if you have not exited the saved file, the Reset button will erase information on your "saved" form. Be careful to avoid this error. You may enter multiple forms for one patient but should use the inner "x" for each form after saving.

5. After closing the saved files for one patient, you may proceed to the next patient's clean screen form image by returning to your FOCUS PDF folder which should be kept open through all data entry transactions.

6. After completing these steps for all of the data forms entered at a given time, check your outbox to make sure all forms were sent. If there are still forms in your outbox, double click on "outbox" and the forms will be sent to the DCC. If this transmission procedure does not work, E-mail Tamar Pair (tpair@som.umaryland.edu) for help with server connections.

F.6 Instructions for Saving a PDF File

1. If you have keyed the patient data into the form and have not created a *Patient ID subdirectory* for this patient, you may create the *Patient ID subdirectories* from this "Save As" Window as follows:

2. Click on the "Folder Icon" with the arrow that points up until you see the Drive letter where your *FOCUS E-mail Forms* directory resides.

3. Double click on the FOCUS E-mail Forms directory to open it.

4. Create a new *Patient ID subdirectory*:

- Click on the "Folder Icon" (image), normally the third icon from the "Save in:" window. When moving the mouse cursor over the icon it will say "Create New Folder".
- Click on "Create New Folder"
- A new folder appears in the window labeled "New Folder".
- Change the name to the Patient's ID number, Example: A999-1001" by typing over the words "New Folder".
- Then press the enter key.

Double click on the new Patient ID sub-directory you just created.

5. To name the File:

- In the "Save As" window, the 3rd white box from the top is "File name:"
- Create a file name: It is suggested that you use the patient ID number and form number, *(e.g., 010-0011Form02.pdf) or use the sequence number when saving a multi-visit form, (e.g., 010-0011Form05Seq02.pdf).*
- Type the name in the File name box.
- Click "Save".

6. Close this form following the same procedures described for completing and sending data (see Section F.5).

F.7 Review of E-mail Procedures

In summary, below are the procedures for sending forms:

- Open the PDF file for the form
- Type in the patient information
- Hit the "Submit" button at the bottom of the form
- You may print and sign the page and keep this in the patient's file at your site
- Save the page to a folder in your PC
- Exit the folder
- Obtain a clean or reset form
- Repeat this procedure for each form to be entered.

F.8 Web-Based Data Entry of Patient Demographic Form

The Patient Demographic Form is the only form to be sent directly to the CCC via Web Entry.

Instructions for Web Entry

You may log onto the FOCUS Demographic and Patient Information Website once you have been notified by the Clinical Coordinating Center staff that you have been authorized as a

Center User. FOCUS study staff who have provided the Clinical Coordinating Center with a Human Subjects Protection in Research certificate and who have received a Staff ID Number from the DCC (assigned upon completion of the FOCUS Certification test) will be authorized as a Center User.

You must have all required information to submit a patient record. Required fields are:
Patient Primary Language;
Patient Identification Number;
Letter Code;
Last Name;
First Name;
Patient (Home) Telephone Number;
Date of Birth;
Gender;
Name of Institution to which patient is discharge; and
Telephone Number of Institution to which patient is discharged.

PLEASE NOTE: The Database Will Not Retain A Partially Complete Record.

If a field is not required, and the data cannot be obtained (e.g., Name of a second individual who does not live with the patient), enter "unknown". This will identify the information as truly missing rather than an inadvertently skipped field. For US patients it is extremely important to obtain a Social Security Number, however if this information is truly missing, use the previously defined coding for missing numeric data (i.e., 999-99-9999).

For the **Other Contact Persons Who Do Not Live With Patient** (**2 names if available**) section on the data entry page, please indicate the relationship to the study subject in parentheses after the name (e.g., "Bob Jones (neighbor),").

Each Center User will be issued a User Name and Password. A User Name will have a maximum length of 10 (letters/digits) and a Password can have a maximum length of 12 (letters/digits). Both the User Name and Password are case sensitive. The User Name will be supplied to you by the Clinical Coordinating Center at the time you receive your authorization to enter the patient data. Note that if you are recruiting patients at more than one hospital, you will be assigned a unique User Name for each hospital. You will have the ability to change your Password (see below).

Log onto the website:

- Enter the url (https://ironclad.umdnj.edu/focus/ClinicalTrial) in your web browser to access the Authorization Web Page Investigator website
- Enter your User Name
- Enter your Password
- Select the hospital name from the drop down menu
- Submit

You will now be on the Main Menu Page.

To change your password, update your E-mail address, and/or telephone number:

- On the Main Menu, scroll down to the Administrative Menu
- Select View & Modify User Information
- Enter your first or last name and submit
- Select your user information
- Click on Update
- Change your password and/or update your E-mail address and telephone number
- Clicking Reset prior to submitting change will return unchanged information
- Click submit

The screen will return "The User's Information was updated"

To enter US patient data into the database:

- On the Main Menu, scroll down to the US Patients Menu
- Select Add New US Patient Information
- Note all fields with a RED * are REQUIRED
- The name of the hospital from which the study subject had been enrolled is automatically entered on the screen. If the hospital name is incorrect, please log out of the website and log in again using the correct hospital name.
- Select the patient's primary language from the drop down menu
- Enter the patient's 7 digit identification number
- Enter the patient's 3 digit letter code
- Enter data for each question; pressing the TAB key will move the cursor to the next data entry field
- Enter the name of the institution or setting to which the patient has been discharged to. (IF STILL IN HOSPITAL AT 30 DAYS enter "Not Discharged")
- Enter the area code and telephone number of the institution or setting to which the patient was discharged (IF THE PATIENT IS NOT DISCHARGED, enter the area code and telephone number of the hospital)
- Review all the entered data for accuracy and completeness
- Print a hard copy of the entered data to be placed in the patient's FOCUS study file that is kept at the clinical site
  A hard copy can be printed by either 1) clicking on the print button on the tool bar of the web browser, or 2) pressing the "ctrl" and "p" keys on your keyboard at the same time and then clicking on "print" in the dialogue box
- Submit

If the patient has been successfully added to the database, the screen will return a blank patient form and there will be a message across the top of the screen stating that the patient information been added; otherwise see **Error Message** (below).

Error Message

- If, after pressing the Submit button on the Patient Information page, the screen returns a form containing completed information, check the top of the screen and review the error message
- The message will indicate the data field missing information
- Complete the missing information and press submit

Repeat as necessary until a blank form is returned and the message across the top of the screen indicates that the patient information has been successfully added to the database.

To enter Canadian patient data into the database:

- On the Main Menu, scroll down to the Canadian Patients Menu
- Select Add New Canadian Patient Information
- Note all fields with a RED * are REQUIRED
- The name of the hospital from which the study subject had been enrolled is automatically entered on the screen. If the hospital name is incorrect, please log out of the website and log in again using the correct hospital name
- Select the patient's primary language from the drop down menu
- Enter the patient's 7 digit identification number
- Enter the patient's 3 digit letter code
- Enter the data for each question; pressing the TAB key will move the cursor to the next data entry field
- Enter the name of the institution to which the patient has been discharged (IF STILL IN HOSPITAL AT 30 DAYS enter "Not Discharged")
- Enter the area code and telephone number of the institution to which the patient was discharged (IF THE PATIENT IS NOT DISCHARGED, enter the area code and telephone number of the hospital)
- Review all the entered data for accuracy and completeness
- Print a hard copy of the entered data to be placed in the patient's FOCUS study file that is kept at the clinical site.
  A hard copy can be printed by either 1) clicking on the print button on the tool bar of the web browser, or 2) pressing the "ctrl" and "p" keys on your keyboard at the same time and then clicking on "print" in the dialogue box
- Submit

If the patient has been successfully added to the database, the screen will return a blank patient form and there will be a message across the top of the screen stating that the patient information been added; otherwise see **Error Message** (below).

Error Message

- If, after pressing the Submit button on the Patient Information page, the screen returns a form containing completed information, check the top of the screen and review the error message

- The message will indicate the data field missing information
- Complete the missing information and press submit

Repeat as necessary until a blank form is returned and the message across the top of the screen indicates that the patient information has been successfully added to the database.

To change patient data already entered in the database:

- On the Main Menu, scroll down to either the US or Canadian Patient Menu
- Select View & Modify Patient Information
- Enter at least one digit contained in the Patient Identification Number
- Select Update for the Patient Identification Number requiring a change in entered information
- Review the information on the Patient Demographic and Information Screen
- Make the necessary change(s) and Submit
- The screen will return "the US (or Canadian) patient information updated"

To view patients already entered in the database for the User Name logged in:

- Scroll down to either the US or Canadian Patient Menu
- Select Display US (or Canadian) Patient Information
- This will return a listing of patients entered into the database for the current User Name. The information displayed will be:
  Patient Identification Number;
  First Name;
  Last Name;
  Birth date;
  Letter Code;
  Center; and
  User Name.

If a patient is not included in this listing, then the data for that patient is not in the database. Note if you have more than one User Name (i.e., you are entering data from study subjects for more than one hospital), this listing will be only for the User Name currently logged in. You will have to log off and log in under the additional User Name(s) to view the patients entered for the additional hospital(s).

CHAPTER 8

HOSPITAL FOLLOW-UP

A. Transfusion and Hemoglobin Levels

Patients will be randomly allocated to the 10g/dL (100g/L) threshold transfusion or symptomatic strategy. Patients randomly allocated to 10g/dL (100g/L) will receive one unit of packed red cells following randomization and receive enough blood to raise the Hgb level above 10 g/dl (100g/L) any time the Hgb level is detected to be below 10g/dL (100g/L) during the hospitalization. Any transfusion following the initial unit of packed red cells must be preceded by blood test documenting an Hgb level below 10g/dL (100g/L). If a patient is actively bleeding, more than one unit of blood may be transfused prior to obtaining the post-transfusion Hgb.

Patients randomized to the symptomatic transfusion strategy are permitted to receive a transfusion if they develop symptoms of anemia. Transfusion is also permitted (but not mandatory) in the absence of symptoms if the Hgb level falls below 8 g/dL (80g/L). Blood is administered one unit at a time and the presence of symptoms is reassessed. Only enough blood is given to relieve symptoms. If the transfusion is given because the Hgb level falls below 8g/dL (80g/L) then only enough blood is given to increase the Hgb level above 8 g/dL (80g/L). Patients with compromised cognitive function whose treating physicians believe might not be able to report symptoms are to be transfused when the Hgb level falls below 8 g/dL (80g/L). Patients enrolled in this study will have been subject to the stress of the hip fracture and surgical repair. They are likely to be receiving pain medication. It is possible that a patient's cognitive status will change over the course of study protocol and the treating physician can best judge if, at the appropriate time, the patient can accurately report symptoms of anemia. It is possible that a patient may be competent to report symptoms at the time of randomization and on a later date not be able to accurately report these symptoms, and vice versa. If consent is signed by someone other than the patient and the patient is randomized into the symptomatic group, any time during the hospitalization a hemoglobin level falls below 8 g/dL (80 g/L), the Clinical Site Coordinator is to contact the treating physician. The Clinical Site Coordinator is to confirm that the physician is aware of the hemoglobin value and confirm that the patient is capable of reporting symptoms of anemia. If the physician indicates that the patient is not able to report these symptoms, there must be a transfusion order for enough red cell units to increase the hemoglobin level to 8 g/dL (80 g/L). The Clinical Site Coordinator is to document each time such contact with the treating physician is made and the results (e.g. patient's ability to accurately report symptoms of anemia, or the need for a red blood cell transfusion) on the previously completed Evaluation to Sign Consent in patient's FOCUS study file (see Chapter 3 Evaluation to Sign Consent).

Symptoms of anemia that will be indications for transfusion in the symptomatic transfusion strategy are as follows:

1. Chest pain thought to be cardiac in origin:

   Retrosternal chest discomfort, chest discomfort described as pressure or heaviness or chest pain thought to be cardiac by physician.

Myocardial Infarction: chest pain as above, elevated troponin or CK-MB enzymes, new ischemic changes on electrocardiogram.

2. Congestive heart failure:

Dyspnea, orthopnea, or paroxysmal nocturnal dyspnea, S3 gallop, edema without other apparent cause, elevated jugular venous pressure without other apparent cause, new or worsening congestive heart failure on chest radiograph.

3. Unexplained tachycardia or hypotension

Signs of volume depletion unresponsive to fluid replacement.

A daily Hgb level will be measured in all patients for the first two days after randomization and on post randomization day 4 (or prior to discharge) and day 7 if the patient remains in the hospital. Additional Hgb levels are measured as clinically indicated. The assigned transfusion strategy must be followed until discharge or up to 30 days post randomization (whichever comes first). Blood must be administered one unit at a time followed by Hgb measurement. A patient in either group may be transfused at any time without an Hgb level if the patient is rapidly bleeding (e.g., brisk gastrointestinal bleeding) and the physician believes emergency transfusion is needed.

B. Detection of Myocardial Infarction

All patients will have an electrocardiogram (ECG) before surgery and just prior to randomization, and on post-randomization day 4 or prior to discharge (if before day 4) and one blood specimen for central troponin analysis prior to surgery, one blood specimen for central troponin analysis prior to randomization, and on post randomization day 1 and day 4 or prior to discharge (if before day 4). These three ECGs (presurgery, post surgery prior randomization, post randomization day 4/hospital discharge) and four blood specimens (presurgery, prerandomization, day 1 post randomization, day 4 post randomization/hospital discharge) will be analyzed centrally. In cases where a preoperative blood specimen is not obtained (e.g. consent is obtained after surgery), site personnel are to contact the hospital laboratory and, if available, obtain left over serum from a preoperative blood sample. It also may be possible to use left over serum drawn for other purposes for the other required blood specimens.

It is not necessary to have the ECGs interpreted locally. All electrocardiograms will be read centrally using standardized criteria. ECG readings will be combined with interpretations of clinical status and troponin information in the ECG Core Laboratory to assess outcome status for myocardial infarction blind to treatment assignment.

B1. ECG Collection

The site is required to retain a duplicate or photocopy ECG in the study chart. Original ECGs are submitted to the ECG Core Laboratory for analysis. ECGs are acquired with a paper speed of 25mm/sec and American Heart Association approved filter settings (100Hz accept 40-

100Hz). Keep artifact to a minimum by careful attention to skin preparation. If it is not possible to send the original and a photocopy is submitted, darken the exposure to copy the grid and do not reduce the image size. Submit ECGs on a single page, if rhythm strip ECG data are collected, the strip must be mounted and LABELED with lead identification on a single sheet. To maintain patient confidentiality, all ECGs will be submitted without patient name and other identifying information. Each ECG should have a FOCUS ECG Label (provided; see sample ECG label in Appendix H) with the Patient ID number and Letter Code, the ECG time frame (preoperative, prerandomization, day 4 post randomization, unscheduled), the date and time (military format) of the ECG completed. Any ECG performed following randomization through post randomization day 30 for an adverse event (unscheduled) is also to be sent to the ECG Core Laboratory.

Send the ECGs directly to the St. Louis University ECG Core Laboratory using the preprinted FedEx Labels provided by the Clinical Coordinating Center. For the first 3 randomized patients at each clinical site, the site is to send the ECGs as soon as they have collected, along with a hard copy of the Required ECG Form (FCS 06) attached to the ECGs with a paper clip. A copy of Cardiac Serum Marker Results and ECG for Clinical Care (FCS 08) (and Cardiac Serum Marker Results and ECG for Clinical Care Additional Days (FCS 8A) if applicable) should be included if there are ECGs performed for a clinical event. After the first 3 randomized cases, all ECGs can be held at the site and sent out monthly.

B2. Blood Specimens for Central Troponin Analysis

Whole blood samples for troponin analysis (preoperative, prerandomization, post randomization day 1, and post randomization day 4/hospital discharge) should be collected according to the following specimen processing procedures:

1. Specimens can be otained from either Serum or Plasma samples

2. Specimens can also be obtained from leftover serum or plasma from previously processed specimens. Discuss with your individual lab the policy for utilizing these specimens

3. Serum Samples: Collect specimen in SST gold (5cc), Red top Tube (10 cc) or Red/black SST (10 cc).

4. Plasma Samples: Collect specimen in Lithium Heparin or Sodium Heparin tube

5. Allow specimen to clot 30 mins for SST or 60 mins for red top.

6. Centrifuge specimen @ 1300 RCF for 10 mins (1500 RCF for 8 mins also acceptable).

7. Transfer @ least 0.4mls of serum into each cryo vial, (2) vials per specimen. Label cryo vials with FOCUS ID labels provided by DCC. (Serum/Plasma 1 and Serum/Plasma 2) see Appendix L for central laboratory labeling instructions) within 30 minutes.

8. Labels must be placed on vials prior to freezing in order to adhere

9. Freeze cyrovial sample at $\leq$ -20 degree centigrade until shipment (can be refrigerated up to 7 days prior to freezing).

10. Send frozen specimens using the NIH shipping protocol. Specimens cannot be shipped until you receive a email confirmation with a list of specimens that are cleared for shipment. Shipping materials can be obtained by completing the BBI Biotech (Seracare) supply order form. These samples will be sent to the NHLBI Repository) for the first two patients enrolled and every three months thereafter, providing all required Troponin Blood Specimen (FCS 07) forms have been entered and cryovial labels accepted by the DCC as correct.

C. Data Collection in Hospital

The study nurse should review the medical record of each randomized patient 5 days per week to identify the data needed to complete the forms. The data collection forms should be completed after the patient is discharged from the hospital or at 30 days after randomization, whichever occurs first (see Appendix D for expectations and windows). The data are entered onto the forms and keyed into Adobe Acrobat and emailed to the Data Coordinating Center.

D. Evaluation of Anemia

The most common etiology for anemia is bleeding resulting from the hip fracture. However some patients may have other underlying illness that contributed to anemia. The patient's baseline complete blood count should be carefully reviewed. Abnormalities of white cell count, differential, or morphology, platelet count or morphology, red cell indices or morphology suggest the possibility of another illness contributing to anemia. In those and other situation in which the cause of anemia is unclear, Internal Medicine / Hematology/Cardiology consultation should be requested for guidance and follow-up.

E. Evaluation and Treatment of Pre-Existing Cardiovascular Disease

Since all patients in this trial have pre-existing cardiovascular disease, clinicians should be familiar with the American College of Cardiology/American Heart Association guidelines on Perioperative Cardiovascular Evaluation for Non Cardiac Surgery published in 2002. Unless there are contraindications, all patients should receive perioperative beta-blockers. These guidelines can be downloaded at http://www.acc.org/clinical/guidelines/perio/update/periupdate_index.htm.

F. Guidelines for Withdrawal from Participation

If at any time following randomization the patient indicates that he/she is uncomfortable with the study procedures and/or wishes to withdraw from the study, the clinical site coordinator should determine the source of the patient's concerns. It is extremely important to the study that we collect as much of the study data as the patient will allow. It is permissible, if necessary, for the patient to refuse specific study procedures and continue with the balance of the study. The clinical site coordinator should carefully address these issues. If a patient objects to undergoing additional phlebotomy or electrocardiograms as required by the study protocol, the clinical site coordinator should assure the patient that he/she is free to do so and continue to participate in the study. If the patient wishes to withdraw from the transfusion protocol, the clinical site coordinator is to request that the patient allow the 30- and 60-day follow-up calls or, at the very least, a 60-day call to see how well the patient is walking. Finally, if the patient is unwilling to be contacted for follow-up, the clinical site coordinator is to request that we be allowed to contact the proxy at 60-days for the sole purpose of establishing the patient's ambulatory status. Study staff are always to respect a patient's request to withdraw from the study. It is possible, however, that once the patient fully understands the available options, we will at the very least be able to obtain data for the primary study outcome. If possible, arrange a telephone call for you and the patient or responsible family member to speak with the Study Chairman (Dr. Jeffrey Carson) at the Clinical Coordinating Center or the Director of the Data Coordinating Center (Dr. Michael Terrin) as soon as a patient or family starts to consider withdrawal from FOCUS. Either Dr. Carson or Dr. Terrin will be pleased to discuss ways to remove obstacles to participation with the patient or family. Complete the Patient Withdrawal Form (See Appendix N) and send it by fax to Dr. Carson at the FOCUS Clinical Coordinating Center.

CHAPTER 9

30 AND 60 DAY FOLLOW-UP

A. Functional Status

Functional status will be assessed at 30 days and at 60 days following randomization. CCC staff will use the contact information collected on the Demographic and Patient Information Form to locate the study subject and a proxy for each subject to complete a short telephone assessment. For selected patients, the primary study outcome, ability to walk 10 feet (or across a room) without human assistance at 60 days will also be corroborated by contacting a proxy. If the patient is not able to complete the telephone questionnaire at the 30-day follow-up, the information will be obtained from a proxy.

Trained CCC staff will telephone all study patients at 30 days (between 30 and 45 days) and 60 days (between 60 and 90 days) after randomization to ascertain vital status, the patient's residence (home, nursing home, etc.) and functional status. The DCC will generate listings of patients due for follow-up, which will be sent to the CCC Study Coordinator. The CCC Study Coordinator will generate a report of contact information for the patients using the data file containing demographic and contact information. This listing will be provided to the CCC personnel responsible for conducting the telephone interviews. The CCC will obtain all follow-up data.

The window for obtaining follow-up data will be 30 to 45 days and then 60 to 90 days. If the patient or family member cannot be contacted by 90 days after randomization, the patient will be considered lost to follow-up. The results of the interview will be recorded on the 30-Day Follow-up Form and 60-Day Follow-up Form and sent by E-mail to the DCC ENTRY system. No direct, individual identifiers are recorded on any of the forms entered and maintained at the DCC. The original copy of the 30-day and 60-Day Follow-Up Form will be filed at the CCC in a locked cabinet separate from the Demographic and Contact Information Form.

B. Orthopaedic Follow-up

Physician follow-up may be supervised by the Orthopaedic Surgeon and/or the patient's primary care physician. Sutures will be removed within 3 weeks of surgery. Follow-up radiographs will be performed as clinically indicated. Within 48 hours of rehabilitation facility, nursing home, or assisted living residence admission, a corroborated history should be obtained, which should include premorbid function and mobility, available social support, current relevant clinical conditions and mental state. Patients with co-morbidity, poor functional ability and low mental test scores prior to admission should undergo rehabilitation in a rehabilitation unit with geriatric orthopaedic expertise, if available. Consideration should be given to supplementing the diet of hip fracture patients in rehabilitation with high energy protein preparations containing minerals and vitamins. A multidisciplinary team, when available, should coordinate the rehabilitation process. Supported discharge plans should be used to facilitate the date discharge of elderly hip fracture patients and reduce acute hospital stay. Guidelines for management are available, "Prevention and management of hip fracture in older people. A national clinical

guideline." Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2002 Jan. 40 p. (SIGN publication; no. 56) http://www.sign.ac.uk/guidelines/fulltext/56/.

CHAPTER 10

REPORTING PROCEDURES FOR ADVERSE EVENTS

A. Serious Adverse Events

A serious adverse event (SAE) for study participants enrolled in the FOCUS trial is defined as any adverse event occurring at any time following randomization that results in the following kinds of outcomes:

- death;
- life threatening (places the subject at immediate risk of death);
- in-patient hospitalization or prolongation of existing hospitalization;
- persistent or significant disability/incapacity.

Important or unexpected medical events that may not result in death, be life threatening, or require hospitalization, may be considered serious adverse events based upon appropriate medical judgment, as they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm or acute renal failure requiring intensive treatment but do not result in in-patient hospitalization. Death from any cause that occurs while the study subject is receiving protocol treatment or during the 60 day follow-up must be reported.

B. Reporting Procedures for Serious or Unexpected Adverse Events

Individual cases of serious or unexpected adverse events requiring medical intervention will be reported immediately (by the end of the **next business day** following the time the investigator first becomes aware of the occurrence) by the local site investigator to the Perry Point Data Coordinating Center (DCC) by email or fax to Connie Glassman (connie.glassman@va.gov). In addition, the site will email or fax a copy of the completed Form 13, "Serious or Unexpected Adverse Event" and the narrative summary (Appendix M), describing the event, to the Perry Point DCC who will forward the documents to the FOCUS SAE Classifying Physician. You may be asked to submit additional supporting medical documentation to the Perry Point DCC if requested by the FOCUS SAE Classifying Physician. *Note: All documents submitted to the Perry Point DCC must contain only non-individually identifiable information.*

The FOCUS SAE Classifying Physician will review cases other than non-fatal events documented on FOCUS Form 09 (Hospital Outcome) with the Clinical Site Director as needed and determine if the event is serious and unexpected, serious and expected, or an event that although reported, is not serious. He will prepare monthly summaries and submit letters to Traci Mondoro, PhD, National Heart, Lung, and Blood Institute (NHLBI) Executive Secretary for the Data and Safety Monitoring Board (DSMB). Dr. Mondoro will then forward a monthly summary of SAEs to the DSMB Chairman. The FOCUS SAE Classifying Physician will immediately report any event(s) judged to require urgent consideration to the Executive Secretary for the DSMB. The DSMB Chairman will review all reports and advise the FOCUS

SAE Classifying Physician and the NHLBI to determine whether further information or action is required, including whether the available data can be reviewed at the next regularly scheduled meeting or whether the entire DSMB should convene prior to the next regularly scheduled (biannual) meeting. For all unexpected adverse events or other serious adverse events temporally related to treatment, the Study Chairman promptly reviews these events, and the DSMB reviews these events at their scheduled meetings.

The clinical site investigator must decide in the course of events whether or not an adverse event is of sufficient severity to require that the subject should be removed from the study treatment.

An adverse event report is to be filed when at least one of the criteria below have been met.

- The event is a Serious Adverse Event.
- The event was unexpected, even if it is not a serious adverse event.
- The adverse reaction is not listed as a risk in the consent form and may have been caused by the study treatment, even if it is not a serious adverse event.
- The adverse reaction is listed as a risk in the consent form but the observed reaction is of a higher severity level than was expected, OR the observed reaction is occurring more frequently than expected.
- If or when there is doubt as to whether to file a report with the IRB - err on the side of caution, and file a report.

CHAPTER 11

SPECIFIC INSTRUCTIONS FOR STUDY FORMS

Form instructions are contained in a separate document labeled FOCUS Forms and Instructions, which provides general instructions as well as item-by-item definitions. Form instructions are available on the Web Site for on-line browsing. On the FOCUS Home Page click on the Form QxQs section.

Certified Research Coordinators and Study Investigators are responsible for screening and enrolling patients and contacting patients to obtain follow-up information.

The required information for each form is obtained by interview of the patient, family members, and/or study physicians and review of appropriate medical records.

Below is a general outline of the forms to be completed.

A. Screening Log Form – FOCUS Form 00

The purpose of the Screening Log is to provide demographic data on all patients presenting with hip fracture. This form is completed for all patients enrolled in the study as well as all patients not enrolled in the study.

Form 00 should be completed as soon as the screening of the patient has been completed, that is, the hip fracture patient has been identified as being eligible or ineligible, or the patient or the referring physician declines to give consent for the patient to participate in the trial.

B. ITTRS Voice Response Worksheet

The purpose of the ITTRS Voice Response Worksheet is to confirm that all major eligibility criteria have been met before a treatment allocation is requested for a patient eligible for the randomized trial. During the screening process complete the Inclusion and Exclusion Checklists (FOCUS Forms D and E) to keep in the patient's folder.

The ITTRS Voice Response Worksheet should be completed by the FOCUS Clinical Site staff (investigators and coordinators) who have been designated to request treatment allocations using the Interactive Touch-Tone Randomization System (ITTRS) in the Clinical Sites (hospitals) that have been assigned a site identification number to utilize the ITTRS.

The summary information on eligibility should be obtained from the patient and the patient’s medical records; appropriate items of FOCUS Study Forms 00 and 01 may be completed to use as the source for completing the ITTRS Voice Response Worksheet.

The ITTRS Voice Response Worksheet should be completed as soon as the screening of the patient has been completed, the informed consent form has been signed by the patient and the patient’s physician has agreed to the patient’s participation.

The information on the ITTRS Voice Response Worksheet is transferred to the DCC by calling the Interactive Touch-Tone Randomization System (ITTRS) at the DCC. During the call the treatment assignment is issued and is to be recorded on the bottom of the patient's Voice Response Worksheet.

At the end of the call the Treatment Allocation Form for the patient is sent by facsimile transmission to the designated FAX number at the Clinical Site. The ITTRS Voice Response Worksheet is kept in the patient's files in the Clinical Site.

C. Demographic and Patient Information Form

The purpose of the Demographic and Patient Information Form is to provide contact information for the patient and other individuals who may help the Clinical Coordinating Center locate and maintain contact with randomized patients at the 30 and 60 day follow-up times. The information on this form is strictly confidential and it is NOT transmitted to the DCC. This form is entered on the web.

The purpose is also to record information required to utilize the National Death Index for patients enrolled in the United States and Statistics Canada for Canadian patients.

The Demographic and Patient Information Form should be completed immediately after the patient has been randomized into the study.

D. Admission Forms – FOCUS Forms 01, 02, and Inclusion and Exclusion Criteria Checklists – FOCUS Forms D and E

The purpose of FOCUS Forms 01, 02, and Inclusion and Exclusion Criteria Checklists (FOCUS Forms D and E) is to guide the Coordinators and Study Investigators through the screening process. The Inclusion and Exclusion Criteria Checklists (Forms D and E) should be completed first to establish eligibility; these forms are not submitted to the DCC but should be retained in the patient's files. The information on these forms confirms that the patient meets all inclusion criteria and does not have any of the exclusion criteria. FOCUS Form 01 provides final documentation that the patient is eligible and agrees to participate in the randomized trial. FOCUS Form 02 provides Patient History and Clinical Data.

These forms should be completed during the period of screening and before completing the ITTRS Voice Response Worksheet.

The completed Forms 01 and 02 should be submitted to the DCC within seven days of randomization.

E. In Hospital Forms – FOCUS Forms 03, 04, 4A, 05, 06, 07, 08, 8A, and 09

The purpose of FOCUS Forms 03, 04, 4A, 05, 06, 07, 08, 8A, and 09 is to collect data for the period from hospitalization for the hip fracture until hospital discharge or 30 days, whichever occurs first.

E.1 Medical Orders Form – FOCUS Form 03

Record medical orders from Day 1 pre-op to Day 2 post-op.

E.2 Hemoglobin Form – FOCUS Form 04, Hemoglobin Additional Days Form – FOCUS Form 4A, and Transfusion Record Form – FOCUS Form 05

The Protocol requires that Hgb levels be measured at least on days 1, 2 and 4 after randomization and on post randomization day 7 (if the patient is still in the hospital). In addition, a Hgb measurement is required within 24 hours after any transfusion given to increase a patient's Hgb to 10 g/dL (100g/L) to determine if post-transfusion Hgb targets have been met. If the patient is discharged on day 3 following randomization, a hemoglobin value should be drawn prior to discharge. Information on preoperative and intra-operative transfusions and detailed information on post-randomization Hgb levels will be recorded on Forms 04 and 4A. Post randomization transfusions will be recorded on Form 05. Information on Hgb levels will be obtained by contacting the hospital laboratory directly or from the chart. Information on transfusions will be obtained from the chart. Obtain information from the medical record (wrong person transfusion (compare name on transfusion slip) and ABO incompatible) and from the blood bank for mislabeled specimens.

E.3 Required ECG Form – FOCUS Form 06

The purpose of the Required ECG form is to document that the electrocardiograms have been obtained, copied and sent to the ECG Core Laboratory.

E.4 Required Troponin Blood Specimen Form – FOCUS Form 07

The purpose of the Required Troponin Blood Specimen form is to document that the blood specimens for central troponin analysis have been collected.

E.5 Cardiac Serum Markers and ECG for Clinical Care Form – FOCUS Form 08 and Cardiac Serum Markers and ECG for Clinical Care Additional Days Form – FOCUS Form 8A

The Cardiac Serum Markers for Clinical Care form is designed to capture the specific measurements that the hospital uses for CK-MB and troponin levels, and the results of any CK-MB and troponin values drawn during the course of routine clinical care from the time of hospital admission through discharge/post randomization day 30 (whichever comes first).

NOTE: In the event there are no cardiac serum markers or ECGs collected for clinical care, a Form 8 or 8A is not required.

E.6 Hospital Outcome Form – FOCUS Form 09

The Hospital Outcome Form will be completed by the Clinical Site Coordinator just after the patient is discharged from the hospital, time of death, or 30 days after randomization

(whichever occurs first). This form requests information necessary to identify discharge status and the study's morbidity outcomes. This form will be completed based on information obtained from the patient's medical record. Site coordinators will consult with the surgeon regarding information on this form as needed.

F. Follow-up Forms – FOCUS Forms 10, 11, and 14

Trained CCC staff will telephone all study patients at 30 and 60 days after randomization to ascertain vital status, the patient's residence (home, nursing home, etc.), level of fatigue and functional status. The DCC will generate listings of patients due for follow-up, which will be sent to the CCC Study Coordinator. The CCC Study Coordinator will generate a report of contact information for the patients using a data file containing demographic and contact information. This listing will be provided to the CCC personnel responsible for conducting the telephone interviews. All follow-up data will be obtained by the CCC. This removes the need for personal identifying information to be maintained at the individual sites or the DCC and helps to protect patient confidentiality.

The window for obtaining follow-up data will be 30 to 45 days for the 30 day follow-up and then 60 to 90 days for the 60 day follow-up. If the patient or family member cannot be contacted by 90 days after surgery, the patient will be considered lost to follow-up. The results of the interview will be recorded on Forms 10 and 11. Form 14 will be completed by contacting a proxy to corroborate the patient's ability to walk 10 feet (or across a room) for the 60-day follow-up. No direct, individual identifiers are recorded on any of the forms entered and maintained at the DCC. The original copy of Forms 10, 11 and 14 will be filed at the CCC in a cabinet separate from the Demographic and Contact Information Form.

G. Death Within 30 Days Form – FOCUS Form 12

The purpose of the Death form is to collect evidence of the 30-day mortality and morbidity (myocardial infarction, DVT, PE, stroke, pneumonia, congestive heart failure) detected during autopsy for any death within 30 days occurring during the marker hospital admission. This form should be completed by Clinical Site staff based on information found in the autopsy report.

H. Serious or Unexpected Adverse Event Form – FOCUS Form 13

The purpose of the Serious or Unexpected Adverse Event form is to collect information concerning each serious or unexpected adverse event requiring medical intervention.

Individual cases of serious or unexpected adverse events requiring medical intervention will be reported immediately (by the end of next business day following the time the investigator first becomes aware of the occurrence) by the site investigator to the Clinical Coordinating Center and Data Coordinating Center. A full summary of the adverse event is to be sent to the DCC. Refer to Chapter 10 for reporting procedures for adverse events.

I. Acute Coronary Event Form – FOCUS Form 15

The purpose of the Acute Coronary Event Form is to describe the characteristics of all suspected myocardial ischemic events including suspected myocardial infarction and acute coronary syndrome.

J. Pre-Randomization Transfusion Record – FOCUS Form 16

The purpose of the Pre-Randomization Transfusion Record Form is to account for and collect information on all transfusions administered to FOCUS patients from the time of hospital admission up to the time of randomization.

CHAPTER 12

STUDY MONITORING

The Data Coordinating Center (DCC) provides administrative, data processing and statistical support for the study. This support is provided by DCC staff at two locations: the DCC in Baltimore, Maryland and the DCC in Perry Point, Maryland. Please refer any questions you may have concerning reports discussed in this chapter to the computer assistant at the Perry Point DCC. Contact information is as follows:

Connie Glassman
Phone: 410-642-2411, ext 6131
connie.glassman@va.gov

A. Confirmation of Interactive Touch-Tone Randomization System (ITTRS) Data

After the FOCUS Forms 00 and 01 have been received at the DCC, the data specified below are compared to the data entered during the ITTRS randomization telephone call.

ITTRS Voice Response Worksheet		Source of Information	
Item		Form	Item(s)
12	Gender	00	4
13	Ethnic origin	00	5
14 & 15	Race	00	6 A-E

If any discrepancies are noted, the Clinical Site is notified.

B. Edit/Clarification Report

1. Data received at the Perry Point DCC will be electronically uploaded into the study database. Before it is accepted into the study database, it will undergo an extensive system of edits and cross-edits. This editing procedure will result in a computerized listing with any identified inconsistencies. This listing is called an **Edit/Clarification Report** (Appendix I or examples in this chapter). This report needs to be completed, signed by the Clinical Site staff (Study Coordinator or Investigator), and returned to the Computer Assistants at the Perry Point DCC within 2 weeks of receipt.

2. The Edit/Clarification Report is used as a means of reporting and correcting "questionable" data. This report lists the questionable values detected, provides a short explanation for the queries, and provides a space for correction.

3. Receipt of this report does not necessarily means that the responses on your forms are incorrect. A data value listed may actually be correct, but is considered "questionable" by the edit program. This could result from failing either an out-of-range check or a validity check against other data values, called cross-edits.

4. Some items that appear on this report may continue to appear, even after corrected, for the next two updates due to the data collection form being subjected to additional edit checks. You should continue to verify these items since changes to other data values may later influence the validity of these items.

5. Each item (or each "questionable item") must be verified as correct ("OK") or modified as you find it necessary. The original data collection form and any source document (i.e., patient's medical record) should be reviewed to determine the correct value. If the item must be modified, it is necessary to document the change on the data collection form, including your initials and date.

6. When changing a value that is not listed on the Edit/Clarification Report, use the supplemental clarification area at the end of each patient edit. Please remember to check all responses affected by the change. This will help to cut down on additional edits resulting from your correction. For instructions on completing a **Supplemental Clarifications Form**, please refer to "C" of this section.

7. The Edit/Clarification Report is sent to each site every four weeks. Please **NOTE:** this report is **not cumulative** and, therefore, does not replace the previous month's report. This report must be completed each month and returned to the Perry Point DCC within two weeks of receipt. Timely completion of this report is very important if we are to ensure that the database is complete and accurate for future analysis. This will also avoid a future Outstanding Edit Report to the site.

8. The Edit/Clarification Report will be sent to the site on 2-part NCR (non carbon reproducing) paper. The following guidelines will help you in completing the report:

   a. Keep the Edit/Clarification Report intact until **all** items have been answered.

   b. Place a piece of cardboard behind the page you are currently working with, to prevent copying through to other pages.
   c. Use a dark (blue or black) ballpoint pen and apply pressure to insure all answers appear clearly on all copies. Do not use pencil.

   d. Take sufficient time to enter all information carefully and legibly. If you make an error, do not write over the incorrect entry; instead cross-out the incorrect entry and rewrite the corrected entry to the right of the field provided. You **must** initial and date all corrections. Please do not use white-out.

e. When working with the report, please refer to your Variable Reference Guide (VRG) and have the forms in question in front of you. **Important: make the same changes to your copy of the form that you make on the edit report.**

The FORMAT of this report is as follows:

- the "date" of the Edit/Clarification Report represents the date the report was generated;
- Starting at the top left of the printout is the number assigned to the "Clinical Site, the Patient Identification Number and the Patient's Letter Code".
- From the left of the printout, the identifying "Header Information" of the form is as follows:
  a. FORM – the FORM NUMBER containing the error
  b. VISIT #, SEQ # (Fm 5, 8A, 13, 15) PERIOD (Fm 7) and DAY NO (Form 4a)
  c. VARIABLE NAME of item to be changed, including Item Number, Description and a BRIEF EXPLANATION of the reason the value is questionable (e.g., "Is missing range = 0 to 1"). Refer to the VRG, which contains all of the variable names.
  d. CURRENT VALUE – represents the value that currently exists in the study database.
  e. CORRECTED VALUE – Each line for a "Corrected Value" must be answered. The corrected value **must** be entered as a **changed value**, a **blank** (please enter the word "blank"), "**OK**" (if the current value is correct), or a valid **MISSING DATA** response**.** Questions which provide choices for "unknown" or "N/A" should be coded as "88" or "99", respectively. Other questions may use **MISSING VALUE CODES** for missing data. The Missing Value Codes are as follows:

     U = If the answer is UNKNOWN
     A = If the patient was NOT AVAILABLE
     R = If the patient REFUSED to answer or take test
     F = If the rater FORGOT to obtain the data
     L = If the result was LOST
     T = If the patient was NOT TESTABLE

     Please refer to the VRG for valid responses relative to all questions on the data collection forms.

  f. When you have answered each line under the "Corrected Value" column, the report is complete, and is ready to be signed by the Clinical Site staff (Study Coordinator or Investigator). After the report has been signed, it can then be separated. <u>Under no circumstances should the pages be mailed separately</u> (e.g., do not tear the report and send in pages 2, 6, and 12). The original must be sent to the Perry Point DCC. A copy should be kept at the site and filed in the patient's study file.

Transfusion Trigger Trial for Functional Outcomes in
Cardiovascular Patients Undergoing Surgical Hip Fracture Repair
(FOCUS)

Edit Report / Clarification Report dated 03MAY2006

Site Number: 641
Patient ID: 641-0013
Letter Code: YND

F O R M	VISIT# SEQ#(FM 5,13,15 & 8a) PERIOD (FM 7) DAYNO (FM 4a)	* VARIABLE IN QUESTION AND * *** EDIT MESSAGE TO BE ACTED UPON ***	CURRENT VALUE	CORRECTED VALUE
01 01		3J. History of or treatment for hypercholesterolemia CHOLHXRX Is Missing Range = 0 TO 1	.	_____
09 01		Discharge date must be answered STATDLS = 1 or 3		
		12. Status at discharge STATDLS Please Correct as Necessary	1	_____
		13. Day of discharge or death DIS_DA Please Correct as Necessary	_	_____
		13. Month of discharge or death DIS_MO Please Correct as Necessary		__ __ __
		13. Year of discharge or death DIS_YR Please Correct as Necessary	_	_____

Supplemental clarifications for form relating to THIS PATIENT ONLY

F O R M	VISIT# DAYNO (FM 4a) SEQ# (FM 5,13,15 8a) PERIOD (FM 7)	VARIABLE NAME of item to be changed from the VRG	CURRENT VALUE	CORRECTED VALUE
__ __	__ __	_____	_____	_____
__ __	__ __	_____	_____	_____
__ __	__ __	_____	_____	_____
__ __	__ __	_____	_____	_____

C. Supplemental Clarifications

1. The **Supplemental Clarifications Form** can be used for any items that may not have been detected by standard editing procedures or for data that was not obtained at the time of the form submission. The columns on the Supplemental Clarification form

are in the same format as the Edit/Clarification Report and the same guidelines should be followed.

2. The supplemental clarification lines are located at the bottom of each page in the Edit/Clarification Report. Be sure to use these spaces only for the patient referenced at the top of the page. For patients not included in the Edit/Clarification Report, blank Supplemental Clarification pads are supplied.

3. It is very important that the Supplemental Clarifications Form be filled out correctly and legibly. All identifying information must match the information currently in the study database; otherwise, the changes will not take place.

4. The Patient Identification Number should always be a 7-position field. (Ex: '10-07' should be "010-0007").

5. The Visit, Day Number, Sequence Number and Period should always be entered as a two-position field. Precede it with a zero when necessary.

6. The variable name (item you wish to change) must be written **exactly** as it appears in the VRG provided to you. There are no spaces between characters. The bars (_) between characters are underscores, not dashes. Using the incorrect variable name will result in the correction not being made, so always make it a point to refer to the VRG when working on Supplemental Clarifications.

7. The Current Value should be entered, as it currently exists in the study database.

8. The Corrected Value must be entered, as you want it to appear in the study database.

9. After the form has been completed and signed by the Clinical Site staff (Study Coordinator or Investigator), the original must be sent to the Perry Point DCC. A copy of the Supplemental Clarifications form should be kept by the clinical site and filed in the patient's study file. The site should also record the correction on the data collection form and initial and date the correction.

Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair

(FOCUS)
SUPPLEMENTAL CLARIFICATIONS

Clinical Site Name: _____Clinical Site #:_____

Date of this Supplemental: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
Day Month Year

PID: ___ ___ ___- ___ ___ ___ ___ LETTERCODE: ___ ___ ___
Site # Patient #

SUPPLEMENTAL CLARIFICATIONS FOR FORMS RELATING TO THIS PATIENT ONLY

FORM #	VISIT# / DAYNO (FM 4A) / SEQ# (FM 5,13,15, 8a) / PERIOD (FM 7)	Variable Name of item to be changed from the VRG	Current Value	Corrected Value
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____

Signed by: _____ _____
(Clinical Site staff) (Date signed)

D. Listing of Missing Records

Informational Report for the site – NOT to be returned to the Perry Point DCC

This report is a listing by patient of each form that is past due for each patient randomized at your clinical site. It is important to review this report upon receipt.

*When working with the **Listing of Missing Records**, the following are a few things that should be kept in mind:*

1. Data can be listed as "missing" if there are any errors in the "Header Information", such as Patient Identification Number, Visit Number.

2. Data Collection Forms submitted later than midnight prior to a scheduled update will not be processed until the next scheduled update.

3. Be sure that sufficient time has elapsed to allow for the data to have been received and processed. If the submission of a form is in question, contact the Perry Point DCC to see if we have received the form.

4. Check your correspondence and memoranda to see if the form has been deleted, returned to your facility, and has not been resubmitted.

5. **Each new report is cumulative and replaces the preceding one.** Any prior report(s) that you may still be working on becomes obsolete when a new listing is received. A good rule of thumb would be to review the Listing of Missing Records and make status notations soon after receiving it. (Keep all prior reports for referencing.)

6. If there are records listed as "missing" and none of the above situations are true, please make note of this and check the next two Listings of Missing Records. If the form(s) is still listed as "missing", please contact the computer assistants at the Perry Point DCC so that they can help locate the problem. Be prepared to provide the Computer Assistant with the header information and the approximate date you submitted the form.

Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients
Undergoing Surgical Hip Fracture Repair (FOCUS)

Listing of Missing Records
For records received at Perry Point DCC by 03/May/2006
Report Generated on 03/May/2006

Test Hospital Site # 641
****

A form shown as missing on this report may have been sent in with incorrect information in the header section (PID, LETCODE, VISIT, DAYNO, SEQNO, PERIOD). If this occurs, the software used to produce this report would result in a missing record until the data are resubmitted.

***** PATIENT ID # 641-0014 LETCODE=ABC was randomized on 01/03/2006

Status: Patient Randomized to Focus

Form 7 - Baseline was due on 02/02/2006

Form 7 - Post-op Prior to Random was due on 02/02/2006

Form 7 - Day 1 - Post Random was due on 02/02/2006

Form 7 - Day 4 or Disch was due on 02/02/2006

Form 9 - Hospital Outcome was due on 02/02/2006

***** PATIENT ID # 641-0015 LETCODE=DEF was randomized on 03/28/2006

Surgery was performed on 03/27/2006

Status: Patient Discharged W/in 30 Days

Form 3 - Medical Orders was due on 04/27/2006

***** PATIENT ID # 641-0016 LETCODE=GHI was randomized on 04/18/2006

Status: Patient Randomized to Focus

Form 0 - Screening Log was due on 04/25/2006

Form 1 - Patient Registration was due on 04/25/2006

Form 2 - History & Clinical Data was due on 04/25/2006

E. Outstanding Edit/Clarification Report

Informational Report for the site – NOT to be returned to the Perry Point DCC

This report will reflect any Edit/Clarification Reports that have not been returned to the Perry Point DCC for processing. Your records should show if the report has been mailed. Please allow sufficient time for the Perry Point DCC to receive and process this report. If, after checking the preceding month's report, a report remains outstanding, contact the Computer Assistants at the Perry Point DCC. Be prepared to give the date of the report, as well as the date the report was mailed.

Transfusion Trigger Trial for Functional Outcomes in
Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS)

OUTSTANDING EDIT REPORT/CLARIFICATION REPORT

Test Hospital 641

03MAY2006

****

THE EDIT REPORT/CLARIFICATION REQUEST DATED 15DEC2005 IS 139 DAYS OVERDUE ****

THE EDIT REPORT/CLARIFICATION REQUEST DATED 09MAR2006 IS 55 DAYS OVERDUE*

THE EDIT REPORT/CLARIFICATION REQUEST DATED 06APR2006 IS 27 DAYS OVERDUE.

F. Forms Submission Report

Informational Report for the site – NOT to be returned to the Perry Point DCC

This list represents form numbers and form types received and processed from your Site since the previous update.

a. **Number of New Forms Edited** - Represents number of forms received.
b. **Forms Re-Edited** - Represents number of forms being re-edited due to changes occurring for that form via Edit/Clarification Report and/or Supplemental Clarifications.
c. All other categories are self-explanatory based on number of forms edited/re-edited.

Transfusion Trigger Trial for Functional Outcomes in
Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS)

FORMS SUBMISSION REPORT FOR 03MAY2006

Test Hospital SITE 641

FORM NO	INSTRUMENT	# NEW FORMS EDITED	# OF FORMS RE-EDITED	# ACCPTD	% ACCPTD	# REJECT	% REJECT	# EDITS	# ERRORS	% ERRORS
0	Screening Log	25	1	26	100.00	0	0.00	858	0	0.00
1	Patient Registration	7	0	5	71.43	2	28.57	231	3	1.30
3	Medical Orders	6	0	6	100.00	0	0.00	420	0	0.00
4	Hemoglobin	6	0	5	83.33	1	16.67	180	1	0.56
5	Transfusion Record	2	0	2	100.00	0	0.00	34	0	0.00
6	Required ECG	4	0	4	100.00	0	0.00	108	0	0.00
9	Hospital Outcome	5	0	4	80.00	1	20.00	305	1	0.33
10	Patient Status	4	1	5	100.00	0	0.00	70	0	0.00
	TOTALS FOR ALL FORMS	XX	X	X	X	X	XX.XX	XXXX	XX	X.XX

G. Patient/Form Status Report

Informational Report for the site – NOT to be returned to the Perry Point

This report shows the status of the patient and forms completion/submission status (for each patient). If the patient status is incorrect and remains that way for 2 reports, contact the Computer Assistants at the Perry Point DCC.

Transfusion Trigger Trial for Functional Outcomes in
Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS)

Patient / Form Status Report

For records received at Perry Point DCC by 05/31/2006

Report Generated on 06/06/2006

Test Hospital Site # 641

Patient ID	Status	# EXP	# REC	# MISS	% RECD
641-0007	Patient Discharged W/in 30 Days	16	16	0	100.00
641-0008	FCS 00 indicates patient not eligible	1	1	0	100.00
641-0009	Patient Discharged W/in 30 Days	15	12	3	80.00
641-0010	FCS 00 indicates patient not eligible	1	1	0	100.00
641-0011	Patient Status Unknown	1	1	0	100.00
641-0012	Patient Discharged W/in 30 Days	16	16	0	100.00
641-0013	FCS 00 indicates patient not eligible	1	1	0	100.00
641-0014	Patient eligible based on FCS 00	2	2	0	100.00
641-0015	Patient Status Unknown	1	1	0	100.00
641-0016	Patient eligible based on FCS 00	2	2	0	100.00
641-0017	Patient eligible based on FCS 00	2	2	0	100.00
641-0018	Patient Status Unknown	1	1	0	100.00
641-0019	Patient Discharged W/in 30 Days	4	4	0	100.00
641-0020	Pat/MD refused consent	1	1	0	100.00
641-0021	FCS 00 indicates patient not eligible	1	1	0	100.00
TOTALS ON 15 PATIENTS		65	62	3	95.38
TOTALS ON 12 PATIENTS (UNK STATUS DELETED)		62	59	3	95.16

H. Medical Record Review

For quality assurance purposes, the medical charts of the first two randomized patients after the start of the study (or at the time the Clinical Site Coordinator changes) from each site and a random sample of 10% of patient medical records will be carefully reviewed by the CCC Head Nurse to insure the accuracy of the data abstraction process. The DCC will generate a listing of the study identification numbers of the patients whose charts will be reviewed. This will be sent to the Clinical Site Coordinator at the Clinical Site who will then copy the chart and

forward to the CCC. All identifying information with the exception of dates should be removed. The DCC will provide labels with the patient ID and letter code to be place on each copied page. The DCC will also forward the listing of identification numbers along with a computer printout of the data items to the CCC. CCC staff will compare the data entered with the data in the medical chart and record whether or not each data point was verified. This review will be designed to identify problems in recording data, data entry, data processing, as well as protocol adherence.

CHAPTER 13

ANSWERS TO COMMON QUESTIONS

Can patients be included in the study if they receive blood transfusions prior to randomization?

Patients are eligible for the study even if they received transfusions during the preoperative, intraoperative or even the postoperative time period. Transfusion prior to randomization is at the discretion of the clinicians. It is possible that clinicians were not initially comfortable randomizing the patient and the patient was transfused. A patient may be randomized as long as the hemoglobin g/dl level is <10g/dL (100g/L) during the immediate postoperative time period (first 3 days after surgery).

Can a patient be recruited into the study if consent was not obtained during the preoperative time period?

Occasionally, an eligible patient for the study will not be identified until the postoperative time period. As long as the eligible patient is identified during the immediate postoperative time period, has a hemoglobin level < 10 g/dL (100g/L), and is able to provide informed consent (or consent can be obtained from relative), the patient may be recruited and randomized.

Can a patient be recruited into the study if the hip fracture occurs while hospitalized for another reason?

Occasionally, an eligible patient for the study will have already been hospitalized, and during the course of that hospitalization, fracture a hip. This patient can be recruited for entry into the study. In this case we will use the date of the hip fracture as the starting point to collect hemoglobin and transfusion data, and disregard hemoglobin measures and transfusions prior to the hip fracture.

Can the patient be recruited or remain in the study if the patient receives erythropoietin injections?

Erythropoietin is not ordinarily administered in this setting and we would prefer it not be used. However, patients may remain in the study.

Answers to these and other frequently asked questions can be found on the FOCUS Website and in FOCUS newsletters.

CHAPTER 14

EDUCATION ON PROTECTION OF HUMAN SUBJECT PARTICIPANTS

A National Institutes of Health (NIH) policy became effective October 1, 2000. This policy requires education on the protection of human subject participants for all investigators and key personnel who are responsible for the design and conduct of research under the NIH grant and contract awards for the research involving human subjects.

Since FOCUS is an NIH funded trial, the investigators and coordinators of all participating sites are required to comply with this new policy. Most academic institutions have already developed educational programs on the protection of research participants and have made attendance at such programs a requirement for their investigators. If your institution has not provided this training, an educational program can be accessed on the NIH web at http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp. This takes 30-60 minutes, and you receive a certificate at the end. This training module was originally developed for NIH staff, but it can be used by your personnel to meet training requirements. The program is simple and you are asked to answer only two questions after two cases. Please submit documentation of this education or a copy of the certificate obtained from the Internet training for each Clinical Site staff member identified as key personnel. The CCC is responsible for maintaining these records.

The NIH describes key personnel as anyone involved in the design or conduct of the research. This would include anyone who obtains informed consent, enrolls, and conducts follow-up with a patient. At a minimum you should consider the Clinical Site Director, the lead Clinical Site Coordinator and any other staff member who consents, enrolls and follows patients to be key personnel and consequently should provide documentation of their training. It is up to the discretion of the Clinical Site Director to determine whether other study staff (co-investigators, other coordinators) would be considered key personnel at his/her site. It is not necessary to document training of non-key personnel.

CHAPTER 15

INSTRUCTIONS FOR USE OF FOCUS WEB SITE

A. Overview

The FOCUS Web Site is available for use by all FOCUS Clinical Site and Central Unit staff. For questions about the Web Site, see the Contact Information page.

Web Access

To access the Public Web Address, type http://focustrial.org/ into your browser's address window. Until you are assigned an individual log-on and password, use log-on = XXX and password = XXXXX (in preparation). The Investigator Web address is http://www.focustrial.org/investigator. In order to access the investigator website, request a user name and password via: http://www2.umdnj.edu/~focusweb/focus/focusregister.html.

Adobe Acrobat Reader and PDF files

Most documents available on the FOCUS Web Site are in Portable Document Format (PDF). Documents in PDF preserve the exact look and content of the originals. Adobe Acrobat Reader is required to read and print the PDF documents. This product is free and is available from Adobe at http://www.adobe.com/products/acrobat/readstep.html. When installing the program from the Adobe Web Site, follow the directions given on that Web Site. Click on the file name to open a PDF document with the Adobe Acrobat Reader.

B. Contents of the FOCUS Web Site

The FOCUS Home Page (in preparation) identifies the categories of information available on the Web Site and provides links to those sections. To review the contents of each section, click on the section heading. The page for that section is then displayed. Each page lists the documents available in that section for the given category.

Protocol/Manual

The Protocol, Procedures Manual, Ancillary study Protocols and related documents in PDF format, are accessible from the Protocol/Manual page.

Memos

Important study issues are distributed by numbered memos, which are available in PDF format on the Memos page.

Minutes

Minutes of Steering Committee meetings.

Q & A

Frequently asked questions and answers about Protocol or Procedures and Contact Information are available for browsing on the Q & A page.

Forms

Study Forms in PDF format are available for printing.

Form QxQs

Instructions (Form QxQs) for each FOCUS Form provide specific details about each item on the form.

Study Tools

Study schedules, time lines and other study management tools are available in PDF format.

News & Events

Announcements of upcoming events as well as the FOCUS Newsletters are available in PDF format.

Presentations

The PowerPoint master slide set for conference presentation of background literature, overview of FOCUS Protocol, and data management training session slides are accessible from the FOCUS Presentations page. Click on the PowerPoint presentation name to open the presentation in PowerPoint.

Reports

Study Reports.

Publications

A list of study publications and presentations is on this page. Abstracts of published publications are in PDF format. Manuscripts in progress are available in MS WORD format on the FOCUS Publications page.

APPENDIX A

SAMPLE PIN CARD

FOCUS #36287

Staff Name

Study Password: XXX
Site: XXX
Hospital Password: XXXX
Pin: XXXXX

Univ. of Maryland Baltimore/Perry Point VA

APPENDIX B

Form 310

OMB No. 0990-0263 (Formerly OF-310) (1/17/2003)
Approved for use through 07/31/2005

Protection of Human Subjects
Assurance Identification/IRB Certification/Declaration of Exemption
(Common Rule)

Policy: Research activities involving human subjects may not be conducted or supported by the Departments and Agencies adopting the Common Rule (56FR28003, June 18, 1991) unless the activities are exempt from or approved in accordance with the Common Rule. See section 101(b) of the Common Rule for exemptions. Institutions submitting applications or proposals for support must submit certification of appropriate Institutional Review Board (IRB) review and approval to the Department or Agency in accordance with the Common Rule.	Institutions must have an assurance of compliance that applies to the research to be conducted and should submit certification of IRB review and approval with each application or proposal unless otherwise advised by the Department or Agency.

1. Request Type [ ] ORIGINAL [ ] CONTINUATION [ ] EXEMPTION	2. Type of Mechanism [ ] GRANT [ ] CONTRACT [ ] FELLOWSHIP [ ] COOPERATIVE AGREEMENT [ ] OTHER: _____	3. Name of Federal Department or Agency and, if known, Application or Proposal Identification No.
4. Title of Application or Activity		5. Name of Principal Investigator, Program Director, Fellow, or Other

6. Assurance Status of this Project *(Respond to one of the following)*

[ ] This Assurance, on file with Department of Health and Human Services, covers this activity:
Assurance Identification No., the expiration date IRB Registration No. _____

[ ] This Assurance, on file with *(agency/dept)*_____, covers this activity.
Assurance No._____, the expiration date_ __ IRB Registration/Identification No._____*(if applicable)*

[ ] No assurance has been filed for this institution. This institution declares that it will provide an Assurance and Certification of IRB review and approval upon request.

[ ] Exemption Status: Human subjects are involved, but this activity qualifies for exemption under Section 101(b), paragraph_____.

7. Certification of IRB Review (Respond to one of the following IF you have an Assurance on file)

[ ] This activity has been reviewed and approved by the IRB in accordance with the Common Rule and any other governing regulations.

by: [ ] Full IRB Review on (date of IRB meeting) _____ or [ ] Expedited Review on (date) _____

[ ] If less than one year approval, provide expiration date _____

[ ] This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by the Common Rule will be reviewed and approved before they are initiated and that appropriate further certification will be submitted.

8. Comments

9. The official signing below certifies that the information provided above is correct and that, as required, future reviews will be performed until study closure and certification will be provided.	10. Name and Address of Institution
11. Phone No. *(with area code)* 12. Fax No. *(with area code)* 13. E-mail:	
14. Name of Official	15. Title
16. Signature	17. Date

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APPENDIX C

SCHEDULE OF MEASUREMENTS AND DATA COLLECTION

Part I: Study Measures

	Pre-Randomization					Post-Randomization				
	Admission	Pre-Op	Post-Op Day 1	Post-Op Day 2	Post-Op Day 3	Post Rand Day 1	Post Rand Day 2	Post Rand Day 3	Post Rand Day 4	Post Rand Day 7
Hemoglobin	X		X	X	X	X	X		X	X*
ECG[1]	X		X*#						X*	
Troponin[2]		X*	X*#			X*			X*	

* Reimbursement will be provided by FOCUS
# ECG and troponin specimen drawn just prior to randomization

[1] Any ECG performed following randomization through post-randomization day 30 for any coronary event will also be sent to the ECG Core Laboratory. For contact/mailing info. (see FOCUS WEB). Labels for ECG (See Appendix H).

[2] If consent not signed pre-op, the pre-op Troponin will not be drawn. In this case, site personnel are to contact the hospital laboratory and, if available obtain left over serum from a preoperative draw. Blood is collected and filled to capacity in one of the following: a 10 mL plain red top tube, a 10 mL red/black Serum Separator Tube, or a 5 mL gold Hemogard Serum Separator Tube (SST). Invert tube five (5) times. Allow specimen to clot for 30 minutes for SST's or 60 minutes for plain red top tube. Centrifuge specimen at 1300 RCF for 10 minutes. Transfer serum by carefully pipetting into two (2) pre-labeled cryovials within 30 minutes. Freeze cyrovial samples within 30 minutes at $\leq$ -20 degree centigrade until shipment. Send frozen specimens using NIH shipping protocol.

APPENDIX C (Continued)

SCHEDULE OF MEASUREMENTS AND DATA COLLECTION

Part II: Forms

Number	Name	EXPECTED X AT VISITS					Send to DCC
		PreRand	Rand	HD	30day	60day	
					30-45	60-90	
00	Screening Log	X					DCC
D	Inclusion Criteria Checklist	X					keep
E	Exclusion Criteria & Consent Criteria Checklist	X					keep
	Evaluation to Sign Consent	X					keep
	Study Informed Consent	X [5]					keep
A	ITTRS Voice Response Worksheet		X				keep
01	Patient Registration		X				DCC
02	Patient History and Clinical Data		X				DCC
03	Medical Orders			X			DCC
04	Hemoglobin			X			DCC
4A	Hemoglobin Additional Days			X [4]			DCC
05	Transfusion Record			If TF			DCC
06	Required ECG			X			DCC
07	Required Troponin Blood Specimen	X [2]	X [3]	(D1, D4)			DCC
08	Cardiac Serum Marker Results and ECG for Clinical Care			X [4]			DCC
8A	Cardiac Serum Marker Results and ECG for Clinical Care Additional Days			X [4]			DCC
09	Hospital Outcome Form			X			DCC
10	Patient Status				X [1]	X [1]	DCC
11	ADL, IADL, and Energy/Fatigue				X [1]	X [1]	DCC
12	Death within 30 days			If death	If death		DCC
13	Serious or Unexpected Adverse Event (AE)			If AE	If AE	If AE	DCC
14	Proxy for primary study outcome					X	DCC
15	Acute Coronary Event (ACI)			If ACI			DCC
16	Pre-Randomization Transfusion Record		If PRTF				
InfoUS	Demographic & Patient Information – US			X			CCC
InfoCan	Demographic & Patient Information - Canada			X			CCC
ITTRS=Interactive Touch-Tone Randomization System used for Randomization of Patient							
InfoUS	Sent to CCC to provide contact information for the 30 and 60 day follow-up and for search of National Death Index						
InfoCan	Sent to CCC to provide contact information for the 30 and 60 day follow-up and for search of Statistics Canada						
1 = Completed by CCC Staff							
2 = Completed at baseline prior to surgery							
3 = Completed at post-op, prior to randomization							
4 = Completed on “as needed” basis							
5 = Completed PRIOR to randomization							

APPENDIX D

WINDOWS FOR SUBMISSION OF FORMS TO THE DATA COORDINATING CENTER

a. ITTRS Voice Response Worksheet – Complete before randomization call. File at site.

b. Treatment Allocation
Received from DCC by fax.

c. Demographic Information Form
Submit to CCC within 7 days of randomization. Do not send to DCC.

d. Form 01 – Submit to DCC within 7 days of randomization.
e. Form 02 – Submit to DCC within 7 days of randomization.
f. Form 03 – Submit to DCC within 30 days of randomization.
g. Form 04 – Submit to DCC within 30 days of randomization.
h. Form 4A – Submit to DCC within 30 days of randomization.
i. Form 05 – Submit to DCC within 7 days of transfusion.
j. Form 06 – Submit to DCC within 30 days of randomization.
k. Form 07 – Submit to DCC within 30 days of randomization.
l. Form 08 – Submit to DCC within 30 days of randomization.
m. Form 8A – Submit to DCC within 30 days of randomization.
n. Form 09 – Submit to DCC within 30 days of randomization.
o. Form 10 – Submit to DCC within 2 weeks of contact.
p. Form 11 – Submit to DCC within 2 weeks of contact.
q. Form 12 – Submit to DCC within 2 weeks of death.
r. Form 13 – Submit to DCC within 24 hours of adverse event.
s. Form 14 – Submit to DCC within 2 weeks of contact.
t. Form 15 – Submit to DCC within 2 weeks of Acute Coronary Event.
u. Form 16 – Submit to DCC within 30 days of randomization.
v. Form 00 – Screening Log – Submit to DCC within 1 week of screening.

APPENDIX E

Directions on Filling out a PDF Form

1. Double click on the form you wish to open.

2. Position the pointer inside a form field, and click. This will then allow you to type a text. When entering a form field always click on the left of the field. (Note that dashes and slashes will automatically appear) Just enter the numbers or letter without a break. For example: 00-000 would be entered as 00000 (the dash will automatically appear).

3. Never use the tab function or key when going from one field to the next or when filling in bubbles. Always use your mouse and click.

4. When filling in bubbles you will see an open hand as your cursor; when the open hand turns into a pointing finger that means you are able to click and select the appropriate bubble of your choice. To deselect the bubble because you selected the wrong one; just click on the correct bubble and the 1st one chosen will deselect.

5. If, prior to submitting the form, you have realized that you have filled the entire form out incorrectly you may reset the form. The RESET button along with the SUBMIT button is located at the end of each form in the center bottom of form.

6. When you've finished entering a form, select the SUBMIT bottom to send the information.

7. A pop up will say that a program is trying to access E-mail addresses and it may be a virus; select YES. (It's not a program; it's you submitting your form). A pop up will then ask you if you will allow this E-mail to be sent; select YES.

8. Now is the time to save your form if you choose to. Go to FILE on the toolbar and select "Save As" and create a name and place to save your form. You should also PRINT a hard copy of the completed form to be kept in the patient's study file.

9. Now close your form by selecting the X in the upper right hand corner.
A pop up will tell you your form was sent via E-mail; select OK.

10. You will have to select X again in the upper right hand corner to attempt to close; a pop up will ask if you want to save the changes before you close. You should select NO. (If you select yes it will save the form as it is and every time you open that form to fill it out for different patients that information will still be there.)

11. Your form will now close.

***Please note: When sending test data PLEASE enter 00-000's in the Staff ID section to distinguish actual data from test data.**

APPENDIX F

INSTRUCTIONS FOR SAVING A PDF FILE

A. Set-up File Directory Before Data Entry

Before keying data for FOCUS forms using the E-mail system perform the following steps

1. Set-up a File Directory
   - Open Windows Explorer
   - To open Windows Explorer: Click on the Start Icon>Programs>Windows Explorer
   - As an alternative to Windows Explorer, you may click on the My Computer icon

   - Determine where on your network or local computer drive you want to set-up a directory folder to retain the data for each form page. Click on that Drive Letter (Example: C:\)

   - On the menu bar of Windows Explorer: Click on File>New>Folder

   - A new folder appears in the window labeled "New Folder"
   - Change the name to "FCS E-mail Forms" by typing over the words "New Folder"
   - Then press the enter key
   - Double click on the new directory you just created - FCS *E-mail Forms*

2. Create Sub-directories for each Patient ID as follows:
   - On the menu bar of Windows Explorer: Click on File>New>Folder

   - A new folder appears in the window labeled "New Folder"
   - Change the name to the Patient's ID number, Example: "999-1001" by typing over the words "New Folder"
   - Then press the enter key

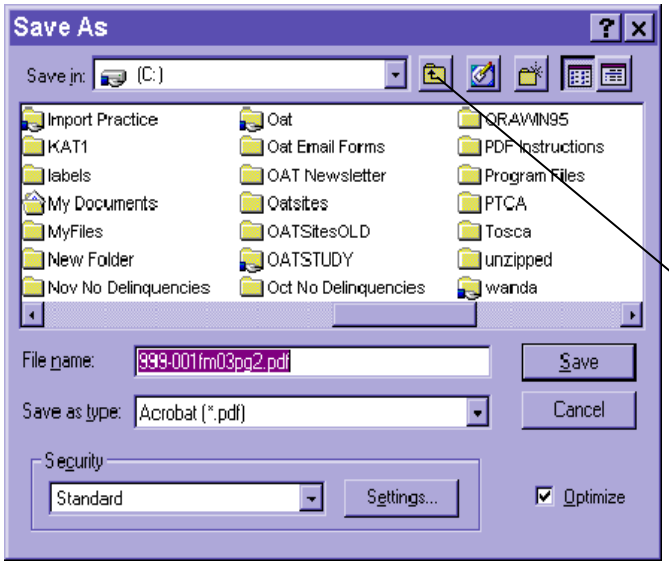
   - Before repeating Step 2 to create another Patient ID sub-directory, click on the folder FCS *E-mail Forms* in the Directory window on the left. Always click on the FCS *E-mail Forms* directory first before creating a new Patient ID sub-directory.

   When finished setting up the directories, close Windows Explorer by clicking on the "X" in the upper right corner of the screen.

4. After keying the patient data into the form, go to the menu bar of your Adobe Acrobat:
   - Click on File
   - Click on "Save As"

APPENDIX F (Continued)

A directory window appears: "Save As"	Look at the "Save in" Window box to see if you are on the correct drive.



If the appropriate drive or folder does not appear move to that drive as follows:

Click on the "Folder Icon" with the arrow that points up; continue to click on this icon until you see the Drive letter where your FCS E-mail directory resides.

Example: (C:).

5. Open the *FCS E-mail Forms Directory* by double clicking on it.

6. Open the appropriate Patient ID sub-directory by double clicking on it.

   Name the File:
   - In the "File name:" window
   - Create a file name: It is suggested that you use the patient ID number, form number and page number, *(e.g., 010-0011Form03.pdf) or use sequence number when saving a multi-visit form, (e.g., 010-0011Form05Seq02.pdf).*
   - Type the name in the "File name:" box.
   - Click Save

8. You may then clear the form to enter data for another patient or you may close this form. Be careful to close saved form files before clearing.

APPENDIX F (Continued)

B. Set-up File Directory After Data Entry

1. If you have keyed the patient data into the form and have not created a *Patient ID subdirectory* for his patient, you may create the *Patient ID subdirectories* from this "Save As" Window as follows:

2. Click on the "Folder Icon" with the arrow that points up until you see the Drive letter where your FCS *E-mail Forms* directory resides.

3. Double click on the FCS E-mail Forms directory to open it.

4. Create a new *Patient ID subdirectory*:

   - The "Save in:" window. When moving the mouse cursor over the icon it will say "Create New Folder".
   - Click on "Create New Folder"
   - A new folder appears in the window labeled "New Folder".
   - Change the name to the Patient's ID number, Example: "9991001" by typing over the words "New Folder".
   - Then press the enter key.
   - Double click on the new Patient ID sub-directory you just created.

5. To name the File:

   - In the "Save As" window
   - The 3rd white box from the top is "File name:"
   - Create a file name: It is suggested that you use the patient ID number, form number and page number, *(e.g., 010-0011Form02.pdf) or use visit number when saving a multi-visit form, (e.g., 010-0011Form05Seq02.pdf).*
   - Type the name in the File name box.
   - Click "Save"

6. You may then clear the page to enter data for another patient or you may close this form page.

APPENDIX G

LETTER TO ORTHOPAEDIC SURGEONS

<date>

Dear Dr. <name>:

We will shortly begin a randomized, clinical trial to evaluate the effect of red blood cell transfusion on functional recovery in elderly hip fracture patients. A summary of the study protocol is attached.

I am writing to request your assistance with the trial. We would like to provide a letter from you to each potential study participant at the time of recruitment. We have attached the letter and would be grateful if you would immediately sign and return it to us, as we will not be able to recruit your patients until we have this signed letter.

For your information, we have attached a summary of the study and wish to thank you for your continued support

If you have any questions or problems about the trial you should feel free to contact me at beeper <number> or <name>, RN at <number>.

Thank you,

<name>, MD

Please return the enclosed letter to <name>, RN, <address>, Fax <number> Thank you.

Study Description

FOCUS
Functional Outcomes in Cardiovascular Patients
Undergoing Surgical Hip Fracture Repair

This study is a multi-center randomized clinical trial that will include a total of 2,600 hip fracture patients with a history of cardiovascular disease or risk factors. We will evaluate if a more aggressive transfusion strategy that maintains postoperative hemoglobin (Hgb) levels above 10g/dL (100g/L) improves functional recovery, morbidity and mortality compared to a more conservative strategy that withholds blood transfusion until the patient develops symptoms of anemia or has a postoperative Hgb level below 8g/dl (80g/L).

All patients who present to the emergency room with hip fracture (that is not a result of multiple trauma requiring surgery other than hip fracture repair) will be identified as potential study participants. The patient and/ or family will be approached for informed consent. A short data collection instrument is completed and placed on the patient's chart. After surgical repair of the hip fracture, a Hgb level is performed daily for 3 days. The patient is eligible for the study if their Hgb level drops below 10 g/dL (100g/L) within the first three postoperative days. Study personnel office will retrieve each day's hemoglobin level and then randomize eligible patients by telephoning a 24 hour automated system. Patients assigned to the 10 g/dl threshold arm receive enough red blood cells to maintain their Hgb level at or above 10 g/dl. Patients assigned to the symptomatic transfusion arm receive a red blood cell transfusion only in the presence of symptoms from anemia or if their Hgb level is below 8 g/dl (80g/L); transfusion is permitted, but not mandatory. However patients with compromised cognitive function whose treating physicians believe might not be able to report symptoms are to be transfused when the Hgb level falls below 8g/dL (80 g/L). Patients will have blood samples drawn preoperatively, postoperatively prior to randomization, and on post randomization days 1 and 4, and electrocardiogram tracings preoperatively, postoperative prior to randomization and post randomization day 4. These blood samples and ECGs will be sent to central processing laboratories where they will be interpreted using standardized criteria to diagnosis myocardial infarction. This diagnosis will be for research purposes only and never linked back to the individual patient. At the time of discharge or death, the hospital data collection instrument will be completed. After discharge, patients will be contacted by telephone at 30 days and 60 days after surgery to determine vital status, ability to walk, and location of residence.

The primary outcome is death or inability to walk without human assistance. Secondary outcomes include myocardial infarction or death, functional status at 30 and 60 days, and nursing home placement at 60 days, 30 day and long-term mortality, significant postoperative morbidity (myocardial infarction, delirium, thromboembolism, pneumonia, and stroke), and the frequency of selected medical errors. Functional status and nursing home placement will be assessed by telephoning all subjects, and long-term survival by vital statistic registries. Postoperative complications (death in hospital or within 30 days and in-hospital morbidity) will be identified using information from the patient's hospital medical chart. An electrocardiogram and troponin levels will be obtained after surgery.

The trial will be conducted at 25 centers from the United States and Canada, and extend over five years. The trial is funded by National Heart, Lung, and Blood Institute, National Institute Institutes of Health.

NOTE: To be printed on Department of Orthopaedic Surgery or Orthopaedic Surgeon Letterhead

Letter to Recruit Hip Fracture Patients

<Date>

<Surgeon name>
<Address>

Dear Hip Fracture Patient:

I wish to make you aware of a research study currently being conducted at Name of Hospital. This study will evaluate how well patients recover from hip fracture surgery.

I have agreed to permit the research study staff to provide you with information about the study. It is up to you whether or not to participate in this study. This decision will not have any effect on the medical care you receive.

Please indicate below by initialing next to the appropriate level of interest.

_____ I am interested in hearing more about this study.

_____ I am not interested in this study.

Sincerely,

<Surgeon name>

Thank You Letters

Date

Dr. Orthopaedic Surgeon
Institution
Address

Re: FOCUS

Dear Dr Surgeon,

I am writing to express my appreciation for your help with the clinical trial called FOCUS. This study will only succeed if surgeons like you assist us to recruit patients into the study and follow the protocol. We believe this trial will provide critical information needed to inform clinicians on how to best use blood transfusion in the perioperative time period.

Sincerely,

Doctor
Principal Investigator

cc: Chair, Department of Orthopaedic Surgery

APPENDIX H

ECG LABELS

FOCUS RESTING SUPINE ECG

ID ___ ___ ___ - ___ ___ ___ ___ Letter Code: ___ ___ ___

__ __ - __ __ __ - __ __ __ __ Time: __ __ : __ __
Day Month Year hr mn

( ) Pre-surgery ( ) Post-Op prior to randomization
( ) Day 4 post randomization ( ) Unscheduled

APPENDIX I

FOCUS
Original Edit Statement

Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS)

Medical Center Name: _____

Date of this Supplemental: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
day month year

PID: ___ ___ ___- ___ ___ ___ ___ LETTERCODE: ___ ___ ___
center patient #

SUPPLEMENTAL CLARIFICATIONS FOR FORMS RELATING TO THIS PATIENT ONLY

FORM #	VISIT# SEQ# (FM 5,13,15) PERIOD (FM 7)	Variable Name of item to be changed from the data dictionary	Current Value	**Corrected Value**
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____
____ ____	____ ____	_____	_____	_____

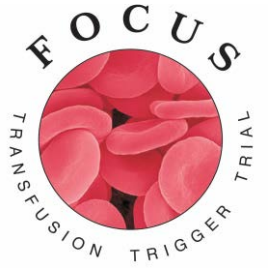
Signed by: _____ _____
(Coordinator) (Date Signed)

APPENDIX J

ID Number	Letter Code	Blood Specimen Labels	PreOp Specimen	Date Assigned	Enrollment	Coordinator Signature
999-0138	ABC	118167 077196 027267 023077	____never collected ____collected and reserved ____collected and destroyed	___/___/___	___yes enrolled ___not enrolled	_____
ID Number	Letter Code	Blood Specimen Labels	PreOp Specimen	Date Assigned	Enrollment	Coordinator Signature
999-0139	DEF	128167 073196 027467 023057	____never collected ____collected and reserved ____collected and destroyed	___/___/___	___yes enrolled ___not enrolled	_____
ID Number	Letter Code	Blood Specimen Labels	PreOp Specimen	Date Assigned	Enrollment	Coordinator Signature
999-0140	GHI	115167 047196 037267 063077	____never collected ____collected and reserved ____collected and destroyed	___/___/___	___yes enrolled ___not enrolled	_____
ID Number	Letter Code	Blood Specimen Labels	PreOp Specimen	Date Assigned	Enrollment	Coordinator Signature
999-0141	JKL	168167 075196 047267 033097	____never collected ____collected and reserved ____collected and destroyed	___/___/___	___yes enrolled ___not enrolled	_____
ID Number	Letter Code	Blood Specimen Labels	PreOp Specimen	Date Assigned	Enrollment	Coordinator Signature
999-0142	MNO	128167 077496 027266 023087	____never collected ____collected and reserved ____collected and destroyed	___/___/___	___yes enrolled ___not enrolled	_____
ID Number	Letter Code	Blood Specimen Labels	PreOp Specimen	Date Assigned	Enrollment	Coordinator Signature
999-0143	PQR	113167 055196 026667 023887	____never collected ____collected and reserved ____collected and destroyed	___/___/___	___yes enrolled ___not enrolled	_____
ID Number	Letter Code	Blood Specimen Labels	PreOp Specimen	Date Assigned	Enrollment	Coordinator Signature
999-0144	STU	118467 076196 087267 103077	____never collected ____collected and reserved ____collected and destroyed	___/___/___	___yes enrolled ___not enrolled	_____
ID Number	Letter Code	Blood Specimen Labels	PreOp Specimen	Date Assigned	Enrollment	Coordinator Signature
999-0145	VWX	118163 077144 027555 026666	____never collected ____collected and reserved ____collected and destroyed	___/___/___	___yes enrolled ___not enrolled	_____

APPENDIX K

Sample Chart Label - US



☐ **Consent Obtained**

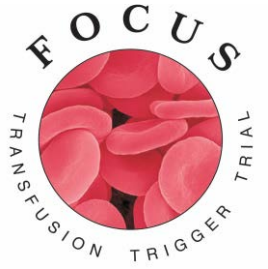
☐ **Randomized 10 g/dL**

- Subject immediately receives 1 unit RBC
- Post transfusion H/H drawn
- Hgb must be >=10 g/dL

☐ **Randomized Symptomatic**

- RBC transfusions held 1 unit RBC
- Transfusion given to relieve symptoms of anemia
- Any Hgb<8 g/dL RBC transfusion permitted to increase Hgb to 8g/dL

Sample Chart Label - Canada



☐ **Consent Obtained**

☐ **Randomized 100 g/L**

- Subject immediately receives 1 unit RBC
- Post transfusion H/H drawn
- Hgb must be >=100 g/L

☐ **Randomized Symptomatic**

- RBC transfusions held 1 unit RBC
- Transfusion given to relieve symptoms of anemia
- Any Hgb<80 g/L RBC transfusion permitted to increase Hgb to 80 g/L

APPENDIX L

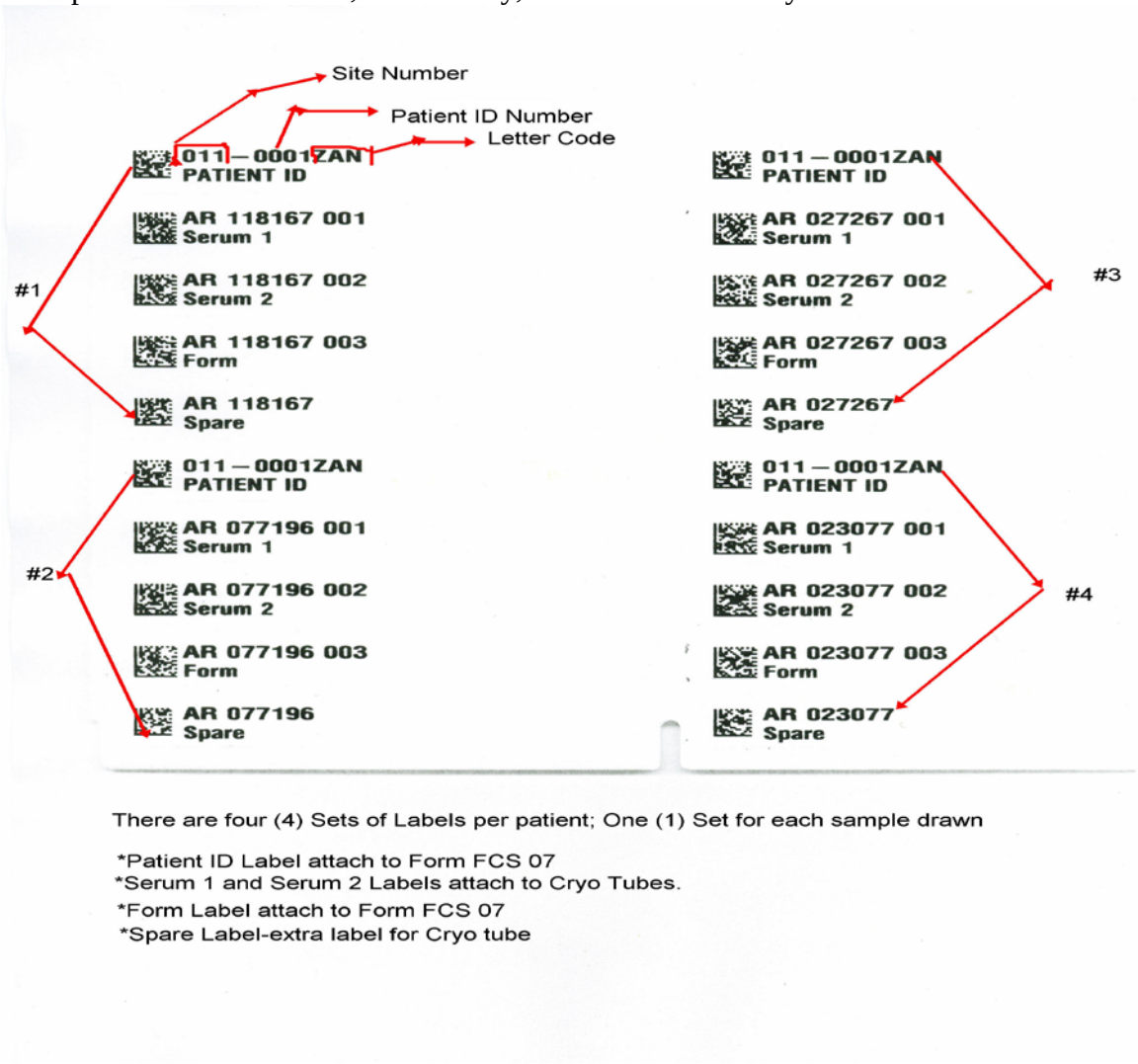
Specific Labeling Instructions for Blood Specimens for Central Troponin Analysis

Each study subject will be assigned 4 sets of 5 labels (total of 20 labels per study subject). A separate set is to be used for each blood specimen for central troponin analysis; preoperative, prerandomizaton, post randomization day 1, post randomization day 4.

The processed serum is to be pipetted into 2 cryovials. One cryovial is to be labeled with the Serum 1 Label and the second cyrovial is to be labeled with the Serum 2 Label.

FOCUS Form 07 Required Troponin Blood Specimen is to be completed, hard copy is to be printed out and the Form Label is to be affixed as marked on the form. These hard copies are to be kept in the study subject's file at the site.

The spare label can be used, if necessary, to label either the cryovial or the Form.



APPENDIX M

Patient ID and Lettercode: _____ Investigator/Coordinator: _____
Event: _____ Event Date: _____ Report Date: _____

Check to identify this event as a serious adverse event _____, acute coronary event _____, both serious adverse and acute coronary events _____.

Narrative Summary
Serious Adverse Event/Acute Coronary Event

1. Key Dates
   - Date of hip fracture
   - Date of surgery
   - Date Entered Into Study
   - 10 g/dL or Symptomatic?
   - Date Discharged

2. Patient Information
   - Age
   - Gender
   - Brief past medical history/relevant medications
   - Complications in Hospital
   - Last Hgb concentration nearest to event

3. Brief Description of Event

4. Pertinent Medical Tests Performed
   (Including laboratory results, ECG, x-ray reports, etc)

5. Reason Current Event is classified as an Adverse Event
   - Death (include date of death);
   - Life threatening (places subject at immediate risk of death);
   - Requires in-patient hospitalization or prolongation of existing hospitalization;
   - Is a permanent or significant disability/incapacity.

6. Outcome of Event

7. Impact on Discharge

8. Relationship to Study Treatment

9. If Acute Coronary Event attach the following (if available)
   - Progress notes that detail the event that occurred
   - ECGs for the event
   - Cardiac diagnostic testing performed
   - Hospital discharge summary

Note: **DO NOT complete this narrative summary** if Form 15 (Acute Coronary Event) was completed because CK-MB or troponin was assessed for screening in a patient with an uncomplicated recovery in hospital to the time of discharge and answers to questions 2A, 2B, 2C, and 3 on Form 15 are all NO. Keep source documentation available because the ECG Core Laboratory classification committee may request a narrative, if one was not initially prepared, in light of review of ECG and other data. If complications or unfavorable outcomes occurred, a complete narrative is required.

APPENDIX N

Patient Identification Number ___ ___ ___ - ___ ___ ___ ____ Lettercode ___ ___ ___

Patient Withdrawal Form

1. Date local FOCUS staff notified of patient's wish to withdraw _____

2. Patient Concerns

	YES	NO
A. Phlebotomy required by the study protocol (if no, skip to B)	_____	_____
1. Was patient assured that he/she is free to refuse these procedures and continue to participate in the study?	_____	_____
B. Electrocardiograms as required by the study protocol (if no, skip to C)	_____	_____
Was patient assured that he/she is free to refuse these procedures and continue to participate in the study?	_____	_____
C. Adherence to transfusion protocol (if no, skip to D)	_____	_____
Was patient assured that he/she is free to refuse the transfusion protocol and continue to participate in the study?	_____	_____
D. Were patient concerns the follow-up telephone calls (if no, skip to #3)	_____	_____
Was the patient asked for permission to telephone the proxy or other contact for the 30 and 60 day assessments?	_____	_____
2. If patient refuses surrogate 30/60 day contact, was patient asked for permission to contact proxy at 60 days to obtain ambulatory status?	_____	_____

3. Outcome of Patient Concerns

	YES	NO
A. Patient agrees to stay in study (if no, skip to #4)	_____	_____
Select all that apply		
Patient agrees to all study procedures?	_____	_____
2. Patient refuses phlebotomy?	_____	_____
3. Patient refuses electrocardiograms?	_____	_____
4. Patient refuses transfusion protocol?	_____	_____
5. 30 and 60 day phone calls are to be answered by surrogate?	_____	_____
6. Only telephone follow-up is proxy contact at 60 days for ambulatory status?	_____	_____

Patient Identification Number ___ ___ ___ - ___ ___ ___ ____ Lettercode ___ ___ ___

	YES	NO
4. Study Chairman called?	_____	_____

A. Date study chairman called ___ ___ - ___ ___ ___- ___ ___ ___

5. Study Chairman/Data Coordinating Center Principal Investigator determination. This patient will:

	YES	NO
A. Remain enrolled in FOCUS	_____	_____
B. Remain enrolled in FOCUS with reduced data expectation	_____	_____
C. Be withdrawn from FOCUS with no data to be included as of ___ ___ - ___ ___ ___- ___ ___ ___	_____	_____

Specify _____
_____
_____

Signature: _____

Date: ___ ___ - ___ ___ ___- ___ ___ ___