GUIDing **E**vidence Based Therapy Using Biomarker **I**ntensified **T**reatment in Heart Failure (**GUIDE-IT**)

Sponsor: NHLBI

Manual of Operations

Version 2.0

Version Date: February 5, 2014

All staff members participating in the conduct of this study at participating institutions should have access to the MOO and be familiar with its contents. The current version of the MOO is posted to the study web site:

https://www.guide-it.org

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List of Abbreviations

6MWT	6-Minute Walk Test
ACE	Angiotensin Converting Enzyme
AE	Adverse Event
ARB	Angiotensin Receptor Blocker
BNP	B-type Natriuretic Peptide
CCC	Clinical Coordinating Center
CEC	Clinical Endpoints Committee
CES-D	Center for Epidemiologic Studies Depression Scale
CRT	Cardiac Resynchronization Therapy
CV	Cardiovascular
DASI	Duke Activity Status Index
DCC	Data Coordinating Center
DCRI	Duke Clinical Research Institute
DSMB	Data Safety and Monitoring Board
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EQOL	Economics and Quality Of Life
HF	Heart Failure
HRQOL	Health-related Quality Of Life
ICD	Implantable Cardioverter Defibrillator
IRB	Institutional Review Board
IVRS	Interactive Voice Response System
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVEF	Left Ventricular Ejection Fraction
mL	Milliliter
NHLBI	National Heart, Lung, and Blood Institute
NTproBNP	Amino-Terminal pro B-type Natriuretic Peptide
SAE	Serious Adverse Event
QOL	Quality of Life

Tab: Overview and Study Design

1 Overview and Study Design

1.1 Introduction

This Manual of Operations (MOO) provides a blueprint for operations for the **GUIDing Evidence Based Therapy Using Biomarker Intensified Treatment in Heart Failure (GUIDE-IT)** study.

The purpose of the GUIDE-IT MOO is to describe clinical research procedures to ensure execution of the clinical trial in accordance with the goals of the GUIDE-IT protocol. Organization of the GUIDE-IT MOO and protocol are similar in topical order and contain complementary, rather than redundant detail. The protocol provides the definitive description of the research plan. The MOO provides practical guidelines for accomplishing research plan objectives.

The MOO is a dynamic document that will be updated throughout the conduct of this study to reflect any protocol or consent amendments and refinements of the CRFs and study procedures.

1.2 Overview

Title:	GUIDing Evidence Based Therapy Using Biomarker Intensified Treatment (GUIDE-IT)
Indication:	Heart Failure
Location:	Approximately 40 clinical centers in U.S. and Canada
Rationale:	Current guidelines recommend that medical therapy be titrated toward the target doses used in clinical trials, but “therapeutic inertia” often represents a barrier to aggressive titration of medical therapy. There is a pressing need to develop strategies to improve utilization of proven therapies for HF in order to improve clinical outcomes and control costs. Observational studies have shown an association between decreasing natriuretic peptide levels over time and improved outcomes in patients with HF.
Objectives:	To compare a strategy of medical therapy titration aimed at achieving and maintaining an NTproBNP target of < 1000 pg/mL (biomarker-guided therapy) to usual care in high-risk patients with systolic heart failure.
Study Design:	Prospective, randomized, parallel controlled groups, unblinded, 2-arm, multicenter clinical trial of approximately 1100 patients.
Primary Endpoint:	Time to cardiovascular death or first HF hospitalization.
Secondary Endpoints:	• Time to all-cause mortality • Cumulative morbidity • Time to cardiovascular death • Time to first HF hospitalization • Health-related quality of life (HRQOL) • Resource utilization, cost and cost effectiveness • Safety

1.3 Study Design

SCREENING

High-risk systolic HF (LVEF ≤ 40% within 12 months)
NT-proBNP > 2000 pg/mL

RANDOMIZATION

For hospitalized patients (or seen in ED), consent obtained at discharge or within 2 weeks

Randomized to either Usual Care (N=550) or Biomarker Guided NT-proBNP < 1000 pg/mL (N=550)

Baseline visit (day 0)

History and physical exam, CV medication history, serum creatinine, BUN and electrolytes and NT-proBNP (local lab), QOL questionnaires, medical resource use and cost assessment, 6MWT, biomarker and DNA sample collection

FOLLOW-UP

2-week follow-up (± 1 week)

History and physical exam, CV medication history, change in HF therapy rationale, serum creatinine, BUN and electrolytes (local lab), NT-proBNP (local lab biomarker guided arm only), medical resource, cost assessment and biomarker samples

6-week follow-up (± 1 week)

History and physical exam, CV medication history, change in HF therapy rationale, serum creatinine, BUN and electrolytes (local lab), NT-proBNP (local lab biomarker guided arm only), medical resource, cost assessment and biomarker samples

3-month follow-up (months 3, 6, 9, 12, 15, 18, 21, and 24) (± 1 week)

History and physical exam, CV medication history, change in HF therapy rationale, serum creatinine, BUN and electrolytes (local lab), NT-proBNP (local lab biomarker guided arm only), medical resource, cost assessment and biomarker samples

Notes:

- Minimum 12 months of follow-up.
- Study visits occur every 3 months until a maximum of 24 months.
- 2-week (±1 week) follow-up after adjustment of therapy or hospitalization.
- Follow-up visits include brief clinical assessment, serum creatinine, BUN and electrolytes (local lab), and NT-proBNP (local lab biomarker guided arm only).
- Follow-up visits continue every 2 weeks until therapeutic targets are reached, or until further titration of therapy is not possible.
- QOL questionnaires to be administered by EQOL group at 3 months, 6 months, 12 months and yearly until the end of the study
- EQOL CC will collect medical resource and cost assessments throughout the length of the study

Tab: Contact Information

2 Contact Information

Trial Website https://www.guide-it.org/

- Study-specific information and resources
- Downloadable forms and study materials
- Updates
- Links for other resources

Urgent Clinical Questions

GUIDE-IT Hotline 1-919-998-9928

Non-urgent questions: contact the DCRI Clinical Research Team by email.

DCRI Clinical Research Team

Email GUIDE-IT@dm.duke.edu

Questions regarding

- Non-urgent clinical issues
- Event reporting
- Safety reporting
- Site payment
- eCRF data entry
- Query resolution

See Appendix A for list of DCRI team members

Submission of Documents to DCRI (including consent forms, patient contact information forms, and medical release forms)

ftp.dcri.duke.edu

Use your site-specific username and password to log in to access your site's secure folder on the FTP site. DCRI will issue your username and password after site activation.

Randomization

Randomize subjects through the InForm eCRF system. See section 5.1 for details.

InForm EDC (eCRF)

https://inform-edc.dcri.duke.edu/guideit/

Training site: https://inform-edc.dcri.duke.edu/guideit_trn/

Training login: Username: crc2

Password: inf5606 (please do not change the password)

Questions regarding technical problems using the eCRF or to reset your password:

U.S. and Canada: 1-866-999-DCRI [3274]

E-mail: edchelp@dm.duke.edu

Coverage: 24 hours a day, 7 days a week

Questions regarding entering subject data, queries, traffic lights, etc., contact the DCRI Clinical Research Team by email: GUIDE-IT@dm.duke.edu

Biorepository and Central Lab

Labcorp Clinical Trials, Cranford, NJ

Questions regarding samples acquisition, preparation, storage, shipping:

Phone: 1 877-788-8861 ext. 7363 or 1-908-709-5700

Fax: 1-615-263-0414

EQOL

Fax: 1-919-668-9816

Use the secure fax or FTP site to submit questionnaires, consent forms, and medical release forms.

Questions regarding administration or submission of baseline questionnaire, consent form, medical release form:

Email: guide-iteqol@duke.edu

Phone: 1-919-668-8892

Clinical Events Committee

Use the secure FTP site to submit de-identified source documents.

Questions regarding event reporting or submission of source documents:

Clinical Trials Coordinator	Deb Greene	1-919-668-8642	deborah.greene@dm.duke.edu
Project Leader	Patrick Loebs	1-919-668-3684	patrick.loebs@dm.duke.edu

Tab: Recruitment and Retention

3 Recruitment and Retention

3.1 Identifying Subjects

The study population will consist of patients at least 18 years of age, who have a diagnosis of systolic heart failure, a left ventricular ejection fraction of ≤ 40% performed within the prior 12 months at least 12 weeks after any intervention likely to improve the LVEF, and an NT-ProBNP > 2000 pg/mL.

Site personnel will follow local process to obtain permission to review hospital and clinic records and assess patient eligibility before reviewing eligibility criteria against hospital/clinic charts. All subjects must sign and date the consent form before any study-related procedures or tests are performed and prior to any data being entered into the InForm EDC system.

Study patients will be identified by the study coordinator through daily screening of the hospital admission records, clinic records, and patient referral, and will be followed by review of each potential study patient's medical chart. If the patient has a documented qualifying LVEF and NT-ProBNP and appears to meet enrollment criteria and if hospitalized, follow the patient until the time of hospital discharge. During the hospitalization, or within 2 weeks of discharge, discuss the study with the patient and family (if applicable). Explain the details of the study and after answering all questions and allowing adequate time, ask the patient to sign an informed consent document.

After signing the consent form and enrolling, confirm all eligibility criteria. If the subject meets all criteria, randomize to biomarker-guided therapy or usual care using the SIRE system within InForm.

3.2 Screening

The investigator or designee will evaluate patient eligibility to enter the study based on clinical signs and symptoms, the clinician's judgment, and the inclusion/exclusion criteria. Patients who fulfill all of the inclusion criteria and none of the exclusion criteria listed in the protocol will be eligible for randomization into the study.

3.3 Eligibility Criteria

Refer to the study protocol for the complete list of eligibility criteria. Study personnel will use the Eligibility worksheet (Appendix C) for determining whether the patient meets the qualifications for study participation.

3.4 Recruitment

Identify potential subjects in both inpatient and outpatient settings. Possible inpatient strategies include:

- Review daily census
- Electronic query of inpatient data—BNP reports
- Referrals from physicians or quality improvement colleagues. A recommendation from a physician is often the primary influence on a patient's decision to participate.
- Set up a "watch list"

In outpatient settings:

- Review charts for post-discharge follow-up visits.

Be inclusive in your review of records.

- Review more than just diagnosis
- Search for chief complaint of chest pain or afib with RVR

Recruitment Challenge	**Planned Mitigating Action**
Patient Identification: Inability of study sites to identify potential patients	• Facilitate subject recruitment through enhanced site support efforts (such as supplemental education materials to distribute to hospital personnel, Dear Doctor letters to increase awareness of the study, etc.) • Evaluate enrollment procedures at each site. Different recruitment strategies may be required depending on the hospital model.
Deviation from Standard of Care: Concern of physicians and clinical personnel about potentially deviating from standard of care.	• Educate site personnel about heart failure, the available literature, the study protocol, and procedures aimed towards establishing an effective heart failure treatment management as specified in the protocol.
Barriers for patients ▪ Lack of resources ▪ Confusion about the difference between research and medical care ▪ Confusion about the study procedures ▪ Fear, distrust or suspicions of research ▪ Not wanting to change current provider or therapy	Solutions/Facilitators ▪ Flexibility ▪ Reimbursement ▪ Personal touch ▪ 24/7 contact pager ▪ Appreciation ▪ Reminder letters ▪ Diversity of personnel ▪ Information and teaching
Be aware of special populations	▪ Older Adults ▪ Psychological changes for the older adult result in motivational changes ▪ Depression ▪ Physical barriers ▪ Family concerns ▪ Women ▪ Time off of work ▪ Childcare ▪ Care of elderly family members

3.5 Patient Contact Information

The Patient Contact Information form (Appendix E) is a critical tool for maintaining contact with subjects. It is important to complete and update this form with current and accurate information.

- Complete all areas of the Patient Contact Information form with the subject.
- Ask the subject for names and contact information for family and friends who do not live with them.
- Ask the subject to inform family and friends that their names were provided as a means to contact the subject. These people will be aware of the study and more likely to cooperate when contacted.
- Maintain the Patient Contact Information Sheet with the subject's study documents. Other than the DCRI EQOL group, do not submit the form to any other entity due to the confidential content.
- Obtain additional authorization for contacting the subject's doctors, if necessary. This allows access to information regarding study events (e.g., hospitalizations, serious adverse events) normally considered confidential and restricted.
- After the baseline visit, upload the Patient Contact Information Form and the Medical Records Release to the FTP site for use by the DCRI EQOL group.

3.6 Retention

Subject retention is critical to the success of any long-term follow-up study. Maintaining the subject's interest, active participation, and commitment to the study can be challenging.

Initiating retention efforts *during the screening phase* for each subject is strongly encouraged. Assess barriers to adherence and retention during the screening process. Monitor potential issues (which often predict retention problems) and try to identify them early, before the subject refuses further study participation.

Subjects who feel that they have been appropriately educated about the study are more likely to take ownership of their responsibilities while enrolled and remain in the study.

Common reasons subjects may decline to enroll in a study or dropout once enrolled include:

- Misunderstanding about clinical trial participation
- Concerns about the protocol complexity and treatments
- Poor motivation, particularly if the dosage or protocol is complex (numerous clinic visits and/or laboratory tests)
- Transportation issues
- Lack of support and guidance during the study

3.6.1 Identify Signs of Potential Study Withdrawal/Drop-Out

Become familiar with signs or changes in subject's behavior indicating adherence issues such as:

- Missed visits, difficulty in reaching subject by phone, failure of subject to return calls, rescheduling study visit, or unexplained changes in adherence to study regimen.
- Complaints about study visits, impatience, lab draws, being quiet or withdrawn during study visits, or unconcerned about adherence to study drug/regimen.

**Suggestion—determine if the behavior is related to study participation or if the subject has a life-altering event such as a relocation, major illness, accident, or death affecting them or a close family member.*

- Changes in subject's health such as hospitalization, development, or recurrence of other illness.

**Suggestion—talk to the subject. In some cases, they may feel their illness is related to their study participation. If the subject expresses concern, work through the issue(s) and help them determine if they should continue.*

- Changes in study site environment such as new clinic personnel, delay in the flow of study visits, new physical location or construction work at the study site.

**Suggestion—let the subjects know in advance about changes at the study site. Introduce them to new personnel. If possible, identify a primary staff member for each subject. "Hand over" to another staff member openly and in the presence of the subject when a staff change is made.*

3.6.2 Tips for Retention

When scheduling and conducting visits:

- Use a schedule to document visits for all subjects and track upcoming visits and reminder tasks.
- Provide subjects the handout with the schedule of all the visits so they know what to expect.
- Call subjects 2–3 days in advance to remind them of a clinic visit, what they can expect during the visit, and items they need to bring (medication, etc.).
- Send a postcard to subjects reminding them of the scheduled visits/phone contact.
- Review the Patient Contact Information form at each visit to verify current contact names and numbers—update as needed.
- Provide reminder appointment cards and/or update their calendar of visits.
- Review the subject's understanding of the study along with their responsibilities. Re-educate as needed and provide additional education materials.

- Call as soon as possible after a missed visit to determine the reason and reschedule the visit.

Promoting interest and commitment to the study

- Stress the importance and value of the subject's participation to further the knowledge of health care providers and for cardiac care.
- Send birthday and/or anniversary cards to subjects.
- Request that the principal investigator write a thank you note to the subject for their participation.
- Provide the subject with routine study updates and progress.

Offering accessibility and convenience

- Provide flexible clinic visits to accommodate after work and or weekend visits.
- Provide parking vouchers, if compensation for parking is available, to eliminate subject's concern about payment or reimbursement for parking.
- Provide public transportation schedules, and phone numbers for taxi services.
- Provide phone number, directions, and map to the study office.
- Provide directions and good signage to the study site. Preprinted maps may be available from sources within your institution. Detailed information such as elevator location, floor, and room number is essential.

Communicating and using a team approach

- Inform the subject's health care providers regarding their participation in the study.
- Send a letter to the subject's primary care physician and/or the referring physician, regarding the study design. Send letters at the beginning of the study as well as during the follow-up phase.
- Involve family members, when appropriate, to support the subject through the study and encourage their continued participation.

The above tips are efforts to help eliminate unnecessary deviation from the protocol and may help with follow-up efforts.

3.6.3 Tips for Locating Subjects

Make every effort to maintain routine contact with each subject. Begin attempts to locate subjects as soon as possible after a missed visit; delays in locating the subject increase the chance of the subject becoming lost to follow-up.
Use the Early Termination/Non-Responder Form (Appendix G) to track attempted contacts to the subject/alternate contact/healthcare provider.
The techniques listed are not in a preferred order. For those subjects who are unable or unwilling to continue or cannot be found, the use of proxy interviews and/or public databases may be acceptable for obtaining vital status information.

Locating Methods

Mail—Contacting the Subject

- Send a certified/recorded delivery letter, with return receipt requested, to each address the subject provided on their contact list. Request that the subject contact the study coordinator by phone and offer reverse calling or a toll free number if they are calling long distance.

  Note: If the signature on the returned receipt matches the signature of the subject on the informed consent form, the subject is determined to be alive as of the date of the signed certified/recorded delivery letter.

  Certified/recorded delivery is preferred for the following reasons:

  - If a subject has moved, the post office will forward the mail to the new address as long as the forwarding period has not expired.
  - If the letter is not delivered and signed after three delivery attempts, a notice is left for the subject to pick up the letter at their nearest post office (couriers will return mail to distribution center).

  Important: Be sure to track the certified/recorded delivery letters and review any returned correspondence for address updates. If a subject has a new address, send another certified/recorded delivery letter to the new address.

Mail—Contacting the Subjects Family/Friends

- Send a certified/recorded delivery letter, with return receipt requested, to each individual the subject listed. The letter should note the subject agreed to be followed for a health study and ask the individual to assist with locating the subject. Request they pass the letter on to the subject and have the subject contact the study coordinator.

Telephone—Contacting Subject, Family and/or Friends

- Call the number(s) for subject, family, and/or friends provided on the Patient Contact Information form.
- Place the calls during the day, after hours, and on weekends (late afternoon and early evening work best).
- Reattempt numbers that are busy or directed to answering machines until contact with a person is made.
- Obtain contact information for other family, friends, or relatives who may know the subject's status, if the individual who answers the phone does not know the subject's status or location.
- Verify that the correct number was dialed when the person answering does not know the subject, or when you receive a message for a disconnected or changed number.

Telephone—Contacting Primary Care Physician or Other Health Care Providers

Call the primary care physician/GP, referring physician and/or other listed physicians, dentists, or known pharmacists for date of last office visit or contact, alive/dead status, or other next of kin contact information.

Computer/Database—Searches

- Review the subject's hospital or clinic records for any details of a hospitalization, doctor's visit, laboratory visit, or other procedure that may indicate status of subject.
- Search public record web sites. Many countries have their public records on line.
- Search national death registers. Where permitted by national law, you may be able to access death information.

3.6.4 Helpful Websites for Finding Subjects

3.6.4.1 Free Sites

Ancestry.com—You must sign up to view the search results and you can immediately unsubscribe from the newsletter.

Anywho.com—Go to the "Person" section and enter the information you have.

People.yahoo.com—This site is easy to work with and also has an email search.

Searchbug.com—Go to "Peoplefinder" or "People by Name" sections and enter the information you have.

Smartpages.com—Go to "Find A Person" and enter the information you have.

SSDI.rootsweb.ancestry.com—This is the Social Security Death Index site and will only search for deceased patients. These listings are updated monthly (though current legislation may limit access).

Whitepages.com—This site provides information found in each state's phone book.

192.com—This site is helpful when searching internationally for patients. Go to the "People finder" section and enter the patient information you have. Try entering information with and without the location to get the best results.

3.6.4.2 For a Fee

Ussearch.com—This site provides only city and state information before requiring a fee. This is good for finding relocation information that can be used in a white pages search.

Vitalcheck.com—This site connects you to several different public records.

3.6.4.3 Website Search Tips

- Use the patient's first initial and last name, instead of the complete first name.
- Use only the patient's last name, without first or middle names.
- Try searching with and without the state, in case the patient has moved.

The above web sites are provided as references. The GUIDE-IT study makes no endorsements, representations, or warranties regarding the website content.

Tab: Informed Consent

4 Informed Consent

4.1 Process

Informed consent is a process initiated prior to the individual agreeing to participate in the study and continuing throughout the individual's study participation. Site staff may employ IRB-approved recruitment efforts prior to the subject consenting; however, a consent form must be signed before performing any protocol-specific procedures to determine protocol eligibility. Extensive discussion of risks and possible benefits will be provided to the subjects and their families, as well as information on the length of study participation, study procedures, available alternative treatments, cost to the subject (if any), and that study participation is entirely voluntary. Provide consent forms describing the study interventions, study procedures, and risks.

Informed consent and HIPAA authorization are required prior to starting any study-related procedure or intervention. The consent form must contain all of the elements of informed consent; the HIPAA authorization must contain all of the core elements and mandatory statements as defined in the code of federal regulations. HIPAA language may be part of the informed consent document or in a separate document. Consent and HIPAA forms will be IRB-approved and the subject will be asked to read and review the document(s). Upon reviewing the document(s), the investigator (or designee) will explain the research study to the subject and answer any questions that may arise. The subject will indicate consent by signing and dating the consent form prior to any procedures being done specifically for the study. By signing the consent form, the subject agrees to complete all evaluations required by the trial unless the subject voluntarily withdraws or is terminated from the trial.

The subject should have the opportunity to think about and discuss the study with their family/friends prior to agreeing to participate. If the subject is unable to provide written consent, then verbal assent must be obtained if required by applicable regional regulations (e.g., for the mentally impaired), and written consent obtained from the legal guardian in accordance with the appropriate state laws, where applicable. The subject may withdraw consent at any time throughout the course of the trial.

Place the signed/dated original consent form and HIPAA authorization form (one document if HIPAA language is included in the consent form) in the investigator's study files unless local procedures require an alternate storage location. Give a signed copy of the consent form (and HIPAA authorization form, if separate) to the subject for their records. The rights and welfare of the subject will be protected by emphasizing to the subject and/or legal guardian that the quality of their medical care will not be adversely affected if they decline to participate in this study.

DCRI will provide the investigator, in writing, any new information that bears significantly on the subject's risk to receive the investigational product. This new information will be communicated by the investigator to subjects who consent to participate in the trial in accordance with IRB requirements. The consent form will be updated and subjects will be consented again, as necessary.

Note: If a subject is withdrawn after enrollment, the signed consent form should still be maintained and not destroyed.

4.2 Genetics and Biorepository Consent

4.2.1 Purpose/rationale of biomarker/genetic components

- Disease characterization and therapeutic responses will play an increasingly important role in the diagnosis and management of chronic diseases such as heart failure.
- A biomarker is anything that can be used as an indicator of a particular disease state or chemical or physical function.
- Subjects will be asked to provide blood samples for deposit into a biorepository at each scheduled visit, including the Baseline Visit.
- These samples will be used for future assessments of molecular biomarkers in plasma and serum.
- Subjects will be asked to consent to allow use of the biorepository samples for genetic testing (DNA).
- Subjects may consent to participate in the biomarker repository and/or the DNA component of the trial.

4.2.2 Potential barriers to participation in biomarkers/genetics

- Overall site recruitment struggle
- Subject is skeptical of participation
- Subject refuses to consent to biomarkers and/or genetics participation
- Blood draw/processing interrupts clinic workflow
- Lack of site staff understanding of the role of biomarker and genetic testing
- Lack of freezer space or access to dry ice for storage and shipping

4.2.3 Possible solutions

- Improve recruitment
  - Engage local colleagues to assist
  - Implement frequent booster sessions within the practice
  - Promote competition among referring physicians/sub-investigators
  - Spread the word about GUIDE-IT using GUIDE-IT provided materials (pocket cards, eligibility worksheets, etc.)
  - Implement patient “flagging” system for pre-screening patients (GUIDE-IT prescription pad, post-it notes, electronic flags, etc.)
- Educate about sample anonymity
  - The link to the subject will be destroyed after all study data is collected, prior to biomarker and/or DNA analyses
  - No links will be retained between the subject and the blood sample from which biomarker and/or DNA will be obtained

- Because the DNA data will be anonymized, it will not be possible to report any incidental findings back to the subject.

- Personalization of donation
  - Remind subject that participation will help not just future generations, but possibly family members, etc.
- Provide real world examples
  - Biomarkers (cholesterol, PSA for prostate screening; CRP for inflammation; hemoglobin A1c for diabetes, etc.)
  - DNA (BRACA breast cancer gene; sickle cell anemia; Huntington's disease)
- Describe volume of blood needed at each visit
  - ~20 mL, 4 teaspoons, less than 1/12th of a can of Coke.

- Solutions to lack of freezer space
  - Samples may be sent on day of collection if absolutely necessary.
  - Samples may be stored temporarily on dry ice if freezer space is not available.

4.2.4 Biorepository Participation Pearls of Wisdom

- PI or Sub-I presents the study to the patient initially
- Patients are informed they will not get results; the samples are stored in a research repository, and there may be no direct benefit to the patient
- The research staff provides examples of how future discoveries may help family/friends with a chronic problem, and that by providing research samples, the patient may be able to help their family and friends in the future
- The Study Coordinator explains that almost all research studies being done now have a biorepository component
- The Study Coordinator explains to the subject that the future of medicine will be based on the information gathered from biomarkers/DNA and that even though it may not benefit the subject directly, it may benefit future generations
- Stress that biorepository participation is voluntary
- Study Coordinator explains that biorepository participation is an optional but important part of the study
- Coordinators go page by page with the subject explaining all aspects of the study, including biorepository participation.
- Biorepository is incorporated into the main consent (not separate).

- Biorepository participation is a separate consent to the main consent and the study coordinator explains that there is no direct benefit to the subject and the reasons for doing these types of studies.
- The main study is presented during a prescreening phone call to the patient. Biorepository participation is not mentioned during the prescreening, just an overall view of GUIDE-IT.
- The consent is sent home with the patient to review while the research staff schedules a separate screening/consenting visit after the initial MD visit.
- The staff shows the patient the lab tubes so the patient knows the amount of blood to be drawn.
- Study Coordinator tells the subject the amount of blood that is more relatable to them such as teaspoons or the amount is less than a certain amount of a can of Coke.
- The staff tries to schedule any visit requiring a draw in the morning or early afternoon.
- The staff minimizes the number of sticks to coincide the sample collection with standard of care lab draws.
- Before the patient is given the ICF, the Study Coordinator explains that there is an optional blood draw component, and that it can be drawn at the same time as SOC draw.
- Patient is informed that the samples will become anonymous and no results will be available to the patient. There will be no way for results to be traced back to the patient that could place them jeopardy at a future date.
- The staff uses the example of how the BRACA gene was discovered for breast cancer by this type of research and sample collection.
- Staff gives examples of the types of tests that have been developed from Biomaker/DNA research (cholesterol, PSA prostate screening, CRP for inflammation, Hemoglobin A1c for diabetes, etc.)

4.3 Informed Consent Template

A consent form template is located on the trial website. The template contains language specific for the GUIDE-IT study. Sites should insert site-specific information and required language and send the form to the DCRI Lead CRA or designee for approval prior to submission to the local IRB. The informed consent process should be documented in the subject's medical record including the date and time of consent and that the subject was provided a copy of the signed consent form.

Tab: Study Procedures

5 Study Procedures

The complete study visit schedule is listed in Appendix A of the protocol. Worksheets for collecting data at the study visits are located in Appendix F and on the trial website.

5.1 Randomization

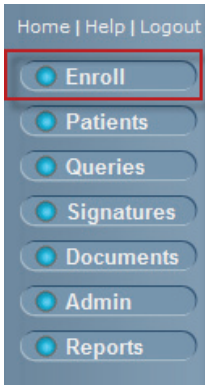
Randomization will occur at the time of discharge or within a 2-week window after hospital discharge. A total of 1100 subjects will be randomized in a 1:1 fashion using the Simple Internal Randomization Engine (SIRE) within the InForm eCRF to either biomarker-guided therapy or usual care. The unit of randomization will be at the patient level rather than the site level. Treatment allocation will be conducted using a complete randomization scheme.

5.1.1 To Randomize a Subject

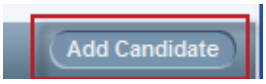
After logging in to InForm, click on the Enroll button on the left side of the screen

Access the GUIDE-IT InForm system to enroll and randomize a subject into the GUIDE-IT trial.

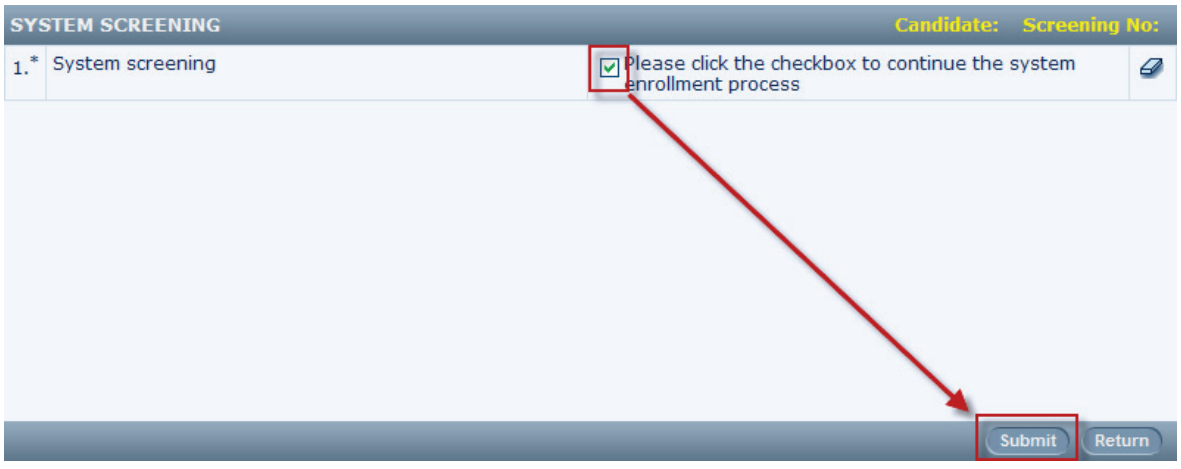
1. Confirm eligibility
2. On the left side navigation pane, select Enroll ⟶



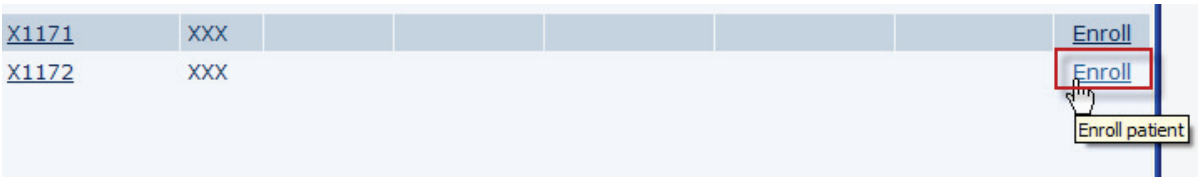
3. On the lower right corner of the screen, select Add Candidate ⟶



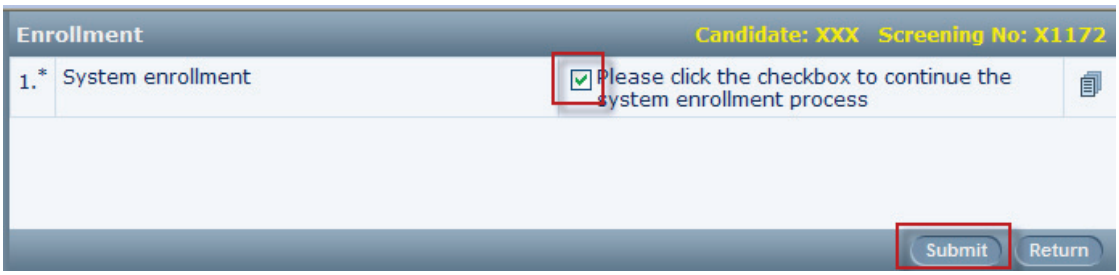
4. On the System **Screening** screen, check the box, then go to the bottom right, and click Submit.



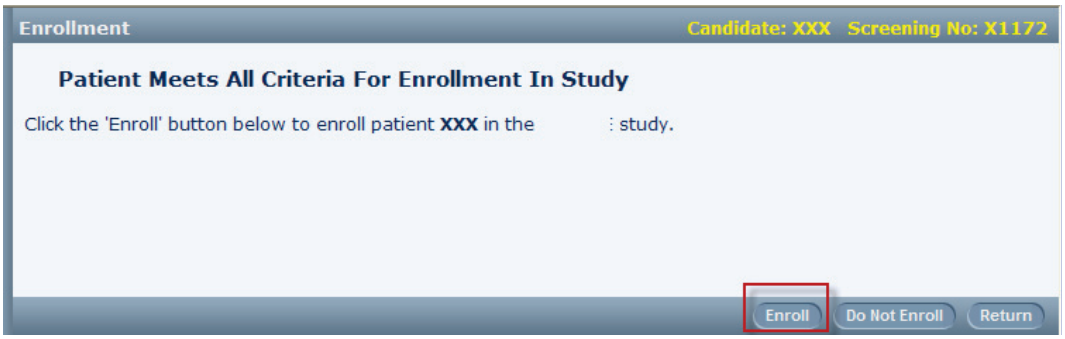
5. The next screen has a list of numbers, and on the right, an Enroll button. Click Enroll.



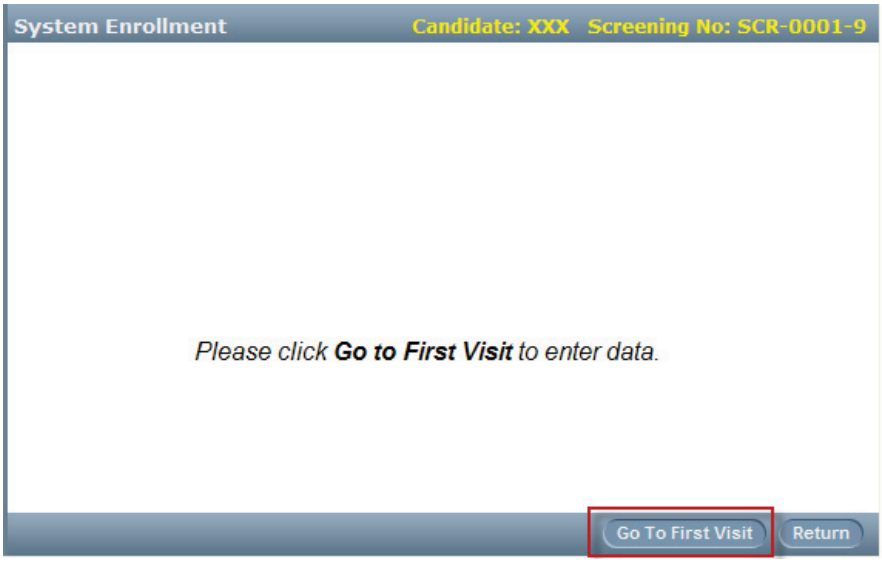
6. On the System **Enrollment** screen, check the box (if not already checked), then go to the bottom right, and click Submit.



7. On the Enrollment screen, confirm that the patient meets eligibility criteria and on the lower right side, click Enroll. A new patient is now entered into the InForm system for your site.



8. To enter information for the subject and to randomize, click Go to First Visit on the bottom right of the screen.



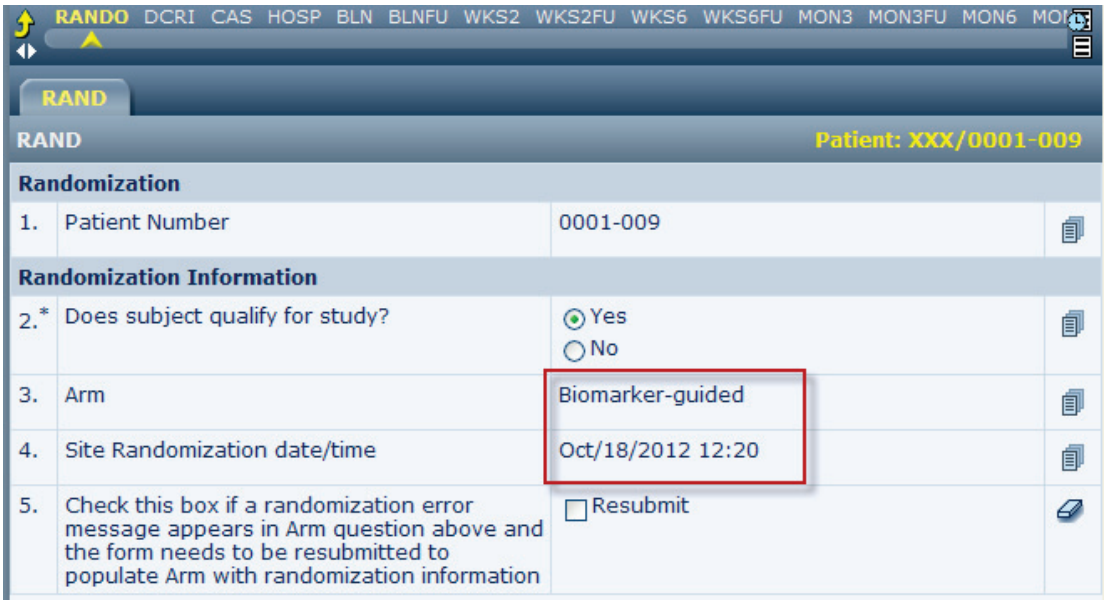
9. Continue to the RAND form to complete the randomization process.

On the Randomization form:

Patient Number: Auto-filled by the SIRE IVRS system. This field is ***read only*** and cannot be modified.

Does the subject qualify for study? Selecting *Yes* will trigger the randomization process.

The subject's assigned arm and site randomization date and time will appear on the screen.



5.2 Visit Windows

Randomization will occur at discharge or within a 2-week window after discharge. Schedule all subsequent study visits based on the date of randomization and complete them within a ± 1-week window.

An Excel visit calculator is available on the website or from your CRA. Create one file per patient to help track scheduled and unscheduled visit windows.

Scheduled visits are based on the date of randomization. In the Excel file, enter the date of randomization and the calculator will populate the dates of visit windows for all subsequent visits.

Unscheduled visits are based on the date of hospitalization or change in treatment. For unscheduled visits, go to a new tab in the Excel Workbook and rename the tab with the most recent scheduled visit (eg, 3 month, 6 month, etc.). Enter the date of the hospitalization or change in treatment and the calculator will populate dates of the window for the 2 week follow-up visit. Enter the actual visit date if another follow-up visit is required. If the Unscheduled visit falls within the window for a scheduled visit, perform the assessments for the scheduled visit and enter the information on the scheduled visit form in the eCRF.

5.3 History and Physical

Perform a physical examination at the time of screening, and a focused physical exam at each study visit. The focused physical exam will consists of the following:

- Current New York Heart Association heart failure class
- Level of orthopnea
- Vital signs sitting or resting: heart rate, respiratory rate, blood pressure
- Heart rhythm assessment for presence of atrial fibrillation or flutter
- Presence of S3 heart sound
- O_2 saturation as measure by pulse oximetry
- Presence of visible jugular venous pressure
- Presence of pulmonary rales
- Presence of hepatomegaly
- Presence of ascites
- Presence of peripheral edema

5.4 Cardiovascular Medication History

At baseline and at each study visit, ask the subject to identify **all** current medications, including prescription, nonprescription, and herbal supplements. If there are changes in any medications, update the information in the subject's medical record. The CRF will collect information about specific medications on the MEDS and ADJUST forms.

Concomitant Medications [MEDS]

ACE inhibitor

Aldosterone antagonist

Angiotensin receptor blocker

Beta Blocker

Loop diuretic

PDE5 Inhibitors

Metolazone

HCTZ

Ambulatory IV Inotropes

Hydralazine

Nitrates (long lasting)

Calcium channel blocker

Antiplatelets

Anticoagulants

Digoxin

Amiodarone or other antiarrhythmic

Statin

Lipid lowering agent (other than statin)

Insulin

Oral anti-diabetic agent

Antidepressant

Allopurinol

Bronchodilator (long lasting)

Therapy Adjustment [ADJUST]

Angiotensin Converting Enzyme (ACE) inhibitor

Angiotensin receptor blocker (ARB)

Beta-blocker

Digoxin

Hydralazine-nitrates

Loop diuretic

Mineralocorticoid receptor antagonist (spironolactone or eplerenone)

Oral thiazide diuretic

5.5 6-Minute Walk Test (6MWT)

The procedure for performing 6MWT is based on the 2002 American Thoracic Society (ATS) guidelines. Worksheets for the 6MWT are in Appendix D.

Description: The 6-minute walk is a simple test for assessing exercise capacity as a measure of functional status. It also reflects the normal daily activity levels of patients.

Equipment Needed

- Watch or clock with second hand
- Tape measure
- Tape
- Chairs
- 6-Minute Walk Worksheet with Borg scale and pen

Preparation

1. Measure an indoor course with a chair or cone at each end. Establish a suitable distance between chairs so that if the patient tires, a chair is easily accessible. A distance of 20 to 25 feet (about 8 meters) is a suitable distance to start with, but this may vary based on the patient's condition and space at your facility. Avoid L-shaped hallways.

2. Provide patient teaching. Explain the test to the patient using the suggested wording on the 6-Minute Walk Patient Worksheet. Answer any questions the patient may have.

Conducting the 6-Minute Walk Test

1. Escort the patient to the start of the course. Show the patient the walking course and ask the patient to begin walking as you begin keeping time. Stay with the patient for the entire walk test and record the number of completed laps.

2. Provide encouragement to the patient. At 1-minute intervals, encourage the patient using the examples provided on the 6-Minute Walk Patient Worksheet. Use your judgment to assess the patient's comfort and clinical state and, if appropriate, recommend that the patient rest or stop the test early. You may stop the test early for any of the following reasons: anginal symptoms (e.g., chest pain or tightness), ataxia, staggering, unsteadiness, confusion, claudication or other significant leg pain, cyanosis, facial expression signifying distress, lightheadedness, marked dyspnea, pallor, signs of peripheral circulatory insufficiency, or unusual fatigue.

3. Stop the test after 6 minutes (or sooner if the subject develops signs or symptoms requiring test termination). Mark the floor where the patient stops with a piece of tape.

4. Determine the total distance walked. Multiply the number of laps times the distance of each lap (round to the nearest foot or meter). Add this figure to the distance covered in the last partial lap. Record the distance.

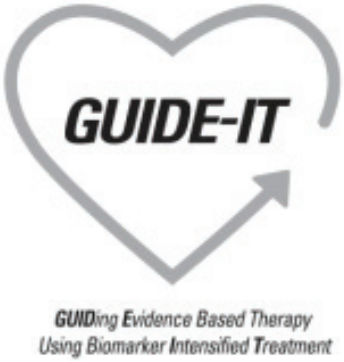
5. Obtain the patient's Borg Rating of Perceived Exertion (RPE) Scale at the end of the walk. Show the patient the scale as you instruct how to rate his or her level of exertion.

Perceived Breathlessness (Borg Scale)

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight (light)
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	
10	Very, very severe (maximal)

Tab: EQOL

6 EQOL Questionnaires, Medial Resource Use, and Cost Assessment



MANUAL OF OPERATIONS:

ECONOMICS AND QUALITY OF LIFE (EQOL) COORDINATING CENTER

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GUIDE-IT EQOL Contact Information

DCRI Outcomes Group

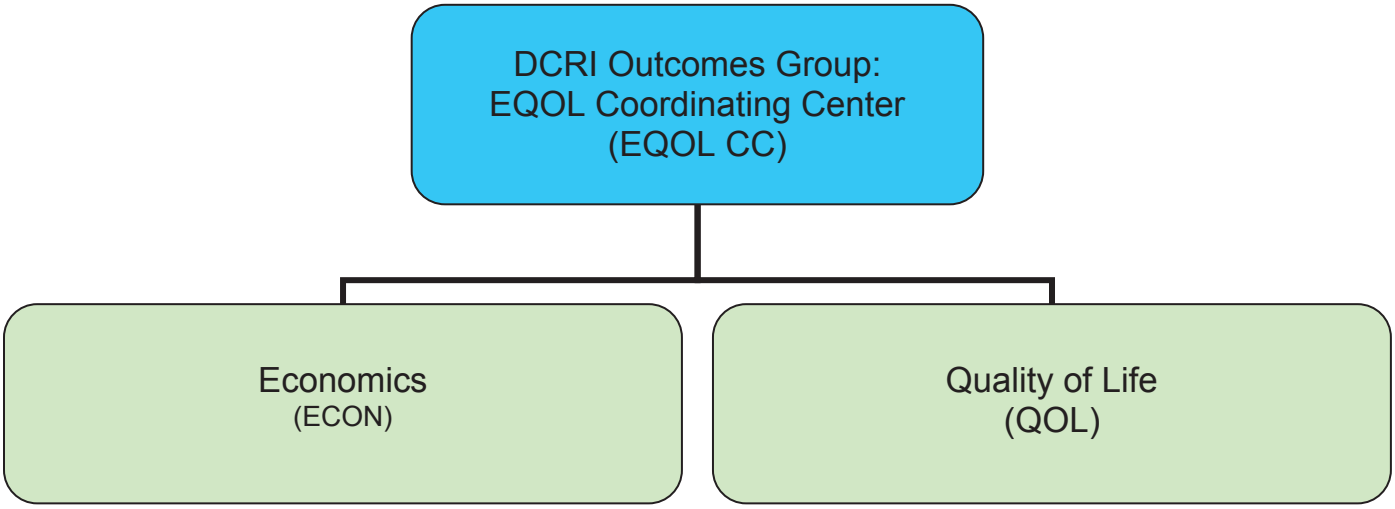
GUIDE-IT Website	www.GUIDE-IT.org	
Mailing Address: (Express mail only)	Duke Clinical Research Institute 2400 Pratt Street Room 0311 Terrace Level Durham, NC 27705 USA	Phone: (919) 668-8892 Fax: (919) 668-9816 **Email:** GUIDE-ITEQOL@duke.edu
Daniel Mark, MD, MPH	Principal Investigator	**Email:** GUIDE-ITEQOL@duke.edu
Tina Harding, BSN, RN	Project Leader	Phone: (919) 668-8430 Fax: (919) 668-9816 Email: tina.harding@duke.edu
Laura Drew	Lead QOL Coordinator	Phone: (919) 668-8892 Fax: (919) 668-9816 Email: laura.drew@duke.edu
Betsy O'Neal	Lead Econ Coordinator	Phone: (919) 668-8878 Fax: (919) 668-9807 Email: betsy.oneal@duke.edu

IMPORTANT: For any GUIDE-IT EQOL operation questions or form requests, contact Laura Drew at 919-668-8892 or GUIDE-ITEQOL@duke.edu.

GUIDE-IT EQOL Operations

The GUIDE-IT Trial is a 1,100 patient multicenter, randomized trial which will identify the best diagnostic approach for people with systolic congestive heart failure who have been hospitalized for decompensated heart failure to one of two management strategies: guideline-based therapy (usual care) or biomarker-guided therapy (BGT). A secondary endpoint of GUIDE-IT is to assess and compare the economic and quality of life consequences of the two treatment strategies being tested in the GUIDE-IT trial.

The Duke Clinical Research Institutes (DCRI) Outcomes Research Assessment Group is responsible for collecting endpoint, quality of life (QOL) and economic information from 3 months after enrollment until the end of the GUIDE-IT Trial.



Patients will be contacted at the following intervals:

Items	Baseline	3 Months	6 Months	12 Months	24 Months
QOL Questionnaire	X	X	X	X	X

GUIDE-IT EQOL Overview of Components

I. QOL Forms can be obtained:

- Site start-up kit (Manual of Operations) ***for reference only***
- GUIDE-IT website (www.GUIDE-IT.org)
- Contact the EQOL Coordinating Center

II. How to Submit Completed Forms:

What?	When?	Where?
Baseline Questionnaire	**Baseline**	Fax to 919-668-9816 **OR** Upload to ftp.dcri.duke.edu
Confidential Patient Contact Information Form	**Baseline**	Fax to 919-668-9816 **OR** Upload to ftp.dcri.duke.edu
Signed Consent and Medical Release Form	**Baseline**	Fax to 919-668-9816 **OR** Upload to ftp.dcri.duke.edu
Hospitalization (HOSP) (e-CRF)	**Every Interval**	**InForm EDC**
Extended Care (EXTCARE) (e-CRF)	**Every Interval**	**InForm EDC**

III. Outcomes Group: Overview

A. Baseline Quality of Life (QOL) Questionnaire

- **Type of Administration**: *In-person at time of consent*
- **Who Administers**: *Site Coordinator*
  - Baseline questionnaires can be administered to the patient by the study coordinator (see Standard Interviewing Guidelines on pages 11-12). Patients can also complete the Baseline Questionnaire on their own and should only take the questionnaire home in extreme circumstances. It is the site's responsibility to make sure a completed Baseline Questionnaire is reviewed for completeness and sent to the EQOL Coordinating Center.
- **Interval:** *Baseline*
  - ALL Baseline Questionnaires should be completed within 30days of consent (and before randomization). Sites are responsible for collecting the baseline questionnaires from patients.
  - A Summary Form must be completed for each patient randomized to GUIDE-IT whether or not a questionnaire is completed (see pg. 17). This provides important tracking for the EQOL CC.
- **Baseline Components**: *General and disease specific health related QOL assessments*
  - Kansas City Cardiomyopathy Questionnaire (KCCQ)
  - Duke Activity Status Index (DASI)
  - Center for Epidemiological Studies Depression Scale (CES-D 10)
  - Medical Outcomes Study Short Form (SF-12)
  - Medical Outcomes Study Short Form (SF-36 subscales; General Health, psychological well-being, vitality, social functioning)
  - EuroQoL (EQ-5D)
  - Bypass Angioplasty Revascularization Investigation (BARI) Work Questions
- **Submitting the QOL:** *Fax to 919-668-9816 or upload to ftp.dcri.duke.edu.*

B. QOL Follow-up Questionnaires

- **Type of Administration**: *Phone Survey*
- **Who Administers**: *EQOL CC Call Center*
- **Intervals:** *3, 6, 12, and 24 months*
- **Follow-up Components:** *(same Baseline Components above)*

IV. Economics: Overview of Components and Collection

The purpose of the Economics study is to describe medical resource patterns and associated medical costs as part of the GUIDE-IT Trial. At each study visit, from enrollment until the study ends, coordinators will ask subjects about hospitalizations, emergency room visits, rehabilitation visits and nursing home care, and enter those data from the main GUIDE-IT case report form into EDC.

U.S. patients are consented as part of the GUIDE-IT ICF for economics data collection by the GUIDE-IT EQOL CC at the DCRI. These data, collected as part of the case report form, are then used by the EQOL CC to contact hospitals and providers for bills collection, data processing and analysis.

A. Economic Resource Utilization

- **Intervals***: Every study interval through Trial Close-out*
- **Economic Components:** *Hospitalization (HOSP) and Extended Care (EXTCARE) forms completed and entered into the case report form from patients' self-reported all-cause hospitalizations, outpatient procedures or institutional facility stay.*
- **Completion and Entry into InForm:** *Site Coordinator [refer to e-CRF instructions for completing these two forms.]*

B. Economic Bill Collection

- **Intervals***: Baseline, other intervals as triggered throughout study by the e-CRF HOSP Form*
- **Economic Components:** *Hospital bills (detailed, summary ledger and UB 92)*
  - Bills will be collected by the GUIDE-IT EQOL CC at the DCRI for all hospitalizations throughout the length of the study. They will include hospitalizations at clinical sites and at institutions not participating in ISCHEMIA. In addition, cost to charge ratios (RCCs) will be obtained from each hospital where an ISCHEMIA baseline or follow-up hospitalization is reported.
  - **Complete bill collection is dependent on case report form capture of all hospitalizations and outpatient procedures as triggered by patients' self-report at each follow-up study interval.**
- **Completion:**
  - ***Site Coordinators*** are responsible for faxing the patient's signed informed consent and Medical Release Form (if applicable) to 919-668-9816 or upload to ftp.dcri.duke.edu
  - ***GUIDE-IT EQOL CC*** *(DCRI Economic team members)* will complete all bill collection for all intervals.

GUIDE-IT Patient Contact Information Form

Collecting legible patient contact information is crucial to obtaining the specific aims of GUIDE-IT. Longitudinal follow-up is dependent on having solid and complete contact data. The EQOL CC will be contacting patients at 3 months, 6 months and then annually until 24 months to complete the Follow-up QOL forms.

To obtain the most accurate contact information from the patients, follow these instructions:

Sample Script of Patient Contact Information Collection:
"You will be contacted by mail or phone several times during this study (3, 6, 12, and 24 months until the study is completed.) They will ask you questions about how you are feeling and if you have been hospitalized. In order to do this, we need your most current phone number and address. Just in case we are unable to contact you, we would like to have the current phone numbers and addresses of one or two people close to you, but don't live with you. Again, this information is collected so that we are able to contact you and find out how you are doing. Thank you for your help!"

Patient Information

- Ask the patient for current address, phone numbers, email and best time to call.
- Ask the patient if it is okay to call him or her at work.
- Ask the patient if it is okay to call and text them on their mobile phone.
- Verify that the patient is giving you their permanent contact information: ask if the patient has any plans to relocate or change numbers in the next 3 months. Also verify if patient has a secondary residence. If so, complete this section.

Spouse/Significant Other

- Ask for the patient's spouse/significant other's phone numbers and email address.
- Ask the patient if it is okay to call and text the spouse/significant other on their mobile phone.

Alternate Contact: Friend/Relative Information

- Ask the patient for the current address, phone numbers and email of a friend or relative **who does not live with them.** This information can be very valuable if the interviewer has a hard time reaching the patient, or if the patient's phone number changes or is disconnected. If the patient does not have complete information for a friend or a relative, get as much detail as you can. Emphasize to the patient that their friends/relatives will only be contacted if we are unable to reach the patient.
- Ask the patient if it is okay to call this contact and text them on their mobile phone.

Health Care Provider Information

- Ask the patient for the name and location of their primary care physician (PCP). The patient may not have the physician's phone number and address committed to memory, but get as much detail as possible. Generally, the first and last name of the physician and the city would be enough to find the correct phone number and contact the physician office.
- If the patient does not have a regular PCP, then provide the name of the physician who will provide follow-up care, i.e., cardiologist.

Remember to Tell Participants that they will be called by "Duke" from a "919" area code

And

Fax the form to the Guide IT COORDINATING CENTER @ *919-668-9816 or upload to ftp.dcri.duke.edu*

GUIDE IT Site#: __ __ __ Patient ID: __ __ __ __ Patient Initials: __ __ __

Patient Contact Information Form

Thank you very much for your participation in this important study. We will be following up with you in the future and would like to make sure that we reach you by your preferred method of contact, at the most convenient time for your schedule. We would like you to provide your most current contact information, as well as contact information for an alternative person to contact if we are unable to reach you.

***Preferred Method of Contact to schedule interview: ❑ Phone ❑ Email* (all interviews by phone)**

PATIENT NAME: (Last Name, First Name)_____

STREET: _____

CITY: _____ STATE: _____ ZIP: _____

HOME TELEPHONE #: (____) -_____Best time to call: _____ ❑ AM ❑ PM

WORK TELEPHONE #: (____) -_____ EXT_____ *May we call you at work?* ❑ Yes ❑ No

CELL/MOBILE TELEPHONE# (____) -_____ Best time to call: ___❑ AM ❑ PM *Can we text?* ❑ Yes ❑ No

EMAIL ADDRESS: _____ Preferred Language: English__ Spanish____ Other_____

SPECIAL COMMUNICATION INSTRUCTIONS: (example: hard of hearing)_____

SPOUSE/SIGNFICANT OTHER: (Last Name, First Name)_____

HOME TELEPHONE #: (____) -_____Best time to call: _____❑ AM ❑ PM

CELL/MOBILE TELEPHONE# (____) -_____Best time to call: ___❑ AM ❑ PM *Can we text?* ❑ Yes ❑ No

EMAIL ADDRESS: _____

If applicable, address of your secondary residence:

STREET_____

CITY: _____ STATE: _____ ZIP: _____

Please provide the name of a friend or relative <u>who does not live with you</u> who would know your whereabouts if we were unable to contact you.

NAME: (Last Name, First Name)_____

RELATIONSHIP:_____

STREET: _____

CITY: _____ STATE: _____ ZIP: _____

HOME TELEPHONE #: (____) -_____Best time to call: _____ ❑ AM ❑ PM

WORK TELEPHONE #: (____) -_____ EXT_____ *May we call/contact at work?* ❑ Yes ❑ No

MOBILE TELEPHONE # (____) -_____ Best time to call: ___❑ AM ❑ PM *Can we text*? ❑ Yes ❑ No

EMAIL ADDRESS: _____

Please provide the name of a friend or relative <u>who does not live with you</u> who would know your whereabouts if we were unable to contact you.

NAME: (Last Name, First Name)_____

RELATIONSHIP:_____

STREET: _____

CITY: _____ STATE: _____ ZIP: _____

HOME TELEPHONE #: (____) -_____Best time to call: _____ ❑ AM ❑ PM

WORK TELEPHONE #: (____) -_____ EXT_____ *May we call/contact at work?* ❑ Yes ❑ No

MOBILE TELEPHONE# (____) -_____Best time to call: ___❑ AM ❑ PM *Can we text*? ❑ Yes ❑ No

EMAIL ADDRESS: _____

Referring health care provider and/or clinic:

HEALTH CARE PROVIDER: (Last Name, First Name) _____❑ MD ❑ DO ❑ NP ❑ PA

OFFICE NAME:_____

STREET: _____

CITY: _____ STATE: _____ ZIP: _____

OFFICE TELEPHONE #: (____) -_____ FAX # (___) _____

GUIDE-IT EQOL Standard Interviewing Guidelines

The GUIDE-IT QOL questionnaires must be administered in a standardized, structured interview format to eliminate as completely as possible any effect an interviewer might have on the patient's responses. Ideally, all interviews in the study should be so standardized that any variability in data only represents changes in patient health from one time to another. Therefore, the ***questions should be asked exactly as worded***, and the interviewers should not ask supplemental questions or reword.

I. Role of the Interviewer:

- Obtains written consent (baseline) or verbal consent (follow up) before proceeding with the questionnaire.
- Administers the questionnaire in a structured format.
- Ensures that the patient understands the instructions and remains aware of them throughout the interview.
- Allows the patient an opportunity to respond to each item.
- Records the patient's responses completely and accurately.
- To eliminate bias and to attempt to standardize the interview, the approach and guidelines (see "Administering the Questionnaire" section below) should be followed during the interview process. Before administering the questionnaire to a patient, practice the interview on family and friends.
- Patients should respond to the items as they are written according to their own perception or interpretation of their meaning. Remember that the expression and tone of your voice will affect the patient's comfort level.

II. Your Interview Style with the Subject:

- Presenting yourself in a friendly and interested manner; however, remain neutral, relaxed, and non-threatening.
- Give the patient the impression that you are basically interested in him or her, but are not personally involved with his/her response to the questionnaire.

III. Administering the Questionnaire:

- Read every item to the patient exactly as written.
- Do not ask any supplemental questions or reword.
- Read the items clearly and slowly.

- Pause briefly between the items so that the patient has enough time to respond.

- Concentrate on the items as you read them, that is, think about what each one is saying.

- Do not speed up your pace or develop a monotone toward the end of the interview.

- Remember that each patient is hearing the items for the first time.

- **Avoid** making assumptions about a patient's behavior and developing expectations about specific responses; assumptions could easily be incorrect, even though they may seem obvious.

- **Avoid** the following potential biases:
  - Giving the impression that you approve or disapprove of any answer the patient gives
  - Acting surprised at any answers given
  - Showing special interest in hearing the answer to any specific question

IV. Possible Issues Encountered During Interview:

- Patient suggests that the wording of a statement be changed
  Tell the patient that you will note his suggestion but right now he should only consider the statement as you have read it.

- Patient refuses to answer a statement
  Record patient refusal on questionnaire. Do not try to convince him to consider the statement.

- Patient changes his/her response
  You may make a correction anytime the patient requests it.

- Patient complain that a statement or group of statements is too personal
  Explain that often personal aspects of our lives are affected by our health. Remind the patient that you are just a recorder and that all information he gives is completely confidential.

- Patient discusses his/her illness, symptoms, or medical care
  Do not encourage a conversation about the patient's health, instead just answer with a nod or smile or "um hum". If the patient continues, tell him that you really need to ask the questions right now, and you can talk after the interview is completed.

GUIDE-IT EQOL Baseline QOL Questionnaire Guidelines

- ***Once a patient has been consented, Baseline QOL data is to be collected.***
- The terms enrollment and randomization are used interchangeably.
- Complete all fields on the QOL Summary form.
- Familiarize yourself with the "Standard Interviewing Guidelines" (see pages 11-12 before administering QOL questionnaires.
- Use pen and print neatly; do not use pencil.
- List all dates according to the QOL (European) date convention of day/month/year (DD/MMM/YYYY) ex. 01/NOV/2012.
- Record the patient study # (hospital site # and patient # assigned to the patient when enrolled in the trial) on each page of the questionnaire to avoid any misidentification of data.
- Record patient initials; please use <u>three</u> initials. It is very important to be consistent from form to form.
- <u>*Corrections*</u> are to be made by drawing a single line through the incorrect entry, then indicating the correct entry as near to the incorrect one as possible and initialing in small print and dating the correction; <u>D*o not white out mistakes*</u>. Example: ~~04/04/2002~~ 04/APR/2012*TMH*
- If data requested are not applicable to the patient, please code NA for Not Applicable. If data requested are not known by the patient, enter DK for Don't Know. If the patient refuses data requested, enter RF. Refer to the QOL Coding Guidelines.
- The originals of each Summary Form and Questionnaire should be kept on file with the clinical data forms.

Important:

- The QOL Questionnaire gives a baseline measurement of life before the patient's enrollment in GUIDE-IT. The Site Coordinator should have the patient reflect and think about how he or she was feeling prior to enrollment into GUIDE-IT when answering the QOL Baseline Questionnaire. It is from this more stable, baseline measurement that we will be able to analyze changes in QOL over time by treatment group.
- **Baseline Questionnaires and Summary Forms are to be faxed to 919-668-9816 or** upload to ftp.dcri.duke.edu**.** Keep a copy on file with your patient's files at your institution.

EQOL Baseline Quality of Life Questionnaire

(Do not use the sample forms for patient administration; use the forms provided on the website: www.guide-it.org)

GUIDE-IT EQOL Baseline QOL Summary Form

A Summary Form must be completed for every patient randomized to GUIDE-IT.

Make sure to fill in site/patient id information for the Summary Form and Questionnaire to ensure accurate tracking of data.

Sites are responsible for the Baseline Summary QOL.

Complete by checking off:

- Final Questionnaire Status (If Incomplete or Not Done, provide reasons why)
- Who Answered the Questions
- Where the patient live
- Comments

Date Convention

- Please use the European Date Convention, listing date by day-month-year, DD/MMM/YYYY. Example: 01/Nov/2012.

Final Questionnaire Status

- Complete = 90% or more of questionnaire completed.
- Incomplete = at least 10% of questionnaire missing.
- Not Done = patient died.

Note: ***If Incomplete or Not Done: Contact the GUIDE-IT team by email at: GUIDE-ITEQOL@duke.edu to provide reasons why a questionnaire is Incomplete or Not Done.***

Who Answered the Questions

- Enter the primary source of information for the questionnaire. *The patient, by protocol, should be the only source* for the Baseline Questionnaire.

Where did the patient reside/ live at the time of this Summary and Questionnaire were completed?

- Enter place where the patient resides at the time of the interview. If hospitalized, code Acute Care.

Comments

- Important text information regarding the patient or questionnaire should be added here. Any information that would be important or useful to the follow-up interviewers. For example, the patient is hard of hearing or has an assistive talking device.

Interviewer Initials

- Enter initials of the person completing the Summary Form.

Guide-IT Summary Form

Check (√) One Interval: ❑ Baseline

FINAL QUESTIONNAIRE STATUS:

❑1 Complete
❑2 Incomplete (Specify the reason)➔ ➔ ➔
❑3 Not Done (Specify the reason)➔ ➔ ➔

REASON FOR INCOMPLETE OR NOT DONE:

❑1 Patient died Date of death: __ / ___ / ____
DD MMM YYYY
❑2 Patient too ill
❑3 Patient refused
❑4 Other: Specify: _____
❑5 Unable to locate ➔ Complete Follow-Up Status below

FOLLOW-UP STATUS IF UNABLE TO LOCATE:

❑1 Alive : Date Last Contact Alive: __ / __ / ____
DD MMM YYYY
❑2 Unknown: Date Last Contact Alive: __ / __ /____
DD MMM YYYY

WHO ANSWERED THE QUESTIONS?

❑1 Patient
❑2 Proxy / Patient Representative

WHERE DID THE PATIENT RESIDE / LIVE AT THE TIME THIS SUMMARY AND QUESTIONNAIRE WERE COMPLETED?

❑1 Community / Home
❑2 Acute Care (in-subject hospital)
❑3 Skilled Nursing Home / End-of-Life Care Institution
❑4 Rehabilitation Institution

INTERVIEWER INITIALS: ____ ____ ____

COMMENTS:_____
_____
_____
_____
_____
_____
_____

Fax Summary and Questionnaire to (919) 668-9816 or upload to ftp.dcri.duke.edu

GUIDE-IT EQOL Baseline QOL Questionnaire

This questionnaire should be administered by the site coordinator or designate following consent for randomization and prior to therapy unless there are significant extenuating circumstances.

Today's Date

This is the date the questionnaire is administered. Please use the European Date Convention, listing date by day-month-year, DD/MMM/YYYY. Example: 01/Nov/2012

Question 1- 23 (KCCQ)

These questions, from the Kansas City Cardiomyopathy Questionnaire (KCCQ) are specific to heart failure over the **past 2 weeks.** It is very important to orient the patient to the questions' time frame.

For Questions 1–6 it is important to carefully read the introduction as it contains the definition of heart failure and its symptoms. This group of questions ask how patients relate their heart failure symptoms to physical functioning, quality of life, and lifestyle. They include both frequency and extent of the symptoms.

Questions 7–9 are specific to heart failure symptoms and how they relate to quality of life and lifestyle.

Site Number: __ __ __ Patient Number: __ __ __ __ Patient's Initials: __-__-__

Guide-IT –Baseline EQOL Questionnaire

The following questions are about your overall health and recent activities. Please check your choice for each question. The numbers beside each answer are there simply to help us record the information. Do not worry about them. Answer each question as best you can. This information is <u>confidential and will not be released to anyone without your permission</u>.

TODAY'S DATE: __ __ /__ __ __ /__ __ __ __ *[Example: 01/Nov/2002]*
d d m m m y y y y

The following questions refer to your heart failure and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

Heart Failure affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities <u>over the past 2 weeks</u>.

Activity . . .	Extremely Limited	Quite a bit Limited	Moderately Limited	Slightly Limited	Not at all Limited	Limited for other reasons or did not do activity
1. Dressing yourself	❑1	❑2	❑3	❑4	❑5	❑6
2. Showering/ Bathing	❑1	❑2	❑3	❑4	❑5	❑6
3. Walking 1 block on level ground	❑1	❑2	❑3	❑4	❑5	❑6
4. Doing yard work, housework, or carrying groceries	❑1	❑2	❑3	❑4	❑5	❑6
5. Climbing a flight of stairs without stopping	❑1	❑2	❑3	❑4	❑5	❑6
6. Hurrying or jogging (as if to catch a bus)	❑1	❑2	❑3	❑4	❑5	❑6

7. <u>Compared with 2 weeks ago</u>, have your symptoms of **heart failure** (shortness of breath, fatigue or ankle swelling) changed?

My symptoms of **heart failure** have become…

- ❑1 Much worse
- ❑2 Slightly worse
- ❑3 Not changed
- ❑4 Slightly better
- ❑5 Much better
- ❑6 I've had no symptoms over the last 2 weeks

8. Over the <u>past 2 weeks</u>, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

- ❑1 Every morning
- ❑2 3 or more times a week, but not every day
- ❑3 1-2 times a week
- ❑4 Less than once a week
- ❑5 Never over the past 2 weeks

9. Over the <u>past 2 weeks</u>, how much has swelling in your feet, ankles or legs bothered you?

It has been…

- ❑1 **Extremely** bothersome
- ❑2 **Quite a bit** bothersome
- ❑3 **Moderately** bothersome
- ❑4 **Slightly** bothersome
- ❑5 **Not at all** bothersome
- ❑6 I've had **no swelling**

Question 10 - 15 (KCCQ)

These questions are specific to heart failure signs and symptoms in frequency, severity and change over time. Please note that the patient is asked to think back over the **past 2 weeks**.

10. Over the past 2 weeks, on average, how many times has **fatigue** limited your ability to do what you want?
    - ❑1 All of the time
    - ❑2 Several times per day
    - ❑3 At least once a day
    - ❑4 3 or more times per week but not every day
    - ❑5 1-2 times per week
    - ❑6 Less than one a week
    - ❑7 Never over the past 2 weeks
11. Over the past 2 weeks, how much has your **fatigue** bothered you?
    It has been…
    - ❑1 **Extremely** bothersome
    - ❑2 **Quite a bit** bothersome
    - ❑3 **Moderately** bothersome
    - ❑4 **Slightly** bothersome
    - ❑5 **Not at all** bothersome
    - ❑6 I've had **no fatigue**
12. Over the past 2 weeks, on average, how many times has **shortness of breath** limited your ability to do what you wanted?
    - ❑1 All of the time
    - ❑2 Several times per day
    - ❑3 At least once a day
    - ❑4 3 or more times per week but not every day
    - ❑5 1-2 times per week
    - ❑6 Less than one a week
    - ❑7 Never over the past 2 weeks
13. Over the past 2 weeks, how much has your **shortness of breath** bothered you?
    It has been…
    - ❑1 **Extremely** bothersome
    - ❑2 **Quite a bit** bothersome
    - ❑3 **Moderately** bothersome
    - ❑4 **Slightly** bothersome
    - ❑5 **Not at all** bothersome
    - ❑6 I've had **no shortness of breath**
14. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?
    - ❑1 Every night
    - ❑2 3 or more times a week, but not every day
    - ❑3 1-2 times a week
    - ❑4 Less than once a week
    - ❑5 Never the past 2 weeks
15. **Heart failure** symptoms can worsen for a number of reasons. How sure are you that you know what to do, or whom to call, if your **heart failure** gets worse?
    - ❑1 **Not at all** sure
    - ❑2 **Not very** sure
    - ❑3 **Somewhat** sure
    - ❑4 **Mostly** sure
    - ❑5 **Completely** sure

Question 16 - 23 (KCCQ)

These questions are specific to heart failure signs and symptoms and how they relate to lifestyle, self-efficacy and social limitation. Please note that the patient is asked to think back over the **past 2 weeks**.

16. How well do you understand what things you are able to do to keep your **heart failure** symptoms from getting worse? (for example, weighing yourself, eating a low salt diet, etc.)
    - ❑1 Do not understand at all
    - ❑2 Do not understand very well
    - ❑3 Somewhat understand
    - ❑4 Mostly understand
    - ❑5 Completely understand

17. Over the <u>past 2 weeks</u>, how much has your **heart failure** limited your enjoyment of life?
    - ❑1 It has **extremely** limited my enjoyment of life
    - ❑2 It has limited my enjoyment of life **quite a bit**
    - ❑3 It has **moderately** limited my enjoyment of life
    - ❑4 It has **slightly** limited my enjoyment of life
    - ❑5 It has **not limited** my enjoyment of life at all

18. If you had to spend the rest of your life with your **heart failure** the way it is <u>right now</u>, how would you feel about this?
    - ❑1 Not at all satisfied
    - ❑2 Mostly dissatisfied
    - ❑3 Somewhat satisfied
    - ❑4 Mostly satisfied
    - ❑5 Completely satisfied

19. Over the <u>last 2 weeks</u>, how often have you felt discouraged or down in the dumps because of your **heart failure**?
    - ❑1 I felt that way **all of the time**
    - ❑2 I felt that way **most of the time**
    - ❑3 I **occasionally** felt that way
    - ❑4 I **rarely** felt that way
    - ❑5 I **never** felt that way

How much does your **heart failure** affect your lifestyle? Please indicate how your **heart failure** may have limited your participation in the following activities <u>over the past 2 weeks</u>.

Activity	Severely Limited	Limited quite a bit	Moderately Limited	Slightly Limited	Did not limit at all	Does not apply or did not do for other reasons
20. Hobbies, recreational activities	❑1	❑2	❑3	❑4	❑5	❑6
21. Working or doing household chores	❑1	❑2	❑3	❑4	❑5	❑6
22. Visiting family or friends out of your home	❑1	❑2	❑3	❑4	❑5	❑6
23. Intimate relationships with loved ones	❑1	❑2	❑3	❑4	❑5	❑6

Questions 24-35 (DASI)

These items comprise the Duke Activity Status Index (DASI) which measures the physical **ability to perform** certain activities **in the past month**, as opposed to not being able to do them or not having the opportunity to do them. They measure what the subject has been **able to do** (i.e. his/her **proven performance or equivalent**). The 12 items cover a spectrum of difficulty and several dimensions of normal life. Only **one response** should be coded **for each question.**

*****If the subject has a **sudden deterioration** in function **just prior to his/her GUIDE-IT enrollment**, then his/her response should reflect what he/she could do in the time just before the deterioration.

- The intent is to determine if the subject can do the activities without difficulty, allowing the **respondent** to define "difficulty".
- Questions 19-27 determine if he/she can do **any** of the listed activities without difficulty. The response of the **activity he/she can do best** should be coded.
  - *Example 1*: Suppose a subject does not do housework ("light or moderate") because someone else does it. If he/she can **currently** do activities of **comparable** difficulty and therefore **knows he/she could** physically do housework with no difficulty or with some difficulty, then his or her answer should be coded as such.
  - *Example 2*: Suppose a subject has not participated in any sports in several years and is now fairly sedentary. Since he/she has not done an activity of that difficulty prior to enrollment and he/she knows that he/she could not do it, his/her answer should be coded "…**OR I couldn't do this**".
  - *Example 3***:** Suppose a subject has had a stroke and cannot do some activities. His/her response should be coded "**…OR I couldn't do this**" to things he/she cannot do, **regardless** of the physical impairment.
- Any response **"Yes, but…"** should be coded as **"Yes, but with some difficulty."**
- Question 25 in regards to sexual relations: if the subject is Widow/Widower/No Partner, etc., code as **"Don't do this for other reasons"**.
- A subject not doing activities because of **doctor's orders** should be coded as **"Don't do this for other reasons"**.
- Similarly, a subject who **does not know** if he/she can do an activity and doesn't know if he/she could OR doesn't have an equivalent activity should be coded as **"Don't do this for other reasons"**
- Any clarifications for understanding a patient's physical functioning should be noted in the **Comments section** of the **EQOL Summary Form**.
  - *Example:* If a subject cannot do an activity independently because of paralysis but can move around via the aide of a power chair.
- If a subject **refuses to respond**, then write in "**RF**".

These questions are about any physical limitations you might have had in the past month. For each question, please rate whether you are physically able to do one or more of the activities without difficulty, with some difficulty OR you couldn't do it, or you don't do it for other reasons (NA).

Could you. . .	Yes, with no difficulty	Yes, with some difficulty or I couldn't do this	Don't do this for other reasons
24. take care of yourself, that is, eating, dressing, bathing, and using the toilet?	❑1	❑2	❑3
25. walk indoors, such as around your house?	❑1	❑2	❑3
26. walk a block or two on level ground?	❑1	❑2	❑3

For some of the rest of these activity questions, there will be more than one activity mentioned like climb a flight of stairs or walk up a hill. Answer each question according to the one activity you can do best.

Could you. . .	Yes, with no difficulty	Yes, with some difficulty or I couldn't do this	Don't do this for other reasons
27. climb a flight of stairs or walk up a hill?	❑1	❑2	❑3
28. run a short distance?	❑1	❑2	❑3
29. do light work around the house like dusting or washing dishes?	❑1	❑2	❑3
30. do moderate work around your house like vacuuming, sweeping floors, or carrying in groceries?	❑1	❑2	❑3
31. do heavy work around the house like scrubbing floors or lifting or moving heavy furniture?	❑1	❑2	❑3
32. do yard work like raking leaves, weeding, or pushing a power mower?	❑1	❑2	❑3
33. have sexual relations?	❑1	❑2	❑3
34. participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?	❑1	❑2	❑3
35. participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?	❑1	❑2	❑3

Questions 36-45 (CES-D)

The Center for Epidemiologic Studies-Depression measures depression and has been widely used in Outcomes research. Note that the responses can be defined by quantity or actual number of days. The timeframe for these is **one week** before randomization in GUIDE-IT.

Questions 46-48 (SF-12, SF-36)

These questions, originally from the Medical Outcomes Study Short-Form 12 and 36, comprise measures of general health and physical functioning. Orient the patient to think about the **past 4 weeks.**

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you have felt this way during the **past week**: *(circle **one** number on each line)*

During the past week…	Rarely or none of the time (< 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of the time (3-4 days)	All of the time (5-7 days)
36. I was bothered by things that usually don't bother me	❑1	❑2	❑3	❑4
37. I had trouble keeping my mind going	❑1	❑2	❑3	❑4
38. I felt depressed	❑1	❑2	❑3	❑4
39. I felt that everything I did was an effort	❑1	❑2	❑3	❑4
40. I felt hopeful about the future	❑1	❑2	❑3	❑4
41. I felt fearful	❑1	❑2	❑3	❑4
42. My sleep was restless	❑1	❑2	❑3	❑4
43. I was happy	❑1	❑2	❑3	❑4
44. I felt lonely	❑1	❑2	❑3	❑4
45. I could not "get going"	❑1	❑2	❑3	❑4

These first questions are about your health now and your current daily activities. Please try to answer every question as accurately as you can.

46. **In general, would you say your health is:**
- ❑1 Excellent
- ❑2 Very good
- ❑3 Good
- ❑4 Fair
- ❑5 Poor

Now I'm going to read a list of activities that you might do during a typical day. As I read each item, please tell me if your health now limits you a lot, limits you a little, or at all in these activities.

47. . . . moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf. Does your health now limit you a lot, limit you a little, or not limit you at all?
- ❑1 Yes, limited a lot
- ❑2 Yes, limited a little
- ❑3 No, not limited at all

48. . . . climbing several flights of stairs. Does your health now limit you a lot, limit you a little, or not limit you at all?
- ❑1 Yes, limited a lot
- ❑2 Yes, limited a little
- ❑3 No, not limited at all

Questions 49-54 (SF-12, SF-36)

These questions, also from the Medical Outcomes Study Short-Form 12 and 36, are measures of physical functioning and bodily pain. In addition, questions are asked about the role of emotional problems and physical health on daily activities during the **past 4 weeks**.

The following two questions ask about your physical health and your daily activities.

49. During the past four weeks, how much of the time have you accomplished less than you would like as a result of your physical health?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

50. During the past four weeks, how much of the time were you limited in the kind of work or other regular daily activities you do as a result of your physical health?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

The following two questions ask about your emotions and your daily activities.

51. During the past four weeks, how much of the time have you accomplished less than you would like as a result of any emotional problems, such as feeling depressed or anxious?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

52. During the past four weeks, how much of the time did you do work or other regular daily activities less carefully than usual as a result of any emotional problems, such as feeling depressed or anxious?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

53. During the past four weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?
    - ❑1 Not at all
    - ❑2 A little bit
    - ❑3 Moderately
    - ❑4 Quite a bit
    - ❑5 Extremely

The next questions are about how you feel and how things have been with you during the past four weeks.

As I read each statement, please give me the one answer that comes closest to the way you have been feeling; is it all of the time, most of the time, some of the time, a little of the time, or none of the time?

54. How much of the time during the past four weeks . . . did you feel full of life?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

Questions 55-63 (SF-12 & SF-36)

These questions, from the Medical Outcomes Study Short-Form 12 and 36, measure vitality and well being/mental health.

55. How much of the time during the past four weeks . . . have you been very nervous?
- ❑1 All of the time
- ❑2 Most of the time
- ❑3 Some of the time
- ❑4 A little of the time
- ❑5 None of the time

56. How much of the time during the past four weeks . . . have you felt so down in the dumps that nothing could cheer you up?
- ❑1 All of the time
- ❑2 Most of the time
- ❑3 Some of the time
- ❑4 A little of the time
- ❑5 None of the time

57. How much of the time during the past four weeks . . . have you felt calm and peaceful?
- ❑1 All of the time
- ❑2 Most of the time
- ❑3 Some of the time
- ❑4 A little of the time
- ❑5 None of the time

58. How much of the time during the past four weeks . . . did you have a lot of energy?
- ❑1 All of the time
- ❑2 Most of the time
- ❑3 Some of the time
- ❑4 A little of the time
- ❑5 None of the time

59. How much of the time during the past four weeks . . . have you felt downhearted and depressed?
- ❑1 All of the time
- ❑2 Most of the time
- ❑3 Some of the time
- ❑4 A little of the time
- ❑5 None of the time

60. How much of the time during the past four weeks . . . did you feel worn out?
- ❑1 All of the time
- ❑2 Most of the time
- ❑3 Some of the time
- ❑4 A little of the time
- ❑5 None of the time

61. How much of the time during the past four weeks . . . have you been happy?
- ❑1 All of the time
- ❑2 Most of the time
- ❑3 Some of the time
- ❑4 A little of the time
- ❑5 None of the time

62. How much of the time during the past four weeks . . . did you feel tired?
- ❑1 All of the time
- ❑2 Most of the time
- ❑3 Some of the time
- ❑4 A little of the time
- ❑5 None of the time

Questions 55-63 (SF-12 & SF-36) (continued)

These questions, from the Medical Outcomes Study Short-Form 12 and 36, measure vitality and well-being/mental health.

Questions 64-67 (SF-12, SF-36)

These questions, from the Medical Outcomes Study Short-Form 12 and 36, comprise measures of general health and social functioning.

63. During the past four weeks, how much of the time has your physical health or emotional problems interfered with your social activities like visiting with friends or relatives? Has it interfered . . .
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

These next questions are about your health and health-related matters.

Now, I'm going to read a list of statements. After each one, please tell me if it is definitely true, mostly true, mostly false, or definitely false. If you don't know, just tell me.

64. I seem to get sick a little easier than other people. Would you say that's . . .
    - ❑1 Definitely true
    - ❑2 Mostly true
    - ❑3 Don't know
    - ❑4 Mostly false
    - ❑5 Definitely false

65. I am as healthy as anyone I know. Would you say that's . . .
    - ❑1 Definitely true
    - ❑2 Mostly true
    - ❑3 Don't know
    - ❑4 Mostly false
    - ❑5 Definitely false

66. I expect my health to get worse. Would you say that's . . .
    - ❑1 Definitely true
    - ❑2 Mostly true
    - ❑3 Don't know
    - ❑4 Mostly false
    - ❑5 Definitely false

67. My health is excellent. Would you say that's . . .
    - ❑1 Definitely true
    - ❑2 Mostly true
    - ❑3 Don't know
    - ❑4 Mostly false
    - ❑5 Definitely false

Question 68-73 EuroQoL (EQ-5D)

These questions measure health related quality of life by asking various questions about a person's mobility, self-care, usual activities, pain, and anxiety.

Please answer the following questions by indicating which statement best describes your own health state today.

68. **Mobility**
- ❑1 I have no problems in walking about
- ❑2 I have some problems in walking about
- ❑3 I am confined to bed

69. **Self-care**
- ❑1 I have no problems with self-care
- ❑2 I have some problems washing or dressing myself
- ❑3 I am unable to wash or dress myself

70. **Usual activities** (i.e. work, study, housework, family or leisure activities):
- ❑1 I have no problems with performing my usual activities
- ❑2 I have some problems with performing my usual activities
- ❑3 I am unable to perform my usual activities

71. **Pain/Discomfort**
- ❑1 I have no pain or discomfort
- ❑2 I have moderate pain or discomfort
- ❑3 I have extreme pain or discomfort

72. **Anxiety/Depression**
- ❑1 I am not anxious or depressed
- ❑2 I am moderately anxious or depressed
- ❑3 I am extremely anxious or depressed

Question 73 EuroQoL (EQ-5D)

This question measures health related quality of life by asking the patient to draw a line from the box on the left to a number on the thermometer scale that represents how they are feeling. It's important they mark to a line (with or without a number).

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst state you can imagine is marked by 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your current health state is.

Best imaginable health state

Your own health state today

Worst imaginable health state

73. **Response** :___ ___ ___

Questions 74-79 (Bari Work Questions)

These items assess the patient's work status. **Work is defined as a job for pay.** Persons are considered working if they are paid employees (paid in wages, salary, commission or "in kind"); self-employed in their own business profession, or in farming; or unpaid employees on a family business or farm. A person is retired if he or she considers himself or herself to be retired and is not looking for work. **Volunteer activities, activities around the house, or unpaid work such as for church should not be included as "work".**

Question 74

This question is asked to determine the patient's working status just prior to his/her enrollment in GUIDE-IT. If the patient indicates more than one category applies, ask him or her to choose the category which best describes his or her current working status. If the patient cannot decide, the category closest to the **top** of the list should be coded, e.g., part-time vs. retired should be coded "part-time" to indicate current employment.

- **It is important to elicit work dates, month and year; *code DK*, if "Don't Know".**
- Allow the **patient** to define "full-time" and "part-time"; the general rule is full-time >= 38 hours.
- If currently not working, ask date stopped, and if the date is **within the past six months,** proceed with the remaining work questions; otherwise, go to Question 9. If someone has not worked in the past 6 months, there is less likelihood of future employment.
- On **short-term sick leave** = on leave for **less** than 3 months due to **health reasons**.
- On **long-term sick leave** = on leave for **more** than 3 months due to **health reasons**.
- **Temporarily laid off** = patient is not currently working (for reasons **other** than health) but still has an employer. This designation is frequently used for **"seasonal laborers"** such as farmers, painters, builders, teachers, etc.
- **Disabled** = someone who **perceives** him or herself to be **disabled**, whether or not he or she is receiving medical disability. Note: workmen's compensation = disabled.
- **Unemployed (and/or) Looking for work:** "Looking for work" is actively seeking employment, any effort to procure a job or establish a business or profession.

EXAMPLES:

- **Example 1:** A patient retired from a job as a factory worker two years ago, and now works 20 hours a week at McDonald's. He or she should be coded as "working part-time" since that is his/her current job activity.
- **Example 2:** A patient had been working full time until four weeks ago when he or she had a heart attack. He or she has not gone back to work. Since he or she has worked in the past three months, he or she should be coded as "on short term sick leave."
- **Example 3:** A patient has had progressive angina and has been on sick leave for four months, but has not formally retired. He or she should be coded as "on long-term sick leave."
- **Example 4**: Another patient has had progressive angina for the past three months and has had to quit his or her job because of his or her heart condition. Because he or she no longer has a job to return to, he or she is either "disabled" or "unemployed" (even if he or she intends to look for more work) or "retired."
- **Example 5:** A patient's only job is seasonally selling seed corn. He or she is not currently working and has not worked in the past 6 months, because it is not the working season. He or she should be coded as "temporarily laid off."

Questions 76-79

These questions define the patient's **job class**. It is important that a **detailed, descriptive job title and tasks** be written out along with number of hours worked. A patient's job class is more dependent on job activities than job title.

The next questions are about your work and daily activities.

74. Which <u>one</u> of the following best describes your current working status?
- ❑1 Working full-time
- ❑2 Working part-time
- ❑3 On short-term sick leave
- ❑4 On long-term sick leave (at least three months)
- ❑5 Temporarily laid off
- ❑6 Homemaker ➔ ➔ ➔ ➔ ➔ ➔➔➔➔➔➔
- ❑7 Disabled ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔
- ❑8 Unemployed or looking for work➔ ➔ ➔ ➔ ➔
- ❑9 Retired ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔
- ❑10 Other *Please specify:* _____

Did you ever work for pay?

❑1 Yes ➔ **When did you stop?**

_ _ / _ _ _ / _ _ _ _
d d m m m y y y y

❑2 No ➔ **SKIP to Question 80**

Is this date <u>within the past 6 months</u>?

❑1 Yes

❑2 No ➔ **SKIP to Question 80**

75. Are you planning to return to work?
- ❑1 Yes
- ❑2 No
- ❑3 DK

76. What kind of work did you do for pay in the <u>past six months?</u> Main Job:_____

77. What were the most important activities or duties of your <u>main</u> job? Examples: Drive truck, Operate tool and dye machine, supervise road crew._____

78. Which best describes how you are (or were) paid?
- ❑1 Hourly wages
- ❑2 Annual/Monthly salary
- ❑3 Work on commission or tips
- ❑4 Self-employed and/or own business, professional practice or farm
- ❑5 Work in family business or farm

79. During the time you worked, how many hours per week did you <u>usually</u> work at your job? # _____

Question 80 (Demographics: Education)

This question asks for the last grade of education or year completed. For example, if someone attended but did not complete the 11th grade, enter "10."

**Any scenarios which are difficult to compute should be noted in the Comments section of the EQOL Summary Form.

Question 81 (Demographics: Marital Status)

This question asks the patient's marital status. Separated generally means not living together. If not living together but the patient considers himself/herself married (for example, the spouse is living in a nursing home), then code = married.

Question 82 (Demographics: Income)

This item is asking for the level of total household income, not actual amount. Remind the patient that this is confidential, and the information is used solely to describe the GUIDE-IT patient. To help a patient feel more comfortable, the interviewer may ask the question, hand the questionnaire to the patient and ask them to circle the most appropriate answer.

The next set of questions are about you and your household

80. What is the highest grade (# of years) you completed in school? *(Circle one.)*

0							
1	2	3	4	5	6	7	8
9	10	11	12	Equivalency Certificate			
13	14	15	16				
17	18	19	20	21+			

81. Are you presently:
- ❑1 Married or living as married
- ❑2 Divorced
- ❑3 Separated
- ❑4 Widowed
- ❑5 Never Married

Finally, we would like to ask your total household income level. It will not affect your medical care in any way; it's strictly for demographic purposes for this study.

82. Roughly how much income from all sources (including earnings, pensions, investments, etc.) did your household have last year (before taxes)?
- ❑1 $10,000 or less
- ❑2 $10,001 to $20,000
- ❑3 $20,001 to $30, 000
- ❑4 $30,001 to $45,000
- ❑5 $45,001 to $60,000
- ❑6 $60,001 to $105,000
- ❑7 $105,001 to $120,000
- ❑8 $120,001 or greater
- ❑9 Refused

GUIDE-IT Medical Release Form

The GUIDE-IT study involves the collection of hospital information. At the time patients sign a consent they are asked to also sign a medical release form so that billing information regarding any hospitalizations that occurred during the 24 month follow up period can be requested from any hospital other than the enrolling facility. Patients are asked to sign the Medical Release Form in order for bills to be collected from any outside hospital in the event of hospitalization.

Additional instructions:

- Always fill in the patient identifiers at the top of the page
  (If your site or a patient does not allow release of social security number skip that section but enter the rest of the identifiers. When ECON requests billing information many times the SS# is used to identify a patient if they have a common name "Mary Smith".)

- Do not fill in the section that requests the facility name. The Economics group will fill this in when requesting a patients billing information. A patient may not always be hospitalized at the "site" facility and all bills are to be collected when an event or hospitalization is reported.
  If the patient or your site requests that this be filled in :
  - ✓ *Enter every hospital a patient may use-local and any near where they travel. The site will be responsible to request additional medical release forms if form cannot be completed*
- Leave information to be disclosed blank
  If your facility needs this checked off then:
  - ✓ *Check off hospital bill, discharge summary and Emergency Department records. The latter two will not be requested unless a bill cannot be provided.*
- Signature and Date need to be filled in. Use the date of consent and then enter date two years from this date.

As always, contact the EQOL coordinator for any questions regarding this document.

GUIDE-IT	Site #:_ _ _ Patient ID: _ _ _ _ Patient Name:_____ Date of Birth:_____ Social Security Number: _____

If mailing this form please send to:

GUIDE IT Coordinating Center
Duke Clinical Research Institute
2400 Pratt Street, P.O. Box 17969
Durham, N.C. 27705

I authorize and request that

_____

<insert facility name>

release the following protected health information from my medical record to the GUIDE IT Coordinating Center at Duke Clinical Research Institute, Durham, North Carolina. Information is requested for the following dates of service:

_____

INFORMATION TO BE DISCLOSED (check the appropriate boxes and include other information where indicated):

- ☐ Hospital Bill
- ☐ Discharge Summary
- ☐ Emergency Department Reports
- ☐ Procedure Reports (cardiac catheterization, percutaneous coronary intervention (Angioplasty, stent, PTCA)
- ☐ Operative Report (e.g., coronary artery bypass grafting (CABG))
- ☐ Laboratory Reports
- ☐ Radiology Reports
- ☐ Autopsy Report
- ☐ Patient Discharge Instructions
- ☐ Other:_____

THE INFORMATION TO BE DISCLOSED WILL BE USED FOR THE FOLLOWING PURPOSE:
The patient has consented to participate in the GUIDE IT Study. The Guide IT study will gather data to see if using the results of a blood test for NT-proBNP (a hormone released from the heart also known as a Biomarker) can help doctors decide the best drug treatment for patients with heart failure (HF). By signing this form, I authorize the staff/representatives of the GUIDE IT Study at the Duke Clinical Research Institute (DCRI) to use the above information [Patient's Name, Date of Birth, Medical Record Number, and Social Security number] to collect my **Hospital Bills** and **Medical Records** for any hospitalizations which occur during the time I am enrolled and followed in the GUIDE IT study. In doing so, I authorize the Patient Accounting/Medical Records Department at any hospital where I may receive care during this time period to disclose these hospital bills and medical records to the GUIDE IT study group. This process may take up to 3 years following my enrollment in the study. I understand that this information collected by GUIDE IT study will be kept strictly confidential and be used solely to assess my medical care and the medical expenses that occur during the course of the GUIDE IT Study. The information will not be re-disclosed to any party outside of the GUIDE IT study team. Additionally, I understand that I have the right to: 1) refuse to sign this authorization, 2) withdraw this authorization at any time by giving written notice to the address listed at the bottom of this form, with the knowledge that this action will not affect any information collected before the notice withdrawal and 3) receive a copy of this authorization.

This medical record/hospital billing information may be collected from_____ (study enrollment date) to _____ (2 years from date of enrollment).

Signature: Patient name printed

_____ _____

Date Signed: ____/____/_____ (mm/dd/yyyy)

Witnessed by:
Research Coordinator: _____ Date Signed: ____/____/_____ (mm/dd/yyyy)
(Signature)

---------- ----------
(Please print name) (Please print enrolling hospital name)

GUIDE-IT EQOL Scheduler

Below is a sample scheduler that will be sent by the GUIDE-IT EQOL Coordinating Center at the beginning of each month. This is a reminder for sites when forms are due or may be late.

Reminder: Baseline Questionnaires are expected for each patient enrolled at the site.

Fax forms to 919-668-9816 or upload to ftp.dcri.duke.edu

GUIDE IT EQOL SCHEDULER - SAMPLE

Thursday, November 1, 2012

Forms and Consents
Fax to :

DCRI EQOL CC (919)-668-9816

Site No.:	100	**Attention:**	**Jane Smith**	Demo Site	
Site Name:	Demo Site	**Fax: Phone:**	919-555-1212 919-555-1212	12 Main St Durham, NC 27705	
		Email:	nobody@mail.com		

Study No.	Date of Randomization	Item	Description	Due Date	Note
100-1003	**09-Aug-2011**	QOL	Baseline QOL Summary/Questionnaire	11/09/2011	**LATE**
100-1004	**10-Aug-2011**	QOL	Baseline QOL Summary/Questionnaire	08/10/2011	**LATE**
100-1006	**12-Aug-2011**	QOL	3 Month QOL Summary/Questionnaire	11/12/2011	Due

GUIDE-IT EQOL Queries

Queries are sent by the GUIDE-IT EQOL Coordinating Center at the beginning of each month.

If necessary, patients may need to be contacted to resolve some queries. The queries should be completed and faxed to 919-668-9816 or emailed to GUIDE-ITEQOL@duke.edu within 7 business days.

DATA CLARIFICATION FORM - SAMPLE GUIDE IT EQOL

Site: 100

Attention: Jane Smith 123 Main St Fax: 919-555-1212

Site Name: Demo Site **Phone: 919-555-1212** **Durham, NC USA 27705**

Pt#	Form	Missing Data	Corrected Data
100-1000	Baseline Questionnaire	**A response to Question 76 is missing. Please provide the "kind of work within the past 6 month" that the patient did (job role or title).**	
100-1002	Baseline Summary page	**Please provide the "Reason for Incomplete or Not Done" questionnaire.**	

The following are routine queries for missing or unclear data on the GUIDE IT Health Outcomes Questionnaires. Please clarify the data in the "Corrected Data" column for each query. Please date and initial all changes on the questionnaires retained at your site.

Thank you for your assistance in guaranteeing a quality dataset for GUIDE IT EQOL. Please sign and date this form, then fax back ASAP to +1 (919) 919-668-9816 . If you cannot fax, scanned forms can be sent to Guide-ITEQL@duke.edu.

_____

Site Coordinator Signature **Date**

Tab: Clinical Endpoints Committee

7 Clinical Endpoints Committee (CEC)

7.1 Roles and Responsibilities of the CEC

Clinical endpoints classification is the process of systematically identifying clinical events (endpoints) and consistently applying pre-defined criteria to these events. The CEC physicians will use these criteria to review and adjudicate all endpoints in an independent and blinded fashion to prevent bias.

The endpoints listed below will be collected during the GUIDE-IT trial from time of randomization until the final study visit. A subject may have multiple endpoints. **Report all endpoint events**, not just the first occurrence.

Primary Endpoint Events

- Death (all-cause mortality)
- Hospitalization (all-cause)

CEC Event Queries

The CEC will issue queries for source documents, or to request additional source documents if the documents submitted do not provide the necessary information to adjudicate the event. CEC queries will be sent through InForm. CEC queries will begin with **CEC:** so as not to be confused with other data queries.

7.2 Source Document Submission

After reporting the clinical event on the eCRF, obtain the necessary source documentation (see list of recommended source documents). Complete source documentation should be submitted to the CEC as soon as possible after identification of the event.

Prior to submission, blind all subject identifiers in order to protect subject confidentiality. This includes:

- Subject name, address, phone number
- Social security/insurance numbers
- Medical record numbers
- Any other Protected Health Information (PHI)

Label each page of the source documentation with the protocol name and complete 7-digit subject number (XXX-XXXX).

Attach the completed CEC Event Source Document Coversheet (see Appendix H) and submit the documents (event packet) to the CEC by fax or by FTP upload.

CEC Fax: 919-668-9816 **ftp.dcri.duke.edu**

7.3 Recommended Source Documentation for Endpoints

Please ensure dates and times are marked clearly on ECGs, CV procedure reports, and all diagnostic testing reports.

Remove all patient identifiers prior to submission.

All-cause Death

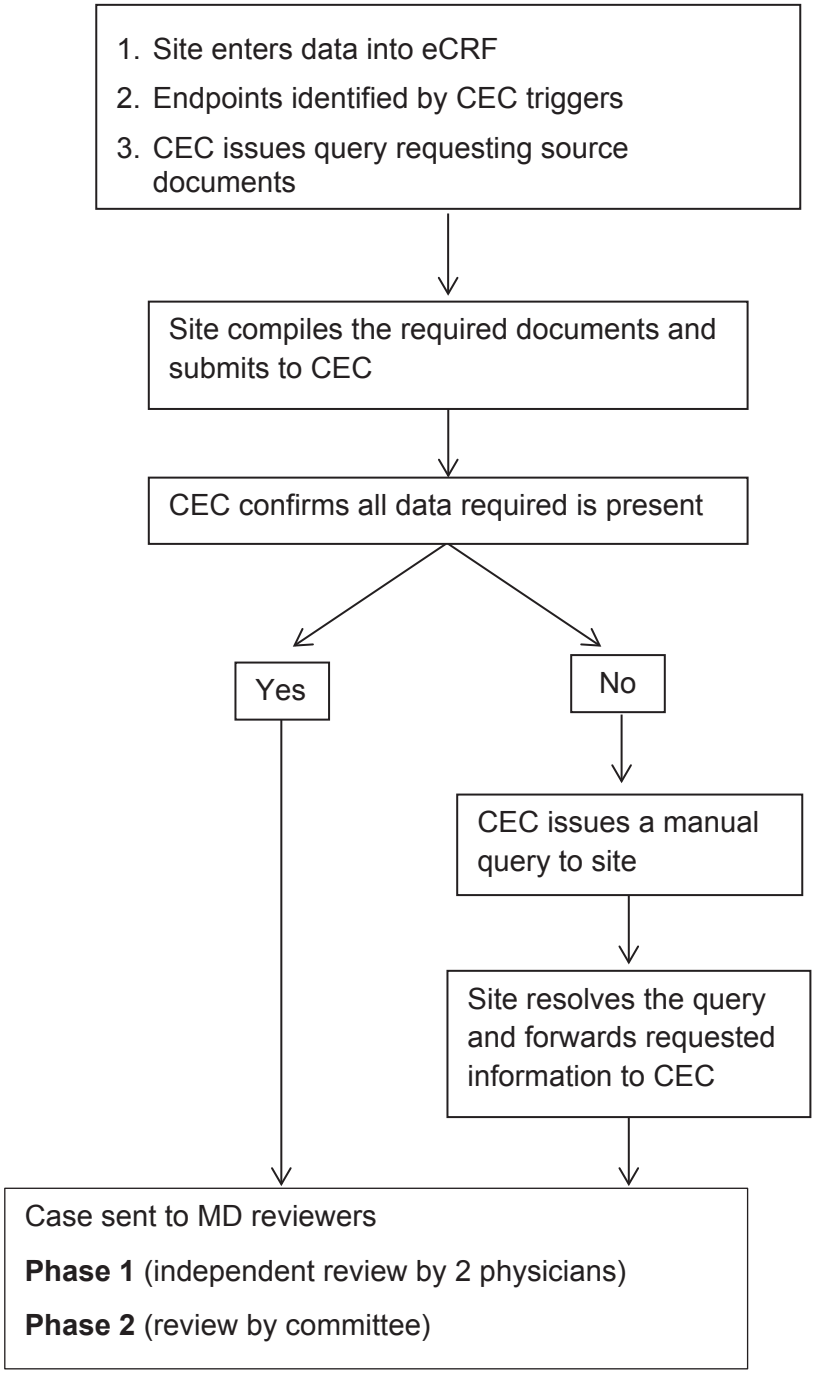
- Death summary or physician narrative* (include signs/symptoms/events leading up to death)
- Autopsy report (if performed)

All-cause Hospitalization

- Physician narrative*
- Discharge summary
- ECGs, if requested (pre-event, event, post-event)
- Cardiac markers, if requested
- Medication administration records, if requested

*If other recommended source documents are not available for death event, or with any event when all data is not available, a physician narrative will be needed. The narrative may be entered into the eCRF on the pre-populated page where the date of the event is placed. Physician narratives should provide a coherent and well-documented descriptive summary of pertinent details. The narrative should contain a clear, concise, and accurate description of the circumstances surrounding the event, and enough information about the associated signs, symptoms, and treatments that the CEC can make an independent classification of the event.

7.4 CEC Process Flow



Tab: Laboratory

8 Laboratory

8.1 Laboratory Sample Collection

The following tests will be performed at the time points specified in the GUIDE-IT protocol:

8.1.1 Local Laboratory Assessments

- ❑ NT-proBNP
- ❑ Hematology and chemistry to include:

Chemistry

- Sodium
- Potassium
- BUN/Urea
- Serum creatinine
- Total cholesterol

Hematology

- Hemoglobin
- Hematocrit
- Platelets
- WBC
- Lymphocytes (%)

8.1.2 Central Laboratory Assessments

See appendix I for a figure of central laboratory sample collection.

- ❑ **All subjects:** Core Lab NT-proBNP
- ❑ **Optional:** DNA (once only) and/or biorepository plasma and serum

Laboratory kits will be provided by LabCorp and all samples will be shipped to the LabCorp facility in Cranford, NJ. For more information on blood collection procedures and biological sample collection procedures and management, see the LabCorp Laboratory Manual posted on the GUIDE-IT website (www.GUIDE-IT.org).

8.1.3 DNA collection

Sample for DNA should be collected at the screening visit, however, if a subject is reluctant to participate, the sample may be collected at a future visit to allow the subject time to reconsider participation.

8.2 Central Laboratory Sample Collection Procedure

1. Select the LabCorp kit for the correct visit. Make sure that the requisition demographics match the cryovials. Every vial is pre-labeled with a barcode matching the requisition, but LabCorp requires that the Subject ID must also be entered on every specimen.
2. Use a tourniquet for **all** blood draws.
3. The LabCorp kit includes a 21G Eclipse needle and Vacutainer holder, but samples may be collected using a 19G butterfly needle with an adapter for vacutainer tubes, and should be drawn using a smooth, easy flow*,* avoiding hemolysis.
4. Draw tubes in the recommended order specified in the lab manual. Tubes must be filled to proper capacity to ensure correct anticoagulant ratio.
5. Mix contents by gently inverting the tubes at least 8–10 times, including the gold-top SST tube.
6. Centrifuge samples as soon as possible after collection**,** within 30–120 minutes.
7. Transfer plasma and serum into all cryovials as directed in the lab manual, using care to choose correct color-coded vial.
8. Store samples in -70° C freezer. Ship monthly in bulk on dry ice to LabCorp in Cranford, NJ. Assure that all vials for each visit are maintained together in one zip-loc biobag with a copy of the requisition, using the LabCorp packaging materials.
9. Each visit must be bagged separately.

8.3 Central Laboratory Sample Shipping Instructions

Store samples in a -70° C freezer until ready to ship. If necessary, -20° C is adequate for temporary storage.

Ship frozen specimens in bulk once per month to the processing center in Cranford, NJ.

Sites should follow local, state, and federal regulations for training related to shipment of hazardous materials. IATA training is required to ship biological samples with dry ice.

Sites are responsible for supplying dry ice. To find a dry ice supplier, visit http://www.dryicedirectory.com/

Tab: Study Intervention & Therapy Adjustments

9 Study Intervention & Therapy Adjustments

9.1 Biomarker-guided arm interventions

The treating physician will make decisions for interventions to achieve the NT-pro-BNP target. The order of implementation will be based on clinical judgment, and more than one intervention can occur in a single encounter.

It is recommended that titration of neurohormonal antagonists be considered over titration of diuretics except in the case of clinically apparent congestion, or in the case of very high NT-proBNP levels, which usually indicate subclinical volume overload. Specific changes in therapy and the rationale for them (e.g., in response to clinical change or NT-proBNP levels) will be captured on the eCRF.

Potential interventions to decrease NT-proBNP levels include:

- Up-titrate or add Angiotensin Converting Enzyme (ACE)-inhibitor or Angiotensin Receptor Blocker (ARB)
- Up-titrate or add beta-blocker (if not clinically congested)
- Up-titrate or add hydralazine-nitrates in African-American patients
- Increase loop diuretic dosage (if clinically congested or NT-proBNP > 5000 pg/mL)
- Up-titrate or add spironolactone if tolerated by renal function and potassium
- Add oral thiazide diuretic
- Add digoxin
- Consider adding ARB to ACE-I (if not on spironolactone)
- Consider hydralazine-nitrates in non-African-American patients
- Intensified or repeated heart failure education regarding diet, sodium restriction, etc.
- Consider optimization of cardiac resynchronization therapy (if CRT device implanted)
- Reconsider potential indications for CRT (if not previously implanted)
- If in atrial fibrillation, maximize rate control or consider more aggressive attempts to achieve normal sinus rhythm
- Consider exercise training or cardiac rehabilitation

9.2 Criteria for dosing changes

From: ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012 European Heart Journal (2012) 33, 1787–1847 doi:10.1093/eurheartj/ehs104

Evidence based doses of disease-modifying drugs used in key randomized trials in heart failure (or after MI).

	Starting Dose (mg)	Target Dose (mg)
ACE inhibitor		
Captopril[a]	6.25 t.i.d.	50 t.i.d.
Enalapril	2.5 b.i.d.	10–20 b.i.d.
Lisinopril[b]	2.5–5.0 q.d.	20–35 q.d.
Ramipril	2.5 q.d.	5 b.i.d.
Trandolapril[a]	0.5 q.d.	4 q.d.
Beta-blocker		
Bisoprolol	1.25 q.d.	10 q.d.
Carvedilol	3.125 b.i.d.	25–50 b.i.d.
Metoprolol succinate (CR/XL)	12.5/25 q.d.	200 q.d.
Nebivolol[c]	1.25 q.d.	10 q.d.
ARB		
Candesartan	4 or 8 q.d.	32 q.d.
Valsartan	40 b.i.d.	160 b.i.d.
Losartan[b,c]	50 q.d.	150 q.d.
MRA		
Eplerenone	25 q.d.	50 q.d.
Spironolactone	25 q.d.	25–50 q.d.

[a]Indicates an ACE inhibitor where the dosing target is derived from post-MI trials.
[b]Indicates drugs where a higher dose has been shown to reduce morbidity–mortality compared with a lower dose of the same drug, but there is no substantive placebo-controlled randomized controlled trial and the optimum dose is uncertain.
[c]Indicates a treatment not shown to reduce cardiovascular or all-cause mortality in patients with heart failure or after acute MI (or shown to be non-inferior to a treatment that does).

9.3 Dosages of diuretics commonly used to treat heart failure

	Initial Dose (mg)		Usual Daily Dose (mg)	
Loop diuretics[a]				
Furosemide	20–40		40–240	
Bumetanide	0.5–1.0		1–5	
Torasemide	5–10		10–20	
Thiazides[b]				
Bendroflumethiazide	2.5		2.5–10	
Hydrochlorothiazide	25		12.5–100	
Metolazone	2.5		2.5–10	
Indapamide[c]	2.5		2.5–5	
Potassium-sparing diuretics [d]				
	+ACEi/ARB	−ACEi/ARB	+ACEi/ARB	−ACEi/ARB
Spironolactone/ eplerenone	12.5–25	50	50	100–200
Amiloride	2.5	5	5–10	10–20
Triamterene	25	50	100	200

[a]Oral or intravenous; dose might need to be adjusted according to volume status/ weight; excessive doses may cause renal impairment and ototoxicity.
[b]Do not use thiazides if estimated glomerular filtration rate is < 30 mL/min., except when prescribed synergistically with loop diuretics.
[c]Indapamide is a non-thiazide sulfonamide.
[d]A mineralocorticoid antagonist (MRA) i.e., spironolactone/eplerenone, is always preferred. Amiloride and triamterene should not be combined with an MRA.

9.4 Subject Follow-up

9.4.1 Frequency

Subjects will continue visits every 3 months for a minimum of 12 months and up to a maximum of 24 months. If a subject is unable to come to the study site, remote laboratory assessments of renal function, electrolytes, and NT-proBNP (biomarker-guided arm only) may be substituted, though every effort should be made to assist the subject in returning to the study site for assessments.

9.4.2 Early Termination/Withdrawals

Subjects may discontinue study participation at any time. Subjects who wish to withdraw from all aspects of the study should notify the investigator in writing. Withdrawn consent can apply to certain aspects of the trial. Subjects can refuse to continue participation in the biorepository or EQoL portion of the study and still be included in the GUIDE IT study.

If a subject expresses doubt about continuing in the study:

- Talk with subject to see if you can identify issues or specific reason(s) they want to withdraw. Sometimes recent lifestyle changes or health issues create a temporary adherence problem.
- Do not coerce the subject to remain in the study; the subject can withdraw at any time for any reason.
- Listen carefully and restate the subject's value to the study.
- Ask if the subject would continue to attend follow-up visits by phone.
- If contact becomes a problem, stress the importance of keeping in touch. It may be possible to arrange for the subject to contact the study site at a specified time, annually, or even at the "final visit" stage of the study.
- In all cases, the individual who spoke with the subject should document the withdrawal of consent in writing. This should include the date consent is withdrawn.

9.4.3 For Subjects Considering Withdrawal

Talk with the subject and see if the reason(s) can be resolved. Some reasons may be related to study requirements the subject perceives as burdensome. If so, consider if any of the following options are feasible:

- Providing transportation to and from clinic.
- Accepting test or procedure results from an alternate laboratory or physician's office.
- Relocating a subject to an alternate study site. Contact your site manager/CRA who will assist in locating the nearest site and work with the new site to ease the subject's transition.
- As a last resort, follow the subject by telephone—please contact your site manager/CRA to discuss this option.

Tab: Safety Reporting and SAEs

10 Safety Reporting and Serious Adverse Events

10.1 Adverse Events – Events of Interest

Non-serious adverse events will not be routinely collected for this study. However, events of interest, which may or may not meet criteria for a serious adverse event, occurring from randomization through the final study visit, will be collected in the InForm eCRF. Events of interest include:

- Symptomatic hypotension
- Symptomatic bradycardia
- Hyperkalemia (potassium > 6.0 meq/dL or requiring change in therapy)
- Worsening renal function (increase in creatinine by 0.5 g/dL from last visit or requiring change in therapy)

10.2 Serious Adverse Events (SAEs)

In this trial, an SAE is any untoward medical occurrence that may result in any of the following outcomes:

- Is life-threatening
- Results in persistent or significant disability/incapacity
- Results in prolongation of existing hospitalization
- Is a congenital anomaly/birth defect
- Is an important medical event that may not result in death, be life-threatening, or require hospitalization that may be considered an SAE when, based upon appropriate medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

Death and hospitalizations will be collected in InForm as trial endpoints and **will not** be captured separately as SAEs.

SAEs occurring from randomization through the final study visit should be documented in the subject's medical records and will be collected in the InForm eCRF. All SAEs documented at a previous study visit and designated as *ongoing* should be reviewed at subsequent visits.

The Investigator will follow all SAEs until resolution, stabilization or the event is otherwise explained. The site will follow institutional guidelines for reporting SAEs to their Institutional Review Board (IRB).

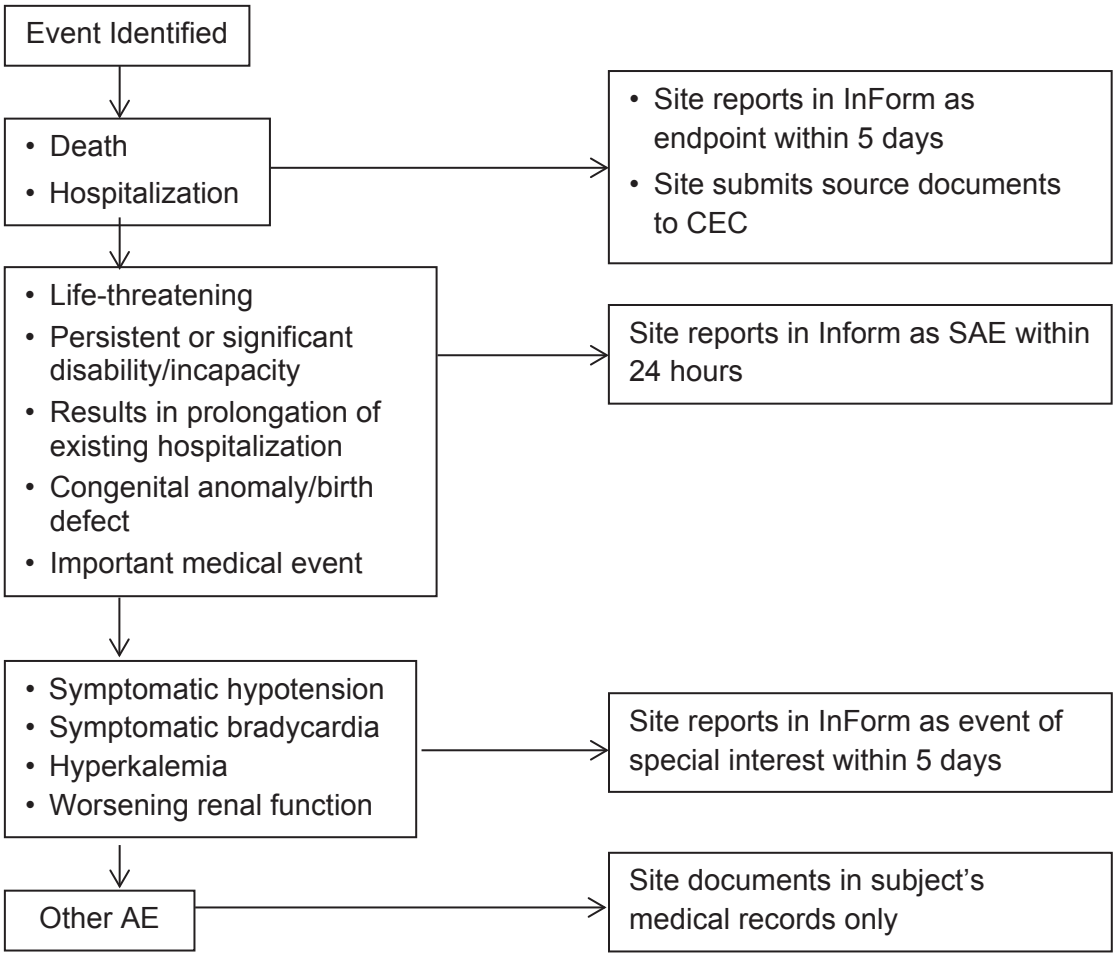
10.3 Reporting Procedures

The site investigator is responsible for documenting all events and should follow usual clinical practices at their institution for reporting to regulatory authorities serious, unexpected events related to standard of care medications and devices.

Report SAEs and endpoints on the InForm eCRF form **within 24 hours of knowledge of the event.**

As additional information pertaining to an event becomes available, update the eCRF form.

Report events of interest in the eCRF within 5 days of learning of the event.



Tab Data Collection and eCRF

11 Data Collection and eCRF

11.1 Electronic Case Report (eCRF)

Qualified study staff at each site will perform primary data collection from source-document reviews. DCRI will perform clinical monitoring, including review of eCRFs with verification to the source documentation. The focus of source documentation verification will be on critical variables that have been identified as supporting patient eligibility and study analysis.

This study will use web-based electronic CRFs developed through a validated, electronic records and electronic signatures (ERES)-compliant platform (21 CFR Part 11). Prior to initiation of the trial, each site will be contacted as to computer availability, hardware specifications, and internet connectivity, to evaluate the capacity of the site to use this type of data collection system.

InForm system requirements:

- Pentium II processor
- Display 1024x768 resolution
- MS Windows 98 or later
- High-speed internet connection
- Microsoft Internet Explorer 6.0, 6.1, 7.0 and 8.0 (in compatibility mode).

At this time InForm is not supported by Netscape, Mozilla Firefox, Google Chrome, or any Mac applications (e.g., Safari).

Site staff who will be entering data will receive training on the system, after which each person will be issued a unique user identification and password.

For security reasons, and in compliance with regulatory guidelines, it is imperative that only the person who owns the user identification and password access the system using the unique access code. Access codes are non-transferable. The password is considered a binding electronic signature. Site personnel who have not undergone training may not use the system and will not be issued user identification and password until appropriate training is completed. After training, a temporary password will be issued.

11.1.1 Password Requirements

The first time you log in, you will need to change your password. During this process you will set up the password recovery system. Enter an e-mail address, challenge question, and an answer to your challenge question. Providing this information will allow you to reset your account in the event you forget your password.

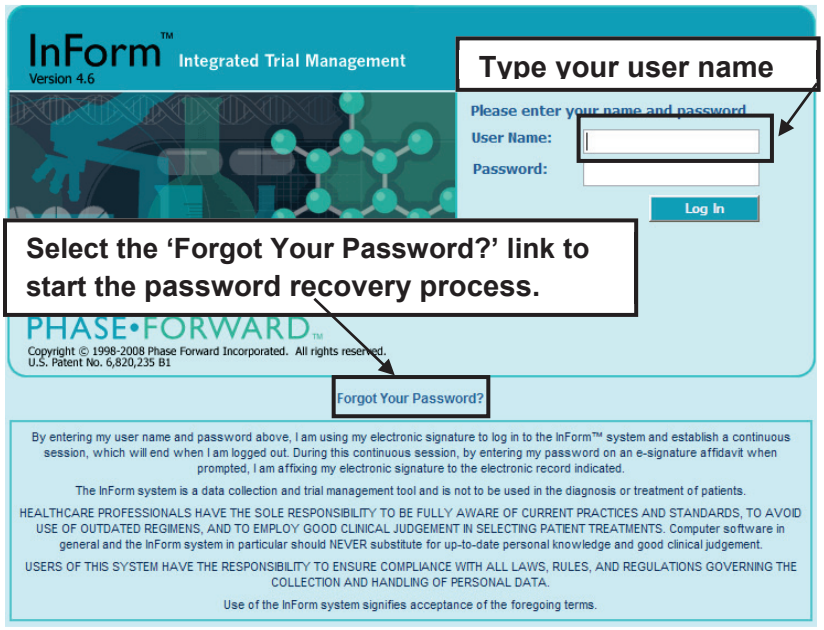
Password requirements:

- Minimum length: 8 characters
- Must include a number
- Must include an upper-case letter
- May include a non-alphanumeric character (&^%&#$)
- Will expire every 120 days
- Cannot be re-used

After three unsuccessful login attempts your user account will become inactive. If you do not remember your password, use the password recovery option **prior to** the third attempt.

1. Type your user name
2. Select the 'Forgot Your Password?' link on the login screen.
3. Submit the answer to your challenge question and select the 'Reset Password' button.

4. InForm will send a newly generated password to the e-mail account used during the initial log in process.
5. Use the new password to log in and then change your password (as prompted by InForm).



If you are locked out of the InForm system, contact the DCRI Helpdesk to request a password re-set.

11.2 Data Quality Control

The investigator is responsible for the integrity and accuracy of the data. The investigator must ensure completeness, legibility, and timeliness of the data reported. In addition, the PI must review and sign electronically to verify data accuracy. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Black ink is required to ensure clarity of reproduced copies. When making changes or corrections, cross out the original entry with a single line, and initial and date the change. Do not erase, overwrite, or use correction fluid or tape on the original source documents.

The source document is the first place information is documented. Source documents include but are not limited to patient charts, lab reports, medication administration records, ECG, etc.

All data relating to the study will be entered into eCRF provided by DCRI. Data will be entered from the subject medical records into the eCRF. Subject medical records will be maintained at the site and considered the source documents for this clinical trial. The investigator is responsible for the data entered into the eCRF, and for verifying that all data entries in the eCRFs are accurate and correct.

The eCRF will flag out of range values entered and ask site staff to confirm accuracy of entry.

All data collected in the context of this study will be stored and evaluated in such a way as to guarantee subject confidentiality in accordance with the legal stipulations applying to

confidentiality of data. Study records and regulatory documents will be retained at the study site, along with adequate source documentation, according to NIH requirements. All study records, including source documents, must be available for inspection by the DCRI, the FDA, and the NIH.

11.3 eCRF Instructions

See appendix J for detailed instructions for entering data into the GUIDE-IT eCRF.

11.4 Timing and Reports

Data will be collected on an ongoing basis and the DCRI site management team will review the eCRFs on a continual basis throughout the trial. The site management team will review the electronic data prior to and between monitoring visits.

Tab: Study Conduct

12 Study Conduct

12.1 Site Training

Training is an ongoing process and therefore the training plan will be updated as needs change throughout the course of the study. All personnel listed on the Site Staff Delegation & Signature Log delegated one or more responsibilities by the Principal Investigator (Site PI) are required to be qualified to perform the activity at the time of delegation.

12.1.1 Forms of Training

All persons listed on the Site Staff Delegation and Signature Log should have documentation of training in Human Research Subject Protection. Training is available at the following websites:

http://phrp.nihtraining.com/users/login.php

https://www.citiprogram.org/

Forms of study-specific training for personnel involved in the GUIDE-IT study will include, but are not limited to:

- Face-to-face meeting training sessions
    - Investigators meeting
    - Steering committee meeting
    - Clinical site meetings (eg, CRA and PI training of support personnel)
- Site initiation visits
- Periodic monitoring visits as applicable
- MOO instruction manuals
- Teleconferences
- Webinars
- Newsletters

12.1.2 Training Topics

Training on all aspects of the study will occur prior to enrolling study subjects. All forms of training listed above may be utilized for the training of study personnel. For example, site initiation visits will cover a brief overview of the protocol as well as site logistics such as facility requirements, while webinars may be used to provide EDC training, or ad hoc refresher training. Additional and/or refresher training will occur as determined by the GUIDE-IT Steering Committee and/or DCRI. Training topics may include:

- Protocol
    - Scientific review, previous research
    - Background and rationale

    - Procedures and schedule of events
- Regulatory requirements
    - Good clinical practice
    - Protection of human research subjects
- Adverse event/serious adverse events
    - Definition and reporting requirements and process
- Study materials
    - Manual of procedures
    - GUIDE-IT website
- Site investigator and site staff responsibilities
- Recruitment and retention of subjects
- Patient enrollment procedures
- Patient management and dosing/intervention recommendations
- Laboratory procedures
- Monitoring plan and visits
- Audit procedures and record retention guidelines
- CRF data entry and query resolution/InForm training

12.2 Study Logs

Blank copies of the study logs are available on the trial website. In-progress and completed logs are located in the Regulatory Binder. Examples of the logs may be found in Appendix B.

- Site Staff Delegation and Signature log
- Site Visit Log
- Confidential Master Subject Log
- Protocol Waiver Log
- Training Log
- A Screening Log will be maintained electronically at each site. This log will not be routinely collected by monitors, but should be available for review at monitoring visits.

12.3 Principles of Good Clinical Practice

The integrity and ultimate credibility of the study depends on factors such as ensuring adherence to the protocol, obtaining complete follow-up information on all participants enrolled, and using quality control measures to establish and maintain high standards for data

quality. The following clinical monitoring is implemented to ensure subject safety and rights, protocol adherence, and complete, accurate, verifiable data:

1. Study initiation-investigator meeting and site initiation visit
2. Interim on-site monitoring visits
3. Remote monitoring of electronic data entry and query resolution
4. Final close-out visit

12.4 Standard Operating Procedures (SOPs)

Site-specific operating procedures will be used when available for study-related processes and procedures.

12.5 Site Monitoring Plan

The DCRI has developed a universal monitoring plan. The DCRI Lead CRA will train both the DCRI and SRA monitors to assure consistency during all study visits. The monitoring plan details visit frequency and identifies critical variables for source document verification. The Lead CRA will review all monitoring reports and address site issues with CRAs as they arise and hold periodic teleconferences with the monitors and sites. The monitoring plan and all monitoring reports will be submitted for review by DMID.

The DCRI Project and Site Management team conducted an Investigators' Meeting on October 25-26 to train the investigators and their staff. Phone initiation visits will also be conducted for all sites, and an on-site visit will be conducted for any new US sites added after this Investigators' Meeting. These meetings/visits will occur prior to the enrollment of the first subject to review study procedures recording the findings in the eCRFs

12.6 Site Monitoring Overview

As part of the quality enhancement plan and in full agreement with the NIH policy which states all clinical trials require monitoring to ensure the safety of participants and the validity and integrity of the data (NIH Guide, NIH Policy for Data and Safety Monitoring, June 10, 1998), monitoring is considered a continuous, ongoing, and multifaceted process. This process may include external on-site monitoring by DCRI site monitors, sponsor staff, and site IRBs.

Site monitoring for GUIDE-IT will include remote and on-site monitoring and will be based on the August 2011 Draft Guidance for Industry Oversight of Clinical Investigations—A Risk-Based Approach to Monitoring. A copy of the complete document is available on the study website.

Site monitoring visits are conducted to ensure required human participant protection, study procedures, laboratory, study intervention administration, and data collection processes are of high quality and meet Sponsor, ICH E6, and other appropriate regulatory guidelines. Site visits are conducted by an authorized representative of the DCRI, or other regulatory agencies to

inspect study data, participants' medical records, and eCRFs in accordance with International Conference on Harmonization (ICH) guidelines, Good Clinical Practice (GCP), and respective local or government regulations and guidelines.

A representative from the DCRI will contact participating clinical sites to facilitate the conduct of monitoring visits. A confirmation will be distributed to the clinical site and designated staff members. The purpose of the monitoring visit is to determine compliance with protocol and regulatory requirements and with study policies and procedures defined in the protocol or MOO. A full or partial audit of selected participants will be conducted to determine consistency of data recorded on source documents with data entered in EDC. Monitoring visits are expected to be conducted at a mutually agreeable time between site monitors and participating staff for the purpose of exchanging information regarding the visit findings, and to discuss any observations related to protocol implementation or compliance with the protocol. The investigator will agree to provide access to the office, clinic, and/or hospital records of all subjects entered in this study. Access for inspection of these records may be required by the DCRI, NIH, and/or their representative(s) at the time of each monitoring visit. In addition, all records may be subject to inspection by officials of the FDA or other health authorities.

12.7 Site Activation

Once all regulatory requirements have been received and all training requirements fulfilled, a site activation letter from the DCRI will be distributed notifying the PI, study coordinator, and other appropriate personnel of approval to initiate study enrollment. This letter should be filed in the regulatory binder as documentation of the date in which the site was activated.

12.8 Site Interim Monitoring Visits

A DCRI representative will conduct the first monitoring visit within 1 month after the first 2 subjects are enrolled and have completed the 6-Week follow-up visit. Subsequent visits will occur annually unless otherwise indicated.

The overall goals of site interim monitoring visit are to:

- Verify completion of previous site visit action items (if applicable).
- Assess continued compliance with ICH, GCP, and CFR guidelines.
- Ensure proper consent/assent procedures.
- Review required essential documents and regulatory binders for accuracy and currency.
- Review overall clinic and laboratory operations.
- Ascertain site compliance with the protocol and MOO-defined procedures.
- Monitor data quality and consistency by conducting a data audit.
- Ensure compliance with protocol and IRB with respect to AEs, SAEs and protocol deviation reporting requirements.

- Assess security of confidential records.
- Communicate observations made during the visit and provide data discrepancies to the site PI and study coordinator.

12.9 Site Close-out Visits

At the request of the PI, the site monitor will schedule a site close-out visit following completion of all required study visits by enrolled participants, completion of required eCRF forms, and resolution of any outstanding data queries.

The overall goals of the site close-out visit are to:

- Ensure site compliance with regulatory and procedural requirements described by the study protocol and MOO.
- Review required source documents to verify accuracy with data entered in EDC.
- Ensure all laboratory samples are shipped according to the protocol.
- Ensure all regulatory documents are submitted appropriately and retained.

The site close-out visit is also a time to communicate procedures with respect to archiving of study records, site IRB notification regarding cessation of enrollment, the potential for future data queries prior to final database lock, and procedures to follow if notification is provided of an FDA inspection/audit.

12.10 Site Monitoring Reports

Following a monitoring visit, the DCRI CRA will distribute a written, detailed site visit report summarizing visit findings and action items with targeted dates of completion of those items. The report is expected to be distributed to the site PI and study coordinator within three weeks of the visit. Site staff is expected to review the findings and resolve action items by the specified target dates. In some instances, verification of selected action items will require verification by the CRA at a subsequent visit. Questions pertaining to the content of the report should be directed to the DCRI Lead CRA.

12.11 Study Completion and Close-Out Procedures

12.11.1 Site Procedures for Close-Out

Site procedures for close out will be followed as documented in the Clinical Monitoring Plan. Sites should also follow their local policies for site closure procedures

12.11.2 Overall Study Completion and Close-Out Procedures

Upon completion of enrollment and follow-up of all study subjects, the DCRI will prepare to lock the database and close-out the study. The database lock process will be followed according to the DCRI SOPs for Data Base Lock and Unlock. Study files, both site and project history files, will be internally audited and confirmed to contain all required information.

12.12 Study Records Retention

It is recommended that investigators retain all records and documents (including electronic data capture materials) pertaining to the conduct of the study for at least 3 years after submission of the final study report in the event follow-up is necessary to help determine any potential hazards to subjects who took part in this study. The investigator agrees to obtain NIH agreement prior to disposal, moving, or transferring of any study-related records. Additionally, if the investigator retires, relocates, or for other reasons withdraws from the responsibility of the study, then another investigator must be assigned if the study is still active. Any new investigator must be approved by NIH and DCRI.

Tab: Regulatory Requirements

13 Regulatory Requirements

13.1 Regulatory Document Requirements

All required regulatory documents must be accurately maintained at each clinical site. The DCRI will provide a regulatory binder for the maintenance of required study and regulatory documents. The purpose of the regulatory binder is to keep an ongoing record of the implementation of the research protocol. The binder maintains required study regulatory documentation in a single location to decrease the likelihood that important documents will be misplaced and to ensure documents are readily available for reference by study staff, site monitors, and auditors. Study staff at each clinical site is required to maintain a current Regulatory Binder by updating documents when there are staffing changes, when documents expire, or when they require updating. Both historical and current copies of all documents are required to be present in the binder. Regulatory Binders will be reviewed during site monitoring visits to ensure that documents are current and all required documents are present.

Submit required documents to the DCRI prior to study start-up and throughout the study as documents are updated. The study site should ensure that all copies are legible and that no part of the document is cut off the page when imaged. The back of any hard copy page should be imaged unless it is completely blank.

The following list provides a summary of contents for placement in the Regulatory Binder provided by the DCRI:

Protocol

- Original and all revisions/amendments
- Signature pages

Consent Forms

- All IRB-approved versions

Investigator Qualifications

- Curriculum Vitae (CVs)
- Medical Licenses

Investigator Forms

- Conflict of interest
- Investigator agreement

IRB Approvals and Correspondence

- Federalwide Assurance (FWA) number
- IRB Membership roster (optional)
- IRB Correspondence
- IRB Approvals, progress reports, close-out report

Training

- Certificate of training for human research subject protection
- Investigator meeting attendance

InForm EDC training certificate

Laboratory

Local laboratory CLIA certificate

Local laboratory normal/reference ranges

Safety Reporting

Safety reports

Study Logs

Site Staff Delegation and Signature Form

Site Visit Log

Subject Screening/Enrollment Log

Confidential Master Subject Log

Training Log

Protocol Waiver Log

Study Correspondence

13.2 Protocol Deviations

A protocol deviation is an intended or unintended departure from the protocol-specific study procedures or schedules, GCP or MOO requirements that does not result in a significant added risk to the participant. Noncompliance with study documents may result due to an action on the part of the participant, the PI, or the clinical site staff. Examples of deviations include, but are not limited to: out of window visits, missed procedures, or missed visits. Site personnel or study monitors may identify protocol deviations. Corrective actions may need to be developed by the clinical site and implemented promptly to minimize deviations. These practices are consistent with ICH GCP Sections 4.5.1, 4.5.2, 4.5.3 (Compliance with Protocol), and 4.5.4.

13.3 Protocol Violations

Protocol violations are a specific type of protocol deviation that results in significant added risk to the participant and may affect the integrity of the study data. Examples include, but are not limited to: failure by the investigator to adhere to significant inclusion/exclusion criteria, failure to follow informed consent procedures, incorrect use of a study device (NT-proBNP point-of-care device), or failure to report an SAE within the protocol-defined timelines. Each investigator is expected to adhere to the study protocol and be responsible for enrolling only participants who have met all eligibility criteria.

13.4 Protocol Waivers

A protocol waiver is a request by the site to proceed with a planned deviation from the protocol; for example, a request to enroll a patient who does not meet all eligibility criteria is

considered to be a protocol waiver. Protocol waivers are expected to be rare in the GUIDE-IT study.
If a patient does not meet eligibility criteria, but the PI would like to consider him or her for enrollment, the PI should contact the GUIDE-IT hotline to discuss. The site should document the waiver request on the Protocol Waiver Log. Copies of the Protocol Waiver Log are available on the study website.

13.5 FDA Audits

During the course of the trial and following trial completion, the FDA may determine that a site inspection will be performed. Any time a participating site receives a communication from the FDA, the sponsor and DCRI must be informed immediately. The sponsor and DCRI will assist the site in preparation for the visit and can address questions from site personnel pertaining to the FDA audits/inspections. Typically, an assessment of investigator compliance with stated obligations, protocol amendments, safety reporting, and overall site compliance with the protocol are determined. The items listed below are areas FDA inspectors will review while auditing investigational sites. Additionally, the FDA has an SOP to follow when inspecting investigational sites. Participating sites are expected to read Bioresearch Monitoring Compliance Program Guidance (#7348.811, which is the one for clinical investigators). Particular attention should be paid to Part III, Inspectional, online at:

http://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/ucm133773.pdf.

Areas for Review during an FDA Audit:

- Study protocol and any amendments to the protocol
- Informed consent and informed assent forms and any amendments to the informed consent and informed assent forms due to protocol amendments
    1. Are all required elements included on the form?
    2. Are additional elements relevant?
    3. Was the consent/assent form approved by the IRB?
    4. Were consent/assent forms signed and dated by the participants (or legal guardian, if applicable)?
    5. Did each participant (or legal guardian, if applicable) provide proper informed consent/assent prior to study entry?
    6. Were study procedures performed prior to obtaining the consent/assent?
- Sponsor/IRB correspondence including IRB approvals/Progress reports/AE reports
- Investigator Agreements
- Methods for recording and correcting study data
- Supporting Files

    - Hospital chart
    - Participant binders
- Review of hospital charts versus other source documents with case reports forms
- Protocol non-adherence (protocol violations)
- Documentation of concomitant medication
- Adverse event reporting
- Serious adverse event reporting to the IRB and sponsor
- Verification that study procedures were performed by personnel who are listed on the site authorization log or study training documents

Tab: Human Subjects Protection

14 Human Subjects Protection

14.1 Confidentiality and HIPAA Considerations

Investigators at each study site will be responsible for insuring compliance with the Privacy Rule, a Federal regulation under the Health Insurance Portability and Accountability Act (HIPAA), in accordance with the investigator's institution's policy. The Privacy Rule establishes the right of a research subject or subject's legally authorized representative to authorize an investigator to use and disclose the subject's personal health information (PHI) for research purposes. This requirement is in addition to the informed consent and assent to participate in the study. A valid Privacy Rule Authorization is a subject's or subject's legally authorized representative's signed permission that allows an investigator to use or disclose the subject's PHI for the purposes, and to the recipient or recipients, as stated in the authorization. The subject or the subject's legally authorized representative has the right to revoke the authorization, in writing, at any time. The signed authorization must be retained by the investigator for 3 years from the date of creation or the date it was last in effect, whichever is later.

HIPAA authorization can be combined with a consent form. Whether combined with a consent form or separate, an authorization must contain the following specific core elements and required statements stipulated in the Privacy Rule.

Study personnel must:

- Have permission to perform the initial screening and main study assessments
- Notify local IRB of recruitment plans
- Receive acknowledgment from the IRB
- Obtain participant authorization

The elements of authorization include:

- Who may use or disclose the information
- Who may receive the information
- Purpose of the use or disclosure
- Expiration date or event
- Individual's signature and date
- Right to revoke authorization
- Right to refuse to sign authorization
- A statement about the potential for personal health information (PHI) to be re-disclosed by the recipient.

Authorization must be written in plain language and contain the core elements and required statements listed above. A signed copy of the authorization must be provided to the individual signing it (if the HIPAA authorization is combined in the consent form, the signed copy of the consent form will serve this purpose).

14.2 Patient Confidentiality

All subject records will be identified only by initials and a subject ID study number. Do not transmit patient names to DCRI. The investigator will keep a Confidential Master Subject Log with the subject ID number, date randomized, date of birth, and full name, address, and telephone number of each subject.

Subject confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their agents. This confidentiality is extended to cover testing of biological samples and genetic tests, in addition to the clinical information relating to participating subjects.

The study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party with the exception of FDA and NHLBI.

The study monitor or other authorized representatives of the sponsor, the FDA, and NHLBI may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study. The clinical study site will permit access to such records.

14.3 Institutional Review Boards

Before initiating this study, the protocol, site-specific consent forms, HIPAA forms, recruitment materials, and other relevant information will be reviewed by a properly constituted IRB at each participating clinical site. A copy of the signed and dated IRB approval at each clinical site will be retrieved prior to site activation and archived at the DCRI. Any amendments to the protocol, other than simple administrative and typographical changes, must be approved by each IRB before they are implemented. The sites will seek annual renewals of their IRB approvals in accordance with local procedures.

This study will be carried out in full compliance with FDA guidelines for Good Clinical Practices (GCPs). Approval by the IRB prior to the start of the study will be the responsibility of the investigator. A copy of the approval letter must be supplied to DCRI along with DHHS Federal wide Assurance Number. During the course of the study, the investigator shall make timely and accurate reports to the IRB on the progress of the study, at intervals not exceeding one year (or as appropriate), and notify the IRB of SAEs or other significant safety findings.

14.4 Amendments to the Protocol

Any amendment to this protocol will be provided to the investigator in writing by DCRI. No protocol amendment may be implemented (with the exceptions noted below) before it has been approved by the IRB and the signature page, signed and dated by the investigator, has been received by DCRI. Where the protocol is amended to eliminate or reduce the risk to the subject, the amendment may be implemented before IRB review and approval. However, the IRB must be informed in writing of such an amendment and approval obtained within reasonable time limits. Deviating from the protocol is permitted only if absolutely necessary for the safety or clinical management of the subject, and must be immediately reported to DCRI.

14.5 Study Discontinuation

The DCRI, NIH, FDA, DSMB and Executive Committee reserve the right to terminate the study in its entirety or at a specific site, at any time.

Tab: Appendices

Appendices

Appendix A. DCRI Contact Information

Clinical Hotline: 919-998-9928 (urgent questions)

Email: GUIDE-IT@dm.duke.edu (preferred method of contact)

FTP site: ftp.dcri.duke.edu
Use your site-specific username and password to access your site's secure folder on the FTP site.

Trial website: https://www.guide-it.org/

	Office Phone	Cell Phone	Email
Gayle Paynter, Project Leader	1-919-668-8641	1-919-314-7414	gayle.e.paynter@duke.edu
Chris Beard, Lead CRA	1-919-668-8690	1-919-	christophe.beard@duke.edu
Barb Kuzil, CRA	1-603 526 6615	1-919-323-2640	barbara.kuzil@duke.edu
Tish Boddie, CTA	1-919-668-8102		lattisha.boddie@duke.edu
Beatrice Mengich, CRA	1-919-668-8069	1-919-257-9251	beatrice.mengich@duke.edu
Elouise Watson, CTA	1-919-668-5968		elouise.watson@duke.edu
Nidia Y. Rosado, CCRA	1-786-410-5761	1-786-410-5762	nidia.rosado@duke.edu

Appendix B. Study Log Samples

Duke Clinical Research Institute

SITE STAFF DELEGATION & SIGNATURE LOG
(For NIH Study)

Principal Investigator (printed name)	Site Number	Study/Protocol Number	Sponsor	Page _____ of _____
		GUIDE-IT		

STUDY COORDINATOR: List individuals that have been delegated significant study-related responsibilities and update this log as personnel, roles and/or responsibilities change. At a minimum, all "Key Personnel" must be included. The NIH defines "Key Personnel" as "The PI and other individuals who contribute to the scientific development or execution of a project in a substantive, measurable way, whether or not they receive salaries or compensation under the grant. Typically these individuals have doctoral or other professional degrees, although individuals at the masters or baccalaureate level may be considered key personnel if their involvement meets this definition. Consultants also may be considered key personnel if they meet this definition".

PRINCIPAL INVESTIGATOR (PI): Delegation and authorization of responsibilities is an on-going process during study conduct. **At the time of delegation, enter your initials, date and start date below.** By your initials, you are authorizing that the designated individuals are qualified to perform the activities indicated at the time of delegation. Your initials also confirm your understanding that this in no way alters your responsibilities as defined by applicable regulations, guidelines and the clinical trial agreement (or equivalent).

MONITOR: Ensure listed individuals are delegated activities relevant to their role, education and training. If updated, collect a **copy**. At close-out, collect a **copy** of the completed log.

Key Personnel Check if "Yes"	Print Full Name	Signature	Initials	Study Role	Study Responsibilities Use Description Code List	PI Initials/Date	Start Date	End Date
☐								
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Description Code List

1. Informed Consent	7. Dispense test article	13. Review and/or sign CRFs/e-CRFs	19. Other:
2. Subject screening	8. Administer test article	14. Data Clarification Form/Query resolution	20. Other:
3. Physical examination	9. Test article accountability	15. Oversight of lab sample collection, preparation & shipment	21. Other:
4. Medical history	10. Relationship/causality for AE(s)/SAE(s)	16. Maintain study files	22. Other:
5. Subject eligibility	11. SAE Reporting	17. IRB/IEC/REB communication	23. Other:
6. Subject randomization	12. CRF/e-CRF completion and correction	18. Other:	24. Other

To be Completed by the Principal Investigator at Study Close-out
As the Principal Investigator for the study, I confirm that all listed personnel were delegated study responsibilities as documented above.

Principal Investigator Signature: **Date:**

Duke Clinical Research Institute

GUIDE-IT Site Visit Log

Site Number: __ __ __ **Principal Investigator Name:** _____	**Sponsor Name:** NHLBI **Protocol:** GUIDing Evidence Based Therapy Using Biomarker Intensified Treatment in Heart Failure (GUIDE-IT)

Visit Date	Reason for Visit	Clinical Monitor/Other (Print Name)	Clinical Monitor/Other (Signature)	Site Personnel (Signature)

Please retain a copy of each completed form for your Regulatory Binder.

Duke Clinical Research Institute

GUIDE-IT Confidential Master Subject Log

ICH Guidelines require keeping a master subject identification log at the study site to serve as proof that the site's subjects are real people.

This list is confidential and should not be forwarded to the sponsor or coordinating center.

- Record on this log **all** subjects who are randomized.
- **Hospital/Identification Number:** Record a unique identifier for each subject. Appropriate number may include a medical record number, social security number, or driver's license number (including the state of issue).

Sponsor: NHLBI

Site Number: __ __ __

Principal Investigator Name:	**Site Address:**

Subject # *From InForm*	**Subject Initials**	**Subject Name**	**Date of Birth**	**Hospital/ID #**	**Date/Version of Consent**	**Date of Randomization**
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PI Signature:_____ Date: __ __ / __ __ __ / __ __ __ __

(required after all subject enrollment completed)

Duke Clinical Research Institute

GUIDE-IT Waiver Log

- Document protocol waiver requests for randomized subjects on this log.
- Make additional copies of this log as needed.
- Store logs in your Regulatory Binder.

Site #: __ __ __ PI Name: ____________________

Subject # (if randomized)	Subject Initials	Waiver Requested	Protocol Waiver Request Details	Waiver Granted?	Waiver Granted by	Site Staff Initials and Date
_ _ _ - _ _ _ _	__ __ __	❑ Inclusion/ exclusion ❑ Other		❑ No ❑ Yes	Name: ____________	Initials: __ __ __ _ _ / _ _ _ / _ _ _ _ dd mmm yyyy
_ _ _ - _ _ _ _	__ __ __	❑ Inclusion/ exclusion ❑ Other		❑ No ❑ Yes	Name: ____________	Initials: __ __ __ _ _ / _ _ _ / _ _ _ _ dd mmm yyyy
_ _ _ - _ _ _ _	__ __ __	❑ Inclusion/ exclusion ❑ Other		❑ No ❑ Yes	Name: ____________	Initials: __ __ __ _ _ / _ _ _ / _ _ _ _ dd mmm yyyy
_ _ _ - _ _ _ _	__ __ __	❑ Inclusion/ exclusion ❑ Other		❑ No ❑ Yes	Name: ____________	Initials: __ __ __ _ _ / _ _ _ / _ _ _ _ dd mmm yyyy
_ _ _ - _ _ _ _	__ __ __	❑ Inclusion/ exclusion ❑ Other		❑ No ❑ Yes	Name: ____________	Initials: __ __ __ _ _ / _ _ _ / _ _ _ _ dd mmm yyyy
_ _ _ - _ _ _ _	__ __ __	❑ Inclusion/ exclusion ❑ Other		❑ No ❑ Yes	Name: ____________	Initials: __ __ __ _ _ / _ _ _ / _ _ _ _ dd mmm yyyy

Duke Clinical Research Institute

GUIDE-IT Site Training Log

Use this log as a tool to record study-specific training performed at your site.

Site number: __ __ __ Principal investigator name: _____

Training topic/procedures discussed: _____

Documents, including versions/dates (or attach): _____

Trainer name: _____

Date	Trainee Name (Print)	Trainee Signature	Comments
_____/_____/_____			
_____/_____/_____			
_____/_____/_____			
_____/_____/_____			
_____/_____/_____			
_____/_____/_____			
_____/_____/_____			

GUIDE-IT

GUIDing Evidence Based Therapy Using Biomarker Intensified Treatment

GUIDE-IT Screening Log

Instructions: Record all patients who are considered for the GUIDE-IT study. Screening should take place during evaluation of or hospitalization/equivalent for high risk systolic heart failure.

Screen Failures: Select up to 2 inclusion and 2 exclusion primary reasons why the patient was not consented or failed screening.

Do not submit this log to DCRI unless otherwise instructed.

Site: __ __ __

					Screen Failure—Reason(s)				
Site Number	Screening Number	Screening Visit Date	Consented?	Screen Fail?	Inclusion	Inclusion	Exclusion	Exclusion	Comments
	S-01								
	S-02								
	S-03								
	S-04								
	S-05								
	S-06								
	S-07								
	S-08								
	S-09								
	S-10								
	S-11								
	S-12								
	S-13								
	S-14								
	S-15								
	S-16								
	S-17								
	S-18								
	S-19								
	S-20								
	S-21								
	S-22								

Site: __ __ __

Site Number	Screening Number	Screening Visit Date	Consented?	Screen Fail?	Screen Failure—Reason(s)				
					Inclusion	Inclusion	Exclusion	Exclusion	Comments
	S-23								
	S-24								
	S-25								
	S-26								
	S-27								
	S-28								
	S-29								
	S-30								
	S-31								
	S-32								
	S-33								
	S-34								
	S-35								
	S-36								
	S-37								
	S-38								
	S-39								
	S-40								
	S-41								
	S-42								
	S-43								
	S-44								
	S-45								
	S-46								
	S-47								
	S-48								
	S-49								
	S-50								
	S-51								

Site: __ __ __

Site Number	Screening Number	Screening Visit Date	Consented?	Screen Fail?	Screen Failure—Reason(s)				
					Inclusion	Inclusion	Exclusion	Exclusion	Comments
	S-52								
	S-53								
	S-54								
	S-55								
	S-56								
	S-57								
	S-58								
	S-59								
	S-60								
	S-61								
	S-62								
	S-63								
	S-64								
	S-65								
	S-66								
	S-67								
	S-68								
	S-69								
	S-70								
	S-71								
	S-72								
	S-73								
	S-74								
	S-75								
	S-76								
	S-77								
	S-78								
	S-79								
	S-80								

Site: __ __ __

Site Number	Screening Number	Screening Visit Date	Consented?	Screen Fail?	Screen Failure—Reason(s)				
					Inclusion	Inclusion	Exclusion	Exclusion	Comments
	S-81								
	S-82								
	S-83								
	S-84								
	S-85								
	S-86								
	S-87								
	S-88								
	S-89								
	S-90								

Inclusion

I1. Not ≥ 18 years of age
I2. LVEF not ≤ 40%
I3. No Heart failure event in prior 12 months
I4. NT-ProBNP not > 2000 or BNP not > 400
I5. Not willing to consent

Exclusion

E1. Acute ACS or revasc.
E2. CRT prior or planned
E3. Myocarditis, cardiomyopathy, pericardidits
E4. Stenotic valvular disease
E5. Planned heart transplant or VAD
E6.Chronic inotropic therapy
E7. Complex congenital heart disease
E8. End stage renal disease
E9. Terminal illness (survival < 12 months)
E10. Pregnant or planning pregnancy
E11. Unable to comply with study procedures
E12. Enrollment in another clinical trial or planned
E.13 Other

Appendix C. Eligibility Worksheets

GUIDE-IT Eligibility Worksheet

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

Demographics

Date of birth: __ __ - __ __ __ - __ __ __ __
dd mmm yyyy

Sex: ❑ Male ❑ Female

Protocol Version
Amendment 2 December 3, 2013

Inclusion Criteria

All answers must be "Yes" for the subject to qualify.

I1.	Is the subject greater than or equal to (≥) 18 years of age?	❑ No	❑ Yes
I2.	Is the subject's most recent documented **LVEF ≤ 40%**, performed by any method and within 12 months of randomization?	❑ No	❑ Yes
I3.	Does the subject have high risk heart failure as defined by the following criteria? ❑ A heart failure event in the prior 12 months defined by one of the following: ❑ HF hospitalization ❑ Treatment in the emergency dept. (or equivalent) for HF ❑ Outpatient treatment for HF with intravenous diuretics **AND** ❑ Has the subject had an NT-Pro BNP greater than (>) 2000 pg/mL or BNP greater than (>) 400 pg/mL at least once during the index hospitalization? _____ pg/mL Date: __ __ / __ __ __ / __ __ __ __	❑ No	❑ Yes
I1.	Is the subject willing to provide informed consent?	❑ No	❑ Yes

Exclusion Criteria

All answers must be "No" or "NA" for the subject to qualify.

E1.	Does the subject have a clinical diagnosis of acute coronary syndrome or had a cardiac revascularization procedure within the past 30 days?	❑ No	❑ Yes
E2.	Has the subject had cardiac resynchronization therapy (CRT) within the prior 3 months or is there a current plan to implant a CRT device?	❑ No	❑ Yes
E3.	Does the subject have active myocarditis, hypertrophic obstructive cardiomyopathy, pericarditis, or restrictive cardiomyopathy?	❑ No	❑ Yes
E4.	Does the subject have severe stenotic valvular disease?	❑ No	❑ Yes
E5.	Is there an anticipated heart transplantation or placement of a ventricular assist device within 12 months?	❑ No	❑ Yes
E6.	Is the subject on chronic inotropic therapy?	❑ No	❑ Yes
E7.	Does the subject have complex congenital heart disease?	❑ No	❑ Yes
E8.	Does the subject have end-stage renal disease with renal replacement therapy?	❑ No	❑ Yes
E9.	Does the subject have a noncardiac terminal illness with expected survival less than 12 months?	❑ No	❑ Yes
E10.	Is the subject a woman who is pregnant or planning to become pregnant?	❑ NA ❑ No	❑ Yes
E11.	Is the subject unable to comply with planned study procedures?	❑ No	❑ Yes
E12.	Is the subject enrolled in or planning to enroll in another clinical trial?	❑ No	❑ Yes

Expected date of discharge (if applicable): __ __ / __ __ __ / __ __ __ __
dd mmm yyyy

GUIDE-IT Eligibility Worksheet

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

Demographics

Date of birth: __ __ - __ __ __ - __ __ __ __
dd mmm yyyy

Sex: ❑ Male ❑ Female

Protocol Version
Amendment 2 December 3, 2013

Inclusion Criteria

All answers must be "Yes" for the subject to qualify.

I1.	Is the subject greater than or equal to (≥) 18 years of age?	❑ No	❑ Yes
I2.	Is the subject's most recent documented **LVEF ≤ 40%**, performed by any method and within 12 months of randomization?	❑ No	❑ Yes
I3.	Does the subject have high risk heart failure as defined by the following criteria? ❑ A heart failure event in the prior 12 months defined by one of the following: ❑ HF hospitalization ❑ Treatment in the emergency dept. (or equivalent) for HF ❑ Outpatient treatment for HF with intravenous diuretics **AND** ❑ Has the subject had an NT-Pro BNP greater than (>) 2000 pg/mL or BNP greater than (>) 400 pg/mL at least once during the index hospitalization? _____ pg/mL Date: __ __ / __ __ __ / __ __ __ __	❑ No	❑ Yes
I1.	Is the subject willing to provide informed consent?	❑ No	❑ Yes

Exclusion Criteria

All answers must be "No" or "NA" for the subject to qualify.

E1.	Does the subject have a clinical diagnosis of acute coronary syndrome or had a cardiac revascularization procedure within the past 30 days?	❑ No	❑ Yes
E2.	Has the subject had cardiac resynchronization therapy (CRT) within the prior 3 months or is there a current plan to implant a CRT device?	❑ No	❑ Yes
E3.	Does the subject have active myocarditis, hypertrophic obstructive cardiomyopathy, pericarditis, or restrictive cardiomyopathy?	❑ No	❑ Yes
E4.	Does the subject have severe stenotic valvular disease?	❑ No	❑ Yes
E5.	Is there an anticipated heart transplantation or placement of a ventricular assist device within 12 months?	❑ No	❑ Yes
E6.	Is the subject on chronic inotropic therapy?	❑ No	❑ Yes
E7.	Does the subject have complex congenital heart disease?	❑ No	❑ Yes
E8.	Does the subject have end-stage renal disease with renal replacement therapy?	❑ No	❑ Yes
E9.	Does the subject have a noncardiac terminal illness with expected survival less than 12 months?	❑ No	❑ Yes
E10.	Is the subject a woman who is pregnant or planning to become pregnant?	❑ NA ❑ No	❑ Yes
E11.	Is the subject unable to comply with planned study procedures?	❑ No	❑ Yes
E12.	Is the subject enrolled in or planning to enroll in another clinical trial?	❑ No	❑ Yes

Expected date of discharge (if applicable): __ __ / __ __ __ / __ __ __ __
dd mmm yyyy

Only 1 form is remaining.

Please make additional photocopies.

GUIDE-IT Eligibility Worksheet

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

Demographics

Date of birth: __ __ - __ __ __ - __ __ __ __
dd mmm yyyy

Sex: ❑ Male ❑ Female

Protocol Version
Amendment 2 December 3, 2013

Inclusion Criteria

All answers must be "Yes" for the subject to qualify.

I1.	Is the subject greater than or equal to (≥) 18 years of age?	❑ No	❑ Yes
I2.	Is the subject's most recent documented **LVEF ≤ 40%**, performed by any method and within 12 months of randomization?	❑ No	❑ Yes
I3.	Does the subject have high risk heart failure as defined by the following criteria? ❑ A heart failure event in the prior 12 months defined by one of the following: ❑ HF hospitalization ❑ Treatment in the emergency dept. (or equivalent) for HF ❑ Outpatient treatment for HF with intravenous diuretics **AND** ❑ Has the subject had an NT-Pro BNP greater than (>) 2000 pg/mL or BNP greater than (>) 400 pg/mL at least once during the index hospitalization? _____ pg/mL Date: __ __ / __ __ __ / __ __ __ __	❑ No	❑ Yes
I1.	Is the subject willing to provide informed consent?	❑ No	❑ Yes

Exclusion Criteria

All answers must be "No" or "NA" for the subject to qualify.

E1.	Does the subject have a clinical diagnosis of acute coronary syndrome or had a cardiac revascularization procedure within the past 30 days?	❑ No	❑ Yes
E2.	Has the subject had cardiac resynchronization therapy (CRT) within the prior 3 months or is there a current plan to implant a CRT device?	❑ No	❑ Yes
E3.	Does the subject have active myocarditis, hypertrophic obstructive cardiomyopathy, pericarditis, or restrictive cardiomyopathy?	❑ No	❑ Yes
E4.	Does the subject have severe stenotic valvular disease?	❑ No	❑ Yes
E5.	Is there an anticipated heart transplantation or placement of a ventricular assist device within 12 months?	❑ No	❑ Yes
E6.	Is the subject on chronic inotropic therapy?	❑ No	❑ Yes
E7.	Does the subject have complex congenital heart disease?	❑ No	❑ Yes
E8.	Does the subject have end-stage renal disease with renal replacement therapy?	❑ No	❑ Yes
E9.	Does the subject have a noncardiac terminal illness with expected survival less than 12 months?	❑ No	❑ Yes
E10.	Is the subject a woman who is pregnant or planning to become pregnant?	❑ NA ❑ No	❑ Yes
E11.	Is the subject unable to comply with planned study procedures?	❑ No	❑ Yes
E12.	Is the subject enrolled in or planning to enroll in another clinical trial?	❑ No	❑ Yes

Expected date of discharge (if applicable): __ __ / __ __ __ / __ __ __ __
dd mmm yyyy

Appendix D. 6-Minute Walk Test Worksheets

Subject #: __ __ __ - __ __ __ __

GUIDE-IT 6MWT Worksheet

Did the subject attempt the 6-minute walk?

❑ Yes ➞ Date: _____

❑ No ➞ Reason: _____

BASELINE

Start walk time: __ __:__ __

Heart rate: __ __ __ bpm

Dyspnea: __ __ (Borg scale)

Fatigue: __ __ (Borg scale)

SpO_2: __ __ __ %

End of Test

End walk time: __ __:__ __

Heart rate: __ __ __ bpm

Dyspnea: __ __ (Borg scale)

Fatigue: __ __ (Borg scale)

SpO_2: __ __ __ %

Dyspnea and Fatigue
Show the Borg scale and state: "Please grade your level of shortness of breath using this scale." Then "Please grade your level of fatigue using this scale." At the end, remind patients of the number they chose before the exercise and ask them to grade their levels of dyspnea and fatigue again.

Supplemental O_2? ❑ No ❑ Yes ➞ ___L/min

Number of laps: ___ x ___ (meters/lap) = ___ + final partial lap: ___ meters = _____ (1 foot = 0.3048 meters)

Total distance walked in 6 minutes: _____ meters

Did the patient experience any other symptoms at end of exercise?

❑ No ❑ Yes ➞ If Yes, check all that apply:

❑ Angina ❑ Dizziness ❑ Hip pain ❑ Leg pain ❑ Calf pain

Person administering 6-Minute Walk Test *(must be listed on the Site Staff Delegation and Signature Log)*:

_____ _____

Printed name *Signature*

Suggested explanation of the 6-minute walk:

"The object of this test is to walk as far as possible for 6 minutes. You will walk back and forth in this hallway. Six minutes is a long time to walk, so you will be exerting yourself. You will probably get out of breath or become exhausted. You are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall or sit in the chair while resting, but resume walking as soon as you are able.

You will be walking back and forth to the marks on the floor. You should pivot briskly at each end and continue back the other way without hesitation. Now I'm going to show you. Please watch the way I turn without hesitation."

Demonstrate by walking one lap yourself. Walk and pivot at each end briskly.

Are you ready to do that? I am going to use this counter to keep track of the number of laps you complete. I will click it each time you turn around at this starting line. Remember that the object is to walk AS FAR AS POSSIBLE for 6 minutes, but don't run or jog. Start now or whenever you are ready.

1 minute: *You are doing well. You have 5 minutes to go.*

2 minutes: *Keep up the good work. You have 4 minutes to go.*

3 minutes: *You are doing well. You are halfway done.*

4 minutes: *Keep up the good work. You have only 2 minutes left.*

5 minutes: *You are doing well. You have only 1 minute to go.*

If the subject stops:
You can lean against the wall or sit if you would like; then continue walking whenever you feel able.

15 seconds remaining: *In a moment I'm going to tell you to stop. When I do, just stop right where you are and I will come to you.*

6 minutes: *Stop.*

Borg Scale

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight (light
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	
10	Very, very severe (maximal)

Subject #: __ __ __ - __ __ __ __

GUIDE-IT 6MWT Worksheet

Did the subject attempt the 6-minute walk?

❑ Yes ➞ Date: _____

❑ No ➞ Reason: _____

BASELINE

Start walk time: __ __:__ __

Heart rate: __ __ __ bpm

Dyspnea: __ __ (Borg scale)

Fatigue: __ __ (Borg scale)

SpO_2: __ __ __ %

End of Test

End walk time: __ __:__ __

Heart rate: __ __ __ bpm

Dyspnea: __ __ (Borg scale)

Fatigue: __ __ (Borg scale)

SpO_2: __ __ __ %

Dyspnea and Fatigue
Show the Borg scale and state: "Please grade your level of shortness of breath using this scale." Then "Please grade your level of fatigue using this scale." At the end, remind patients of the number they chose before the exercise and ask them to grade their levels of dyspnea and fatigue again.

Supplemental O_2? ❑ No ❑ Yes ➞ ___L/min

Number of laps: ___ x ___ (meters/lap) = ___ + final partial lap: ___ meters = _____ (1 foot = 0.3048 meters)

Total distance walked in 6 minutes: _____ meters

Did the patient experience any other symptoms at end of exercise?

❑ No ❑ Yes ➞ If Yes, check all that apply:

❑ Angina ❑ Dizziness ❑ Hip pain ❑ Leg pain ❑ Calf pain

Person administering 6-Minute Walk Test *(must be listed on the Site Staff Delegation and Signature Log)*:

_____ _____

Printed name *Signature*

Suggested explanation of the 6-minute walk:

"The object of this test is to walk as far as possible for 6 minutes. You will walk back and forth in this hallway. Six minutes is a long time to walk, so you will be exerting yourself. You will probably get out of breath or become exhausted. You are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall or sit in the chair while resting, but resume walking as soon as you are able.

You will be walking back and forth to the marks on the floor. You should pivot briskly at each end and continue back the other way without hesitation. Now I'm going to show you. Please watch the way I turn without hesitation."

Demonstrate by walking one lap yourself. Walk and pivot at each end briskly.

Are you ready to do that? I am going to use this counter to keep track of the number of laps you complete. I will click it each time you turn around at this starting line. Remember that the object is to walk AS FAR AS POSSIBLE for 6 minutes, but don't run or jog. Start now or whenever you are ready.

1 minute: *You are doing well. You have 5 minutes to go.*

2 minutes: *Keep up the good work. You have 4 minutes to go.*

3 minutes: *You are doing well. You are halfway done.*

4 minutes: *Keep up the good work. You have only 2 minutes left.*

5 minutes: *You are doing well. You have only 1 minute to go.*

If the subject stops:
You can lean against the wall or sit if you would like; then continue walking whenever you feel able.

15 seconds remaining: *In a moment I'm going to tell you to stop. When I do, just stop right where you are and I will come to you.*

6 minutes: *Stop.*

Borg Scale

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight (light
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	
10	Very, very severe (maximal)

Only 1 form is remaining.

Please make additional photocopies.

Subject #: __ __ __ - __ __ __ __

GUIDE-IT 6MWT Worksheet

Did the subject attempt the 6-minute walk?

❑ Yes ➞ Date: _____

❑ No ➞ Reason: _____

BASELINE

Start walk time: __ __:__ __

Heart rate: __ __ __ bpm

Dyspnea: __ __ (Borg scale)

Fatigue: __ __ (Borg scale)

SpO_2: __ __ __ %

End of Test

End walk time: __ __:__ __

Heart rate: __ __ __ bpm

Dyspnea: __ __ (Borg scale)

Fatigue: __ __ (Borg scale)

SpO_2: __ __ __ %

Dyspnea and Fatigue
Show the Borg scale and state: "Please grade your level of shortness of breath using this scale." Then "Please grade your level of fatigue using this scale." At the end, remind patients of the number they chose before the exercise and ask them to grade their levels of dyspnea and fatigue again.

Supplemental O_2? ❑ No ❑ Yes ➞ ___L/min

Number of laps: ___ x ___ (meters/lap) = ___ + final partial lap: ___ meters = _____ (1 foot = 0.3048 meters)

Total distance walked in 6 minutes: _____ meters

Did the patient experience any other symptoms at end of exercise?

❑ No ❑ Yes ➞ If Yes, check all that apply:

❑ Angina ❑ Dizziness ❑ Hip pain ❑ Leg pain ❑ Calf pain

Person administering 6-Minute Walk Test *(must be listed on the Site Staff Delegation and Signature Log)*:

_____ _____

Printed name *Signature*

Suggested explanation of the 6-minute walk:

"The object of this test is to walk as far as possible for 6 minutes. You will walk back and forth in this hallway. Six minutes is a long time to walk, so you will be exerting yourself. You will probably get out of breath or become exhausted. You are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall or sit in the chair while resting, but resume walking as soon as you are able.

You will be walking back and forth to the marks on the floor. You should pivot briskly at each end and continue back the other way without hesitation. Now I'm going to show you. Please watch the way I turn without hesitation."

Demonstrate by walking one lap yourself. Walk and pivot at each end briskly.

Are you ready to do that? I am going to use this counter to keep track of the number of laps you complete. I will click it each time you turn around at this starting line. Remember that the object is to walk AS FAR AS POSSIBLE for 6 minutes, but don't run or jog. Start now or whenever you are ready.

1 minute: *You are doing well. You have 5 minutes to go.*

2 minutes: *Keep up the good work. You have 4 minutes to go.*

3 minutes: *You are doing well. You are halfway done.*

4 minutes: *Keep up the good work. You have only 2 minutes left.*

5 minutes: *You are doing well. You have only 1 minute to go.*

If the subject stops:
You can lean against the wall or sit if you would like; then continue walking whenever you feel able.

15 seconds remaining: *In a moment I'm going to tell you to stop. When I do, just stop right where you are and I will come to you.*

6 minutes: *Stop.*

Borg Scale

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight (light
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	
10	Very, very severe (maximal)

Appendix E. Patient Contact Information Form

EQOL Baseline Questionnaire

Medical Release Form

Download current forms from the GUIDE-IT website. These forms are for reference only.

GUIDE IT Site#: __ __ __ Patient ID: __ __ __ __ Patient Initials: __ __ __

Patient Contact Information Form

Thank you very much for your participation in this important study. We will be following up with you in the future and would like to make sure that we reach you by your preferred method of contact, at the most convenient time for your schedule. We would like you to provide your most current contact information, as well as contact information for an alternative person to contact if we are unable to reach you.

***Preferred Method of Contact to schedule interview: ❑ Phone ❑ Email* (all interviews by phone)**

PATIENT NAME: (Last Name, First Name)_____

STREET: _____

CITY: _____ STATE: _____ ZIP: _____

HOME TELEPHONE #: (____) -_____Best time to call: _____ ❑ AM ❑ PM

WORK TELEPHONE #: (____) -_____ EXT_____ *May we call you at work?* ❑ Yes ❑ No

CELL/MOBILE TELEPHONE# (____) -_____ Best time to call: ___❑ AM ❑ PM *Can we text?* ❑ Yes ❑ No

EMAIL ADDRESS: _____ Preferred Language: English__ Spanish____ Other_____

SPECIAL COMMUNICATION INSTRUCTIONS: (example: hard of hearing)_____

SPOUSE/SIGNFICANT OTHER: (Last Name, First Name)_____

HOME TELEPHONE #: (____) -_____Best time to call: _____ ❑ AM ❑ PM

CELL/MOBILE TELEPHONE# (____) -_____Best time to call: ___❑ AM ❑ PM *Can we text?* ❑ Yes ❑ No

EMAIL ADDRESS: _____

If applicable, address of your secondary residence:

STREET_____

CITY: _____ STATE: _____ ZIP: _____

Please provide the name of a friend or relative <u>who does not live with you</u> who would know your whereabouts if we were unable to contact you.

NAME: (Last Name, First Name)_____

RELATIONSHIP:_____

STREET: _____

CITY: _____ STATE: _____ ZIP: _____

HOME TELEPHONE #: (____) -_____Best time to call: _____ ❑ AM ❑ PM

WORK TELEPHONE #: (____) -_____ EXT_____ *May we call/contact at work?* ❑ Yes ❑ No

MOBILE TELEPHONE# (____) -_____ Best time to call: ___❑ AM ❑ PM *Can we text*? ❑ Yes ❑ No

EMAIL ADDRESS: _____

Please provide the name of a friend or relative <u>who does not live with you</u> who would know your whereabouts if we were unable to contact you.

NAME: (Last Name, First Name)_____

RELATIONSHIP:_____

STREET: _____

CITY: _____ STATE: _____ ZIP: _____

HOME TELEPHONE #: (____) -_____Best time to call: _____ ❑ AM ❑ PM

WORK TELEPHONE #: (____) -_____ EXT_____ *May we call/contact at work?* ❑ Yes ❑ No

MOBILE TELEPHONE# (____) -_____Best time to call: ___❑ AM ❑ PM *Can we text*? ❑ Yes ❑ No

EMAIL ADDRESS: _____

Referring health care provider and/or clinic:

HEALTH CARE PROVIDER: (Last Name, First Name) _____ ❑ MD ❑ DO ❑ NP ❑ PA

OFFICE NAME:_____

STREET: _____

CITY: _____ STATE: _____ ZIP: _____

OFFICE TELEPHONE #: (____) -_____ FAX # (___) _____

Site Number: __ __ __ Patient Number: __ __ __ __ Patient's Initials: __-__-__

Guide-IT Summary Form

Check (√) One Interval: ❑ Baseline

FINAL QUESTIONNAIRE STATUS:

❑1 Complete
❑2 Incomplete (Specify the reason)➔ ➔ ➔
❑3 Not Done (Specify the reason)➔ ➔ ➔

REASON FOR INCOMPLETE OR NOT DONE:

❑1 Patient died Date of death: __ / ___ / ____
DD MMM YYYY
❑2 Patient too ill
❑3 Patient refused
❑4 Other: Specify: _____
❑5 Unable to locate ➔ Complete Follow-Up Status below

FOLLOW-UP STATUS IF UNABLE TO LOCATE:

❑1 Alive : Date Last Contact Alive: __ / __ / ____
DD MMM YYYY
❑2 Unknown: Date Last Contact Alive: __ / __ /____
DD MMM YYYY

WHO ANSWERED THE QUESTIONS?

❑1 Patient
❑2 Proxy / Patient Representative

WHERE DID THE PATIENT RESIDE / LIVE AT THE TIME THIS SUMMARY AND QUESTIONNAIRE WERE COMPLETED?

❑1 Community / Home
❑2 Acute Care (in-patient hospital)
❑3 Skilled Nursing Home / End-of-Life Care Institution
❑4 Rehabilitation Institution

INTERVIEWER INITIALS:____ ____ ____

COMMENTS:_____
_____
_____
_____
_____
_____
_____

Fax Summary and Questionnaire to (919) 668-9816 or upload to ftp.dcri.duke.edu

Site Number: __ __ __ Patient Number: __ __ __ __ Patient's Initials: __-__-__

Guide-IT –Baseline EQOL Questionnaire

The following questions are about your overall health and recent activities. Please check your choice for each question. The numbers beside each answer are there simply to help us record the information. Do not worry about them. Answer each question as best you can. This information is confidential and will not be released to anyone without your permission.

TODAY'S DATE: __ __ /__ __ __ /__ __ __ __ *[Example: 01/Nov/2002]*
d d m m m y y y y

The following questions refer to your heart failure and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

Heart Failure affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

Activity . . .	Extremely Limited	Quite a bit Limited	Moderately Limited	Slightly Limited	Not at all Limited	Limited for other reasons or did not do activity
1.Dressing yourself	❑1	❑2	❑3	❑4	❑5	❑6
2.Showering/ Bathing	❑1	❑2	❑3	❑4	❑5	❑6
3.Walking 1 block on level ground	❑1	❑2	❑3	❑4	❑5	❑6
4.Doing yard work, housework, or carrying groceries	❑1	❑2	❑3	❑4	❑5	❑6
5.Climbing a flight of stairs without stopping	❑1	❑2	❑3	❑4	❑5	❑6
6.Hurrying or jogging (as if to catch a bus)	❑1	❑2	❑3	❑4	❑5	❑6

7. Compared with 2 weeks ago, have your symptoms of **heart failure** (shortness of breath, fatigue or ankle swelling) changed?

My symptoms of **heart failure** have become…

- ❑1 Much worse
- ❑2 Slightly worse
- ❑3 Not changed
- ❑4 Slightly better
- ❑5 Much better
- ❑6 I've had no symptoms over the last 2 weeks

8. Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

- ❑1 Every morning
- ❑2 3 or more times a week, but not every day
- ❑3 1-2 times a week
- ❑4 Less than once a week
- ❑5 Never over the past 2 weeks

9. Over the past 2 weeks, how much has swelling in your feet, ankles or legs bothered you?

It has been…

- ❑1 **Extremely** bothersome
- ❑2 **Quite a bit** bothersome
- ❑3 **Moderately** bothersome
- ❑4 **Slightly** bothersome
- ❑5 **Not at all** bothersome
- ❑6 I've had **no swelling**

10. Over the <u>past 2 weeks</u>, on average, how many times has **fatigue** limited your ability to do what you want?
    - ❑1 All of the time
    - ❑2 Several times per day
    - ❑3 At least once a day
    - ❑4 3 or more times per week but not every day
    - ❑5 1-2 times per week
    - ❑6 Less than one a week
    - ❑7 Never over the past 2 weeks
11. Over the <u>past 2 weeks</u>, how much has your **fatigue** bothered you?
    It has been…
    - ❑1 **Extremely** bothersome
    - ❑2 **Quite a bit** bothersome
    - ❑3 **Moderately** bothersome
    - ❑4 **Slightly** bothersome
    - ❑5 **Not at all** bothersome
    - ❑6 I've had **no fatigue**
12. Over the <u>past 2 weeks</u>, on average, how many times has **shortness of breath** limited your ability to do what you wanted?
    - ❑1 All of the time
    - ❑2 Several times per day
    - ❑3 At least once a day
    - ❑4 3 or more times per week but not every day
    - ❑5 1-2 times per week
    - ❑6 Less than one a week
    - ❑7 Never over the past 2 weeks
13. Over the <u>past 2 weeks</u>, how much has your **shortness of breath** bothered you?
    It has been…
    - ❑1 **Extremely** bothersome
    - ❑2 **Quite a bit** bothersome
    - ❑3 **Moderately** bothersome
    - ❑4 **Slightly** bothersome
    - ❑5 **Not at all** bothersome
    - ❑6 I've had **no shortness of breath**
14. Over the <u>past 2 weeks</u>, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?
    - ❑1 Every night
    - ❑2 3 or more times a week, but not every day
    - ❑3 1-2 times a week
    - ❑4 Less than once a week
    - ❑5 Never the past 2 weeks
15. **Heart failure** symptoms can worsen for a number of reasons. How sure are you that you know what to do, or whom to call, if your **heart failure** gets worse?
    - ❑1 **Not at all** sure
    - ❑2 **Not very** sure
    - ❑3 **Somewhat** sure
    - ❑4 **Mostly** sure
    - ❑5 **Completely** sure

16. How well do you understand what things you are able to do to keep your **heart failure** symptoms from getting worse? (for example, weighing yourself, eating a low salt diet, etc.)
    - ❑1 Do not understand at all
    - ❑2 Do not understand very well
    - ❑3 Somewhat understand
    - ❑4 Mostly understand
    - ❑5 Completely understand

17. Over the <u>past 2 weeks</u>, how much has your **heart failure** limited your enjoyment of life?
    - ❑1 It has **extremely** limited my enjoyment of life
    - ❑2 It has limited my enjoyment of life **quite a bit**
    - ❑3 It has **moderately** limited my enjoyment of life
    - ❑4 It has **slightly** limited my enjoyment of life
    - ❑5 It has **not limited** my enjoyment of life at all

18. If you had to spend the rest of your life with your **heart failure** the way it is <u>right now</u>, how would you feel about this?
    - ❑1 Not at all satisfied
    - ❑2 Mostly dissatisfied
    - ❑3 Somewhat satisfied
    - ❑4 Mostly satisfied
    - ❑5 Completely satisfied

19. Over the <u>last 2 weeks</u>, how often have you felt discouraged or down in the dumps because of your **heart failure**?
    - ❑1 I felt that way **all of the time**
    - ❑2 I felt that way **most of the time**
    - ❑3 I **occasionally** felt that way
    - ❑4 I **rarely** felt that way
    - ❑5 I **never** felt that way

How much does your **heart failure** affect your lifestyle? Please indicate how your **heart failure** may have limited your participation in the following activities <u>over the past 2 weeks</u>.

Activity	**Severely** Limited	Limited **quite a bit**	**Moderately** Limited	**Slightly** Limited	**Did not** limit at all	Does not apply or did not do for other reasons
20. Hobbies, recreational activities	❑1	❑2	❑3	❑4	❑5	❑6
21. Working or doing household chores	❑1	❑2	❑3	❑4	❑5	❑6
22. Visiting family or friends out of your home	❑1	❑2	❑3	❑4	❑5	❑6
23. Intimate relationships with loved ones	❑1	❑2	❑3	❑4	❑5	❑6

These questions are about any physical limitations you might have had in the past month. For each question, please rate whether you are physically able to do one or more of the activities without difficulty, with some difficulty OR you couldn't do it, or you don't do it for other reasons (NA).

Could you. . .	Yes, with no difficulty	Yes, with some difficulty or I couldn't do this	Don't do this for other reasons
24. take care of yourself, that is, eating, dressing, bathing, and using the toilet?	❑1	❑2	❑3
25. walk indoors, such as around your house?	❑1	❑2	❑3
26. walk a block or two on level ground?	❑1	❑2	❑3

For some of the rest of these activity questions, there will be more than one activity mentioned like climb a flight of stairs or walk up a hill. Answer each question according to the one activity you can do best.

Could you. . .	Yes, with no difficulty	Yes, with some difficulty or I couldn't do this	Don't do this for other reasons
27. climb a flight of stairs or walk up a hill?	❑1	❑2	❑3
28. run a short distance?	❑1	❑2	❑3
29. do light work around the house like dusting or washing dishes?	❑1	❑2	❑3
30. do moderate work around your house like vacuuming, sweeping floors, or carrying in groceries?	❑1	❑2	❑3
31. do heavy work around the house like scrubbing floors or lifting or moving heavy furniture?	❑1	❑2	❑3
32. do yard work like raking leaves, weeding, or pushing a power mower?	❑1	❑2	❑3
33. have sexual relations?	❑1	❑2	❑3
34. participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?	❑1	❑2	❑3
35. participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?	❑1	❑2	❑3

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you have felt this way during the **past week**: *(circle **one** number on each line)*

During the past week…	Rarely or none of the time (< 1 day)	Some or a little of the time (1–2 days)	Occasionally or a moderate amount of the time (3–4 days)	All of the time (5–7 days)
36. I was bothered by things that usually don't bother me	❑1	❑2	❑3	❑4
37. I had trouble keeping my mind going	❑1	❑2	❑3	❑4
38. I felt depressed	❑1	❑2	❑3	❑4
39. I felt that everything I did was an effort	❑1	❑2	❑3	❑4
40. I felt hopeful about the future	❑1	❑2	❑3	❑4
41. I felt fearful	❑1	❑2	❑3	❑4
42. My sleep was restless	❑1	❑2	❑3	❑4
43. I was happy	❑1	❑2	❑3	❑4
44. I felt lonely	❑1	❑2	❑3	❑4
45. I could not "get going"	❑1	❑2	❑3	❑4

These first questions are about your health now and your current daily activities. Please try to answer every question as accurately as you can.

46. **In general, would you say your health is:**
- ❑1 Excellent
- ❑2 Very good
- ❑3 Good
- ❑4 Fair
- ❑5 Poor

Now I'm going to read a list of activities that you might do during a typical day. As I read each item, please tell me if your health now limits you a lot, limits you a little, or at all in these activities.

47. . . . moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf. Does your health now limit you a lot, limit you a little, or not limit you at all?
- ❑1 Yes, limited a lot
- ❑2 Yes, limited a little
- ❑3 No, not limited at all

48. . . . climbing several flights of stairs. Does your health now limit you a lot, limit you a little, or not limit you at all?
- ❑1 Yes, limited a lot
- ❑2 Yes, limited a little
- ❑3 No, not limited at all

The following two questions ask about your physical health and your daily activities.

49. During the past four weeks, how much of the time have you accomplished less than you would like as a result of your physical health?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

50. During the past four weeks, how much of the time were you limited in the kind of work or other regular daily activities you do as a result of your physical health?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

The following two questions ask about your emotions and your daily activities.

51. During the past four weeks, how much of the time have you accomplished less than you would like as a result of any emotional problems, such as feeling depressed or anxious?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

52. During the past four weeks, how much of the time did you do work or other regular daily activities less carefully than usual as a result of any emotional problems, such as feeling depressed or anxious?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

53. During the past four weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?
    - ❑1 Not at all
    - ❑2 A little bit
    - ❑3 Moderately
    - ❑4 Quite a bit
    - ❑5 Extremely

The next questions are about how you feel and how things have been with you during the past four weeks.

As I read each statement, please give me the one answer that comes closest to the way you have been feeling; is it all of the time, most of the time, some of the time, a little of the time, or none of the time?

54. How much of the time during the past four weeks . . . did you feel full of life?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

55. How much of the time during the past four weeks . . . have you been very nervous?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time
56. How much of the time during the past four weeks . . . have you felt so down in the dumps that nothing could cheer you up?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time
57. How much of the time during the past four weeks . . . have you felt calm and peaceful?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time
58. How much of the time during the past four weeks . . . did you have a lot of energy?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time
59. How much of the time during the past four weeks . . . have you felt downhearted and depressed?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time
60. How much of the time during the past four weeks . . . did you feel worn out?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time
61. How much of the time during the past four weeks . . . have you been happy?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time
62. How much of the time during the past four weeks . . . did you feel tired?
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

These next questions are about your health and health-related matters.

Now, I'm going to read a list of statements. After each one, please tell me if it is definitely true, mostly true, mostly false, or definitely false. If you don't know, just tell me.

63. During the past four weeks, how much of the time has your physical health or emotional problems interfered with your social activities like visiting with friends or relatives? Has it interfered . . .
    - ❑1 All of the time
    - ❑2 Most of the time
    - ❑3 Some of the time
    - ❑4 A little of the time
    - ❑5 None of the time

64. I seem to get sick a little easier than other people. Would you say that's . . .
    - ❑1 Definitely true
    - ❑2 Mostly true
    - ❑3 Don't know
    - ❑4 Mostly false
    - ❑5 Definitely false

65. I am as healthy as anyone I know. Would you say that's . . .
    - ❑1 Definitely true
    - ❑2 Mostly true
    - ❑3 Don't know
    - ❑4 Mostly false
    - ❑5 Definitely false

66. I expect my health to get worse. Would you say that's . . .
    - ❑1 Definitely true
    - ❑2 Mostly true
    - ❑3 Don't know
    - ❑4 Mostly false
    - ❑5 Definitely false

67. My health is excellent. Would you say that's . . .
    - ❑1 Definitely true
    - ❑2 Mostly true
    - ❑3 Don't know
    - ❑4 Mostly false
    - ❑5 Definitely false

Please answer the following questions by indicating which statement best describes your own health state today.

68. **Mobility**
- ❑1 I have no problems in walking about
- ❑2 I have some problems in walking about
- ❑3 I am confined to bed

69. **Self-care**
- ❑1 I have no problems with self-care
- ❑2 I have some problems washing or dressing myself
- ❑3 I am unable to wash or dress myself

70. **Usual activities** (i.e. work, study, housework, family or leisure activities):
- ❑1 I have no problems with performing my usual activities
- ❑2 I have some problems with performing my usual activities
- ❑3 I am unable to perform my usual activities

71. **Pain/Discomfort**
- ❑1 I have no pain or discomfort
- ❑2 I have moderate pain or discomfort
- ❑3 I have extreme pain or discomfort

72. **Anxiety/Depression**
- ❑1 I am not anxious or depressed
- ❑2 I am moderately anxious or depressed
- ❑3 I am extremely anxious or depressed

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst state you can imagine is marked by 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your current health state is.

Best imaginable health state

Your own health state today

Worst imaginable health state

73. **Response** :___ ___ ___

The next questions are about your work and daily activities.

74. Which one of the following best describes your current working status?
    - ❑1 Working full-time
    - ❑2 Working part-time
    - ❑3 On short-term sick leave
    - ❑4 On long-term sick leave (at least three months)
    - ❑5 Temporarily laid off
    - ❑6 Homemaker ➔ ➔ ➔ ➔ ➔ ➔➔➔➔➔➔
    - ❑7 Disabled ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔
    - ❑8 Unemployed or looking for work➔ ➔ ➔ ➔ ➔
    - ❑9 Retired ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔ ➔
    - ❑10 Other *Please specify:* _____

Did you ever work for pay?

❑1 Yes ➔ **When did you stop?**

_ _ / _ _ _ / _ _ _ _
d d m m m y y y y

❑2 No ➔ **SKIP to Question 80**

Is this date within the past 6 months?

❑1 Yes

❑2 No ➔ **SKIP to Question 80**

75. Are you planning to return to work?
    - ❑1 Yes
    - ❑2 No
    - ❑3 Don't know

76. What kind of work did you do for pay in the past six months? Main Job:_____

77. What were the most important activities or duties of your main job? Examples: Drive truck, operate tool and dye machine, supervise road crew._____

78. Which best describes how you are (or were) paid?
    - ❑1 Hourly wages
    - ❑2 Annual/Monthly salary
    - ❑3 Work on commission or tips
    - ❑4 Self-employed and/or own business, professional practice or farm
    - ❑5 Work in family business or farm

79. During the time you worked, how many hours per week did you usually work at your job? # _____

The next set of questions are about you and your household

80. What is the highest grade (# of years) you completed in school? *(Circle one.)*

0							
1	2	3	4	5	6	7	8
9	10	11	12	Equivalency Certificate			
13	14	15	16				
17	18	19	20	21+			

81. Are you presently:
- ❑$_1$ Married or living as married
- ❑$_2$ Divorced
- ❑$_3$ Separated
- ❑$_4$ Widowed
- ❑$_5$ Never Married

Finally, we would like to ask your total household income level. It will not affect your medical care in any way; it's strictly for demographic purposes for this study.

82. Roughly how much income from all sources (including earnings, pensions, investments, etc.) did your household have last year (before taxes)?
- ❑$_1$ $10,000 or less
- ❑$_2$ $10,001 to $20,000
- ❑$_3$ $20,001 to $30, 000
- ❑$_4$ $30,001 to $45,000
- ❑$_5$ $45,001 to $60,000
- ❑$_6$ $60,001 to $105,000
- ❑$_7$ $105,001 to $120,000
- ❑$_8$ $120,001 or greater
- ❑$_9$ Refused

August 29, 2012

GUIDE-IT	Site #:_ _ _ Patient ID: _ _ _ _ Patient Name:_____ Date of Birth:_____ Social Security Number: _____

If mailing this form please send to:

GUIDE IT Coordinating Center
Duke Clinical Research Institute
2400 Pratt Street, P.O. Box 17969
Durham, N.C. 27705

I authorize and request that _____
<insert facility name>
release the following protected health information from my medical record to the GUIDE IT Coordinating Center at Duke Clinical Research Institute, Durham, North Carolina. Information is requested for the following dates of service:
_____

INFORMATION TO BE DISCLOSED (check the appropriate boxes and include other information where indicated):

- ☐ Hospital Bill
- ☐ Discharge Summary
- ☐ Emergency Department Reports
- ☐ Procedure Reports (Cardiac catheterization, Percutaneous coronary intervention (Angioplasty, Stent, PTCA))
- ☐ Operative Report (e.g., coronary artery bypass grafting (CABG))
- ☐ Laboratory Reports
- ☐ Radiology Reports
- ☐ Autopsy Report
- ☐ Patient Discharge Instructions
- ☐ Other: _____

THE INFORMATION TO BE DISCLOSED WILL BE USED FOR THE FOLLOWING PURPOSE:
The patient has consented to participate in the GUIDE IT Study. The Guide IT study will gather data to see if using the results of a blood test for NT-proBNP (a hormone released from the heart also known as a Biomarker) can help doctors decide the best drug treatment for patients with heart failure (HF). By signing this form, I authorize the staff/representatives of the GUIDE IT Study at the Duke Clinical Research Institute (DCRI) to use the above information [Patient's Name, Date of Birth, Medical Record Number, and Social Security number] to collect my **Hospital Bills** and **Medical Records** for any hospitalizations which occur during the time I am enrolled and followed in the GUIDE IT study. In doing so, I authorize the Patient Accounting/Medical Records Department at any hospital where I may receive care during this time period to disclose these hospital bills and medical records to the GUIDE IT study group. This process may take up to 3 years following my enrollment in the study. I understand that this information collected by GUIDE IT study will be kept strictly confidential and be used solely to assess my medical care and the medical expenses that occur during the course of the GUIDE IT Study. The information will not be re-disclosed to any party outside of the GUIDE IT study team. Additionally, I understand that I have the right to: 1) refuse to sign this authorization, 2) withdraw this authorization at any time by giving written notice to the address listed at the bottom of this form, with the knowledge that this action will not affect any information collected before the notice withdrawal and 3) receive a copy of this authorization.

This medical record/hospital billing information may be collected from_____ (study enrollment date) to _____ (2 years from date of enrollment).

Signature: Patient name printed

_____ _____

Date Signed: ____/____/_____ (mm/dd/yyyy)

Witnessed by:

Research Coordinator: _____ Date Signed: ____/____/_____ (mm/dd/yyyy)
(Signature)

_____ at _____
(Please Print Name) (Please print enrolling hospital name)

Appendix F. Data Collection Checklists

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

Screening Visit Checklist

Date of screening: _____

❑ Hospital chart/medical records reviewed for eligibility (begin Subject Eligibility Worksheet)

❑ Written informed consent obtained

- ❑ Copy of the signed consent form provided to the subject
- ❑ Consent documented in subject's medical record
  Date: _____ Time: __ __ : __ __

❑ Demographics (including race and ethnicity) verified

Ethnicity
❑ Hispanic or Latino
❑ Not Hispanic or Latino
❑ Unknown

Race ➡ check all that apply:
❑ American Indian or Alaskan Native
❑ Asian
❑ Black or African American
❑ Native Hawaiian or other Pacific Islander
❑ White
❑ Other: _____
❑ Unknown

❑ Subject contact information collected (subject to confirm)

❑ History and physical performed, including vital signs (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites,SPO2)

❑ Local laboratory test results obtained

- ❑ NT-proBNP or BNP
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)

❑ Concomitant medications reviewed and recorded in medical record

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

Day 0 Baseline/Randomization Visit Checklist

Date of visit: _____

- ❑ Eligibility confirmed (review and complete Subject Eligibility Worksheet)
- ❑ Randomization performed using SIRE via InForm
- ❑ Subject contact information reviewed (subject to confirm) and uploaded to ftp.dcri.duke.edu or faxed to 1-919-668-9816
- ❑ Quality of Life assessments administered
  - ❑ Questionnaires uploaded to ftp.dcri.duke.edu or faxed to 1-919-668-9816
  - ❑ Patient Contact Form
  - ❑ Medical Release Form
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained
- ❑ 6MWT performed
- ❑ Local laboratory tests obtained
  - ❑ NT-proBNP or BNP
  - ❑ serum creatinine
  - ❑ BUN
  - ❑ Electrolytes (chemistry panel)
  - ❑ Total cholesterol, uric acid (if performed as part of standard of care)
  - ❑ Hematology (if performed as part of standard of care)
- ❑ Medical History
- ❑ Concomitant medications reviewed and recorded in medical record
- ❑ Follow-up visit for 2 weeks ± 1 week after randomization scheduled
- ❑ GUIDE-IT handout with schedule of follow-up visits and study personnel contact information given to subject

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

Biorepository/DNA Samples

Biorepository samples consent?

- ❑ No
- ❑ Yes ➡

Samples collected?

- ❑ No
- ❑ Yes

Consent withdrawn?

- ❑ No
- ❑ Yes ➡ Date: _____

DNA consent?

- ❑ No
- ❑ Yes ➡

Samples collected?

- ❑ No
- ❑ Yes

Consent withdrawn?

- ❑ No
- ❑ Yes ➡ Date: _____

Date/time collected: _____ __ __ : __ __

Was the subject fasting:

- ❑ **Yes**
- ❑ **No**
- ❑ **Last time subject had anything to eat/ drink containing calories: __ __: __ __**

Date/time processing initiated: _____ __ __ : __ __

Date/time frozen: _____ __ __ : __ __

Date sent to lab: _____

Core Lab and Biorepository/DNA Sample Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

ECHO Substudy (if applicable)

ECHO Substudy consent?

- ❑ No
- ❑ Yes ➡ Send in the signed ECHO ICF to DCRI

Resting transthoracic 2-D and Doppler echocardiogram completed?

- ❑ No
- ❑ Yes

Was the image transmitted/transferred to central reader?

- ❑ No
- ❑ Yes

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

2-week Follow-up Visit Checklist

Date of visit: _____

2 weeks (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

    Date/time collected: _____ __ __ : __ __

    Date/time processing initiated: _____ __ __ : __ __

    Was the subject fasting?

    - ❑ Yes
    - ❑ No
    - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

    Date/time frozen: _____ __ __ : __ __

    Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 6-week follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

_____

_____

_____

_____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

6-week Follow-up Visit Checklist

Date of visit: _____

6 weeks (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 3-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

3 Month Follow-up Visit Checklist

Date of visit: _____

3 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 6-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

6 Month Follow-up Visit Checklist

Date of visit: _____

6 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 9-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

9 Month Follow-up Visit Checklist

Date of visit: _____

9 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 12-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

12 Month Follow-up Visit Checklist

Date of visit: _____

12 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 15-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

ECHO Substudy (if applicable)

ECHO Substudy consent withdrawn?

- ❑ No
- ❑ Yes➡ Date: _____

Resting transthoracic 2-D and Doppler echocardiogram completed (12 month follow up)?

- ❑ No **(explain in 'Notes' section below)**
- ❑ Yes

Was the image transmitted/transferred to central reader?

- ❑ No
- ❑ Yes

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

15 Month Follow-up Visit Checklist

Date of visit: _____

15 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 18-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

18 Month Follow-up Visit Checklist

Date of visit: _____

18 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 21-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

_____

_____

_____

_____

_____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

21 Month Follow-up Visit Checklist

Date of visit: _____

21 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

Study Coordinator: _____

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 24-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

_____

_____

_____

_____

_____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

24 Month/End of Study Visit Checklist

Date of visit: _____

24 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No

❑ Yes →

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

GUIDE-IT

Therapy Adjustment

Date of visit: _____

Associated with visit: ❑ BL ❑ 2 Week ❑ 6 Week ❑ 3 Month ❑ 6 Month ❑ 9 Month
❑ 12 Month ❑ 15 Month ❑ 18 Month ❑ 21 Month ❑ 24 Month

Reason(s) for adjustment of therapy:

- ❑ Decompensated HF
- ❑ Clinical indication without decompensated HF
- ❑ Decrease in NT-ProBNP
- ❑ Increase in NT-ProBNP
- ❑ Other investigator decision: _____
- ❑ Side effects or intolerance
- ❑ Other _____

Medication Adjustments

❑ **ACE inhibitor:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **ARB:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Beta-blocker:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

Medication Adjustments *(continued)*

❑ **Digoxin:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Hydralazine-nitrates:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Loop Diuretic:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Mineralocorticoid receptor antagonist** (aldosterone antagonist)**:**

❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Oral thiazide diuretic:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

Other Therapy Adjustments

❑ **Cardioversion or Rate control**

Date performed: _____

Procedure type: _____

Reason for adjustment: _____

❑ **Cardiac resynchronization therapy:** ❑ New ❑ Optimization

Date performed: _____

Procedure type: _____

Reason performed: _____

❑ **Exercise training or cardiac rehab**

Date of first training/rehab: _____

Reason for recommendation: _____

❑ **Additional HF education**

Date: _____

Topics: _____

Performed by: _____

Reason for additional education: _____

❑ **Hospitalization**

Date of admission: _____

Reason for admission: _____

Hospital name: _____

Other adjustment type:

Date: _____

Adjustment details: _____

_____

_____

Date	Notes

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

Unscheduled 2-Week Follow-up Visit Checklist

Date of visit: _____ **(Note:** Visit may be in person or a remote laboratory evaluation at the discretion of the treating physician)

2 weeks (± 1 week) after hospitalization or change in therapy

Associated with visit: ❑ BL ❑ 2 Week ❑ 6 Week ❑ 3 Month ❑ 6 Month ❑ 9 Month ❑ 12 Month ❑ 15 Month ❑ 18 Month ❑ 21 Month ❑ 24 Month

❑ Subject contact information reviewed

❑ Interval history obtained

❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO2)

❑ Vital signs obtained

❑ Local laboratory tests obtained

- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes →

- ❑ Records requested
- ❑ 2-week follow-up visit scheduled for _____

Study Coordinator: _____ Version 1.15.2014

Were any changes to heart failure therapy made at this visit?

❑ No→

❑ Subject reminded of 18-month follow-up visit scheduled for _____

❑ Yes →

❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Only 1 set of forms
is remaining.

Please make
additional photocopies.

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

Screening Visit Checklist

Date of screening: _____

❑ Hospital chart/medical records reviewed for eligibility (begin Subject Eligibility Worksheet)

❑ Written informed consent obtained

- ❑ Copy of the signed consent form provided to the subject
- ❑ Consent documented in subject's medical record
  Date: _____ Time: __ __ : __ __

❑ Demographics (including race and ethnicity) verified

Ethnicity
❑ Hispanic or Latino
❑ Not Hispanic or Latino
❑ Unknown

Race ➡ check all that apply:
❑ American Indian or Alaskan Native
❑ Asian
❑ Black or African American
❑ Native Hawaiian or other Pacific Islander
❑ White
❑ Other: _____
❑ Unknown

❑ Subject contact information collected (subject to confirm)

❑ History and physical performed, including vital signs (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites,SPO2)

❑ Local laboratory test results obtained

- ❑ NT-proBNP or BNP
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)

❑ Concomitant medications reviewed and recorded in medical record

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

Day 0 Baseline/Randomization Visit Checklist

Date of visit: _____

- ❑ Eligibility confirmed (review and complete Subject Eligibility Worksheet)
- ❑ Randomization performed using SIRE via InForm
- ❑ Subject contact information reviewed (subject to confirm) and uploaded to ftp.dcri.duke.edu or faxed to 1-919-668-9816
- ❑ Quality of Life assessments administered
  - ❑ Questionnaires uploaded to ftp.dcri.duke.edu or faxed to 1-919-668-9816
  - ❑ Patient Contact Form
  - ❑ Medical Release Form
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained
- ❑ 6MWT performed
- ❑ Local laboratory tests obtained
  - ❑ NT-proBNP or BNP
  - ❑ serum creatinine
  - ❑ BUN
  - ❑ Electrolytes (chemistry panel)
  - ❑ Total cholesterol, uric acid (if performed as part of standard of care)
  - ❑ Hematology (if performed as part of standard of care)
- ❑ Medical History
- ❑ Concomitant medications reviewed and recorded in medical record
- ❑ Follow-up visit for 2 weeks ± 1 week after randomization scheduled
- ❑ GUIDE-IT handout with schedule of follow-up visits and study personnel contact information given to subject

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

Biorepository/DNA Samples

Biorepository samples consent?

- ❑ No
- ❑ Yes ➡

Samples collected?

- ❑ No
- ❑ Yes

Consent withdrawn?

- ❑ No
- ❑ Yes ➡ Date: _____

DNA consent?

- ❑ No
- ❑ Yes ➡

Samples collected?

- ❑ No
- ❑ Yes

Consent withdrawn?

- ❑ No
- ❑ Yes ➡ Date: _____

Date/time collected: _____ __ __ : __ __

Was the subject fasting:

- ❑ **Yes**
- ❑ **No**
- ❑ **Last time subject had anything to eat/ drink containing calories: __ __: __ __**

Date/time processing initiated: _____ __ __ : __ __

Date/time frozen: _____ __ __ : __ __

Date sent to lab: _____

Core Lab and Biorepository/DNA Sample Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

ECHO Substudy (if applicable)

ECHO Substudy consent?

- ❑ No
- ❑ Yes ➡ Send in the signed ECHO ICF to DCRI

Resting transthoracic 2-D and Doppler echocardiogram completed?

- ❑ No
- ❑ Yes

Was the image transmitted/transferred to central reader?

- ❑ No
- ❑ Yes

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

2-week Follow-up Visit Checklist

Date of visit: _____

2 weeks (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

    Date/time collected: _____ __ __ : __ __

    Date/time processing initiated: _____ __ __ : __ __

    Was the subject fasting?

    - ❑ Yes
    - ❑ No
    - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

    Date/time frozen: _____ __ __ : __ __

    Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 6-week follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

_____

_____

_____

_____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

6-week Follow-up Visit Checklist

Date of visit: _____

6 weeks (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 3-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

3 Month Follow-up Visit Checklist

Date of visit: _____

3 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 6-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

6 Month Follow-up Visit Checklist

Date of visit: _____

6 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 9-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

9 Month Follow-up Visit Checklist

Date of visit: _____

9 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 12-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

12 Month Follow-up Visit Checklist

Date of visit: _____

12 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 15-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

ECHO Substudy (if applicable)

ECHO Substudy consent withdrawn?

- ❑ No
- ❑ Yes➡ Date: _____

Resting transthoracic 2-D and Doppler echocardiogram completed (12 month follow up)?

- ❑ No **(explain in 'Notes' section below)**
- ❑ Yes

Was the image transmitted/transferred to central reader?

- ❑ No
- ❑ Yes

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

15 Month Follow-up Visit Checklist

Date of visit: _____

15 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 18-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

18 Month Follow-up Visit Checklist

Date of visit: _____

18 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 21-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

_____

_____

_____

_____

_____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

21 Month Follow-up Visit Checklist

Date of visit: _____

21 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

Study Coordinator: _____

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No→
❑ Subject reminded of 24-month follow-up visit scheduled for _____

❑ Yes →
❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

_____

_____

_____

_____

_____

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

24 Month/End of Study Visit Checklist

Date of visit: _____

24 Months (± 1 week) after randomization

- ❑ Subject contact information reviewed
- ❑ Interval history obtained (including assessment for NYHA HF class, orthopnea, con med update)
- ❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO_2)
- ❑ Vital signs obtained (HR, BP, RR)
- ❑ Central laboratory samples obtained
  - ❑ Serum
  - ❑ Plasma
  - ❑ Core Lab NT-proBNP

  Date/time collected: _____ __ __ : __ __

  Was the subject fasting?

  - ❑ Yes
  - ❑ No
  - ❑ Last time subject has anything to eat/drink containing calories: __ __:__ __

  Date/time processing initiated: _____ __ __ : __ __

  Date/time frozen: _____ __ __ : __ __

  Date sent to lab: _____

Core Lab and Biorepository/DNA Samples Collected (number of cryovials):

_____ Whole blood (1)

_____ Plasma, EDTA (5)

_____ Serum, gold-top (2)

_____ Plasma, lithium heparin (2)

_____ NT-proBNP (1)

❑ Local laboratory tests obtained
- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes → ❑ Records requested
❑ 2-week follow-up visit scheduled for _____

Were any changes to heart failure therapy made at this visit?

❑ No

❑ Yes →

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

GUIDE-IT

Therapy Adjustment

Date of visit: _____

Associated with visit: ❑ BL ❑ 2 Week ❑ 6 Week ❑ 3 Month ❑ 6 Month ❑ 9 Month
❑ 12 Month ❑ 15 Month ❑ 18 Month ❑ 21 Month ❑ 24 Month

Reason(s) for adjustment of therapy:

- ❑ Decompensated HF
- ❑ Clinical indication without decompensated HF
- ❑ Decrease in NT-ProBNP
- ❑ Increase in NT-ProBNP
- ❑ Other investigator decision: _____
- ❑ Side effects or intolerance
- ❑ Other _____

Medication Adjustments

❑ **ACE inhibitor:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **ARB:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Beta-blocker:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

Medication Adjustments *(continued)*

❑ **Digoxin:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Hydralazine-nitrates:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Loop Diuretic:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Mineralocorticoid receptor antagonist** (aldosterone antagonist)**:**

❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

❑ **Oral thiazide diuretic:** ❑ Added ❑ Stopped ❑ Increased ❑ Decreased

❑ Switched to different agent: _____

Date of change: _____

New total daily dose: _____

Reason for adjustment: _____

Other Therapy Adjustments

❑ **Cardioversion or Rate control**

Date performed: _____

Procedure type: _____

Reason for adjustment: _____

❑ **Cardiac resynchronization therapy:** ❑ New ❑ Optimization

Date performed: _____

Procedure type: _____

Reason performed: _____

❑ **Exercise training or cardiac rehab**

Date of first training/rehab: _____

Reason for recommendation: _____

❑ **Additional HF education**

Date: _____

Topics: _____

Performed by: _____

Reason for additional education: _____

❑ **Hospitalization**

Date of admission: _____

Reason for admission: _____

Hospital name: _____

Other adjustment type:

Date: _____

Adjustment details: _____

_____

_____

Date	Notes

Subject initials: __ __ __ Subject number: __ __ __ - __ __ __ __

GUIDE-IT

Unscheduled 2-Week Follow-up Visit Checklist

Date of visit: _____ **(Note:** Visit may be in person or a remote laboratory evaluation at the discretion of the treating physician)

2 weeks (± 1 week) after hospitalization or change in therapy

Associated with visit: ❑ BL ❑ 2 Week ❑ 6 Week ❑ 3 Month ❑ 6 Month ❑ 9 Month ❑ 12 Month ❑ 15 Month ❑ 18 Month ❑ 21 Month ❑ 24 Month

❑ Subject contact information reviewed

❑ Interval history obtained

❑ Focused physical exam performed (including assessment heart rhythm, S3, JVP, rales, hepatomegaly, peripheral edema, ascites, SPO2)

❑ Vital signs obtained

❑ Local laboratory tests obtained

- ❑ NT-proBNP (biomarker-guided arm only)
- ❑ serum creatinine
- ❑ BUN
- ❑ Electrolytes (chemistry panel)
- ❑ Total cholesterol, uric acid (if performed as part of standard of care)
- ❑ Hematology (if performed as part of standard of care)

Since the last visit, has the subject been seen by a clinician as an outpatient?

❑ No

❑ Yes → Number of CV visits: ____
Number of non-CV visits: ____

Since the last study visit, has the subject had any hospitalizations, urgent care/ED visits, or outpatient procedures?

❑ No

❑ Yes →

- ❑ Records requested
- ❑ 2-week follow-up visit scheduled for _____

Study Coordinator: _____ Version 1.15.2014

Were any changes to heart failure therapy made at this visit?

❑ No→

❑ Subject reminded of 18-month follow-up visit scheduled for _____

❑ Yes →

❑ 2-week follow-up visit scheduled for _____

(Explain in 'Notes' section below the rationale for change or lack of change in therapy)

Notes: _____

Appendix G. Early Termination/Non-responder Form

Early Termination/Non-responder Form

Subject #: __ __ __ - __ __ __ __

Begin this form after the first missed visit, or if there are other indicators that a subject may be considering early termination from the trial.

Date & Time	Contact Attempt Made By…	Attempted to Contact…	Contact Method	Communication Synopsis
		❑ Subject ❑ Alt. contact: ____________ ❑ HCP: __________________ ❑ Other: ________________	❑ Phone #: _____________ ❑ Email: ________________ ❑ Text #: _______________ ❑ Other: _______________	
		❑ Subject ❑ Alt. contact: ____________ ❑ HCP: __________________ ❑ Other: ________________	❑ Phone #: _____________ ❑ Email: ________________ ❑ Text #: _______________ ❑ Other: _______________	
		❑ Subject ❑ Alt. contact: ____________ ❑ HCP: __________________ ❑ Other: ________________	❑ Phone #: _____________ ❑ Email: ________________ ❑ Text #: _______________ ❑ Other: _______________	
		❑ Subject ❑ Alt. contact: ____________ ❑ HCP: __________________ ❑ Other: ________________	❑ Phone #: _____________ ❑ Email: ________________ ❑ Text #: _______________ ❑ Other: _______________	

Early Termination/Non-responder Form

Subject #: __ __ __ - __ __ __ __

Begin this form after the first missed visit, or if there are other indicators that a subject may be considering early termination from the trial.

Date & Time	Contact Attempt Made By…	Attempted to Contact…	Contact Method	Communication Synopsis
		❑ Subject ❑ Alt. contact: ______ ❑ HCP: ______ ❑ Other: ______	❑ Phone #: ______ ❑ Email: ______ ❑ Text #: ______ ❑ Other: ______	
		❑ Subject ❑ Alt. contact: ______ ❑ HCP: ______ ❑ Other: ______	❑ Phone #: ______ ❑ Email: ______ ❑ Text #: ______ ❑ Other: ______	
		❑ Subject ❑ Alt. contact: ______ ❑ HCP: ______ ❑ Other: ______	❑ Phone #: ______ ❑ Email: ______ ❑ Text #: ______ ❑ Other: ______	
		❑ Subject ❑ Alt. contact: ______ ❑ HCP: ______ ❑ Other: ______	❑ Phone #: ______ ❑ Email: ______ ❑ Text #: ______ ❑ Other: ______	

Only 1 form is remaining.

Please make additional photocopies.

Early Termination/Non-responder Form

Subject #: __ __ __ - __ __ __ __

Begin this form after the first missed visit, or if there are other indicators that a subject may be considering early termination from the trial.

Date & Time	Contact Attempt Made By…	Attempted to Contact…	Contact Method	Communication Synopsis
		❑ Subject ❑ Alt. contact: ________ ❑ HCP: ________ ❑ Other: ________	❑ Phone #: ________ ❑ Email: ________ ❑ Text #: ________ ❑ Other: ________	
		❑ Subject ❑ Alt. contact: ________ ❑ HCP: ________ ❑ Other: ________	❑ Phone #: ________ ❑ Email: ________ ❑ Text #: ________ ❑ Other: ________	
		❑ Subject ❑ Alt. contact: ________ ❑ HCP: ________ ❑ Other: ________	❑ Phone #: ________ ❑ Email: ________ ❑ Text #: ________ ❑ Other: ________	
		❑ Subject ❑ Alt. contact: ________ ❑ HCP: ________ ❑ Other: ________	❑ Phone #: ________ ❑ Email: ________ ❑ Text #: ________ ❑ Other: ________	

Appendix H. CEC Event Source Document Coversheet

GUIDE-IT CEC Event
Source Document Coversheet

Site #: __ __ __ **Subject #: __ __ __ __**

Event date: __ __ / __ __ / __ __ __ __

Please select event type:

- ❑ **Death**
- ❑ **Hospitalization**

Submit de-identified documents to

- **Fax:** 919-668-9816 or
- **Upload to:** ftp.dcri.duke.edu

Source Document *Please refer to listing of recommended source documents*	**Check If Sent**	**Comment**
Admit Note/History/Physical Exam	❑	
Clinical or Progress Notes	❑	
Discharge Summary	❑	
Death Certificate	❑	
Autopsy Report, if performed	❑	
Death Summary	❑	
Medication Administration Records, if requested	❑	
ECGs, if requested	❑	
Cardiac Markers (CK, CKMB, Troponin T/I with upper limits of normal) **if requested**	❑	
Other	❑	

Additional Comments: _____

_____

_____

_____

Name *(printed)*: _____ Signature: _____

Date: _____

GUIDE-IT CEC Event
Source Document Coversheet

Site #: __ __ __ **Subject #: __ __ __ __**

Event date: __ __ / __ __ / __ __ __ __

Please select event type:

- ❑ **Death**
- ❑ **Hospitalization**

Submit de-identified documents to

- **Fax:** 919-668-9816 or
- **Upload to:** ftp.dcri.duke.edu

Source Document *Please refer to listing of recommended source documents*	**Check If Sent**	**Comment**
Admit Note/History/Physical Exam	❑	
Clinical or Progress Notes	❑	
Discharge Summary	❑	
Death Certificate	❑	
Autopsy Report, if performed	❑	
Death Summary	❑	
Medication Administration Records, if requested	❑	
ECGs, if requested	❑	
Cardiac Markers (CK, CKMB, Troponin T/I with upper limits of normal) **if requested**	❑	
Other	❑	

Additional Comments: _____

_____

_____

_____

Name *(printed)*: _____ Signature: _____

Date: _____

Only 1 form is remaining.

Please make additional photocopies.

GUIDE-IT CEC Event
Source Document Coversheet

Site #: __ __ __ **Subject #: __ __ __ __**

Event date: __ __ / __ __ / __ __ __ __

Please select event type:

- ❑ **Death**
- ❑ **Hospitalization**

Submit de-identified documents to

- **Fax:** 919-668-9816 or
- **Upload to:** ftp.dcri.duke.edu

Source Document *Please refer to listing of recommended source documents*	**Check If Sent**	**Comment**
Admit Note/History/Physical Exam	❑	
Clinical or Progress Notes	❑	
Discharge Summary	❑	
Death Certificate	❑	
Autopsy Report, if performed	❑	
Death Summary	❑	
Medication Administration Records, if requested	❑	
ECGs, if requested	❑	
Cardiac Markers (CK, CKMB, Troponin T/I with upper limits of normal) **if requested**	❑	
Other	❑	

Additional Comments: _____

_____

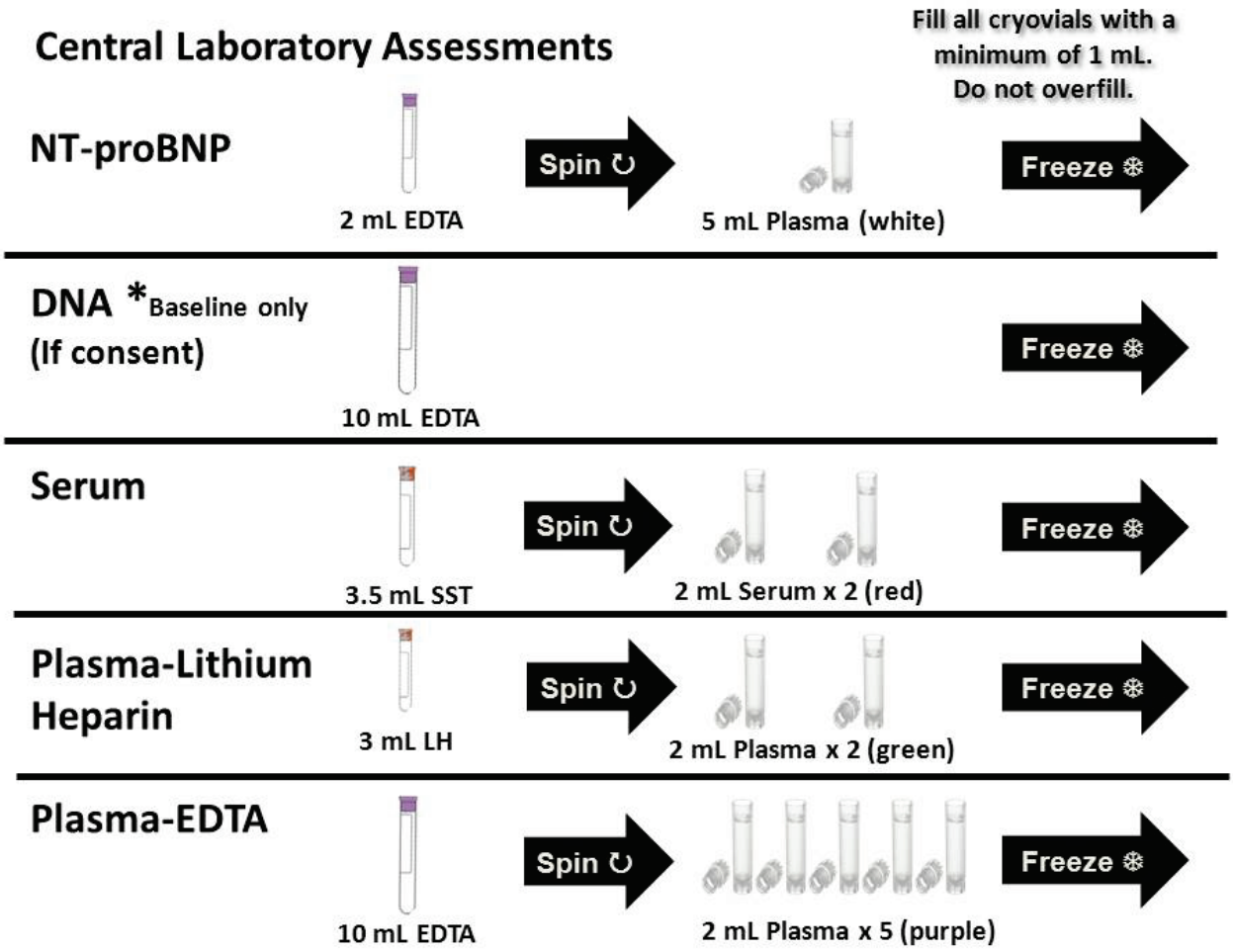
_____

_____

Name *(printed)*: _____ Signature: _____

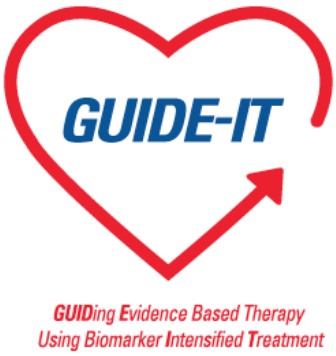
Date: _____

Appendix I. Central Laboratory Sample Collection



Sample	Order of Draw	Tube Type	Processing
Central Lab NT-proBNP	1	EDTA 2 mL	• Mix gently by inverting 8–10 times; centrifuge and transfer within 30–120 minutes of collection • Transfer 1 aliquot of approximately 1 mL of plasma from vacuum tube into 1 labeled white-top cryovial. Avoid transferring cells with the plasma. • Store frozen (-70ºC or lower) in LabCorp packaging, with all vials from each visit to be in one bag, together with a copy of the requisition. • Batch ship on dry ice to LabCorp monthly. Fax shipment alert form to LabCorp.
DNA	2	EDTA 10 mL	• No processing needed. Do not open the tube. • Store frozen (-70ºC or lower) in LabCorp packaging, with all vials from each visit to be in one bag, together with a copy of the requisition. • Batch ship on dry ice to LabCorp monthly. Fax shipment alert form to LabCorp.
Biorepository Serum	3	SST 3.5 mL	• Mix gently by inverting 8–10 times; centrifuge and transfer within 30–120 minutes of collection • Transfer 2 aliquots of approximately 1 mL each of serum from vacuum tube into 2 labeled red-top cryovials. Avoid transferring cells or separator gel with the serum. • Store frozen (-70ºC or lower) in LabCorp packaging, with all vials from each visit to be in one bag, together with a copy of the requisition. • Batch ship on dry ice to LabCorp monthly. Fax shipment alert form to LabCorp.
Biorepository Plasma - Litium Heparin	4	LH 3 mL	• Mix gently by inverting 8–10 times; centrifuge and transfer within 30–120 minutes of collection • Transfer 2 aliquots of approximately 1 mL each of plasma from vacuum tube into 2 labeled green-top cryovials. Avoid transferring cells with the plasma. • Store frozen (-70ºC or lower) in LabCorp packaging, with all vials from each visit to be in one bag, together with a copy of the requisition. • Batch ship on dry ice to LabCorp monthly. Fax shipment alert form to LabCorp.
Biorepository Plasma - EDTA	5	EDTA 10 mL	• Mix gently by inverting 8–10 times; centrifuge and transfer within 30–120 minutes of collection • Transfer 5 aliquots of approximately 1 mL each of plasma from vacuum tube into 5 labeled purple-top cryovials. Avoid transferring cells with the plasma. • Store frozen (-70ºC or lower) in LabCorp packaging, with all vials from each visit to be in one bag, together with a copy of the requisition. • Batch ship on dry ice to LabCorp monthly. Fax shipment alert form to LabCorp.

Appendix J. eCRF Instructions



eCRF Instructions

GUIDing **E**vidence Based Therapy Using Biomarker **I**ntensified **T**reatment in Heart Failure (**GUIDE-IT**)

Version: January 9, 2012

Contents

Abbreviations

ACS	*Acute Coronary Syndrome*
AE	*Adverse Events*
CABG	*Coronary Artery Bypass Graft*
CAD	*Coronary Artery Disease*
CAS	*Cross-active study*
CEC	*Clinical Events Committee*
CRA	*Clinical Research Associate*
CVA	*Cerebrovascular Accident*
DCRI	*Duke Clinical Research Institute*
ECG	*Electrocardiogram*
eCRF	*Electronic Case Report Form*
ED	*Emergency Department*
EDC	*Electronic Data Capture*
FU	*Follow-up*
HF	*Heart Failure*
IABP	*Intra-aortic Balloon Pump*
LVEF	*Left Ventricular Ejection Fraction*
MI	*Myocardial infarction*
PI	*Principal Investigator*
SAE	*Serious adverse event*

General eCRF Instructions

- For all subjects randomized (intentionally or in error) in the RAND form, you must complete a termination [TERM] or end of study [EOS] form. This includes subjects randomized by accident and early terminations.
- Complete the eCRF forms within 5 business days of the study visit.

Database Access

- Once you complete the appropriate training, you will receive a username and password. Use this to log in to the InForm system. Do not share your username/password
- To access the eCRF use the following web address and enter your individual username and password. Bookmark this site on your browser for easy access.

Production database: https://inform-edc.dcri.duke.edu/guideit/

- When logging in for the first time, the InForm system will prompt you to change your password. Passwords are unique and must be at least 6 characters long.
- You will be logged out if no activity occurs in the eCRF for a specified time. If this happens, log back in with your username and password. Any screens in the process of submission will be saved.
- **Training database: This database is for training purposes only.** A username and password will be provided by DCRI. **Do not** change the password on the training database.

Training database:	https://inform-edc.dcri.duke.edu/guideit_trn/
Study Coordinator role:	**Username:** crc2
Principal Investigator role:	**Username:** pi2
	Password: inf5606 (please do not change the password)

Technical Help

- Contact the EDC helpdesk for
  - Technical assistance with the eCRF
  - To reset passwords
  - When trial URL is not accessible
  - With system requirement questions
  - Questions about passwords or the InForm system

    Phone: 1-866-999-DCRI [3274]

    E-mail: edchelp@dm.duke.edu

    Coverage: 24 hours a day, 7 days a week
- Contact your Clinical Research Associate (CRA) or study monitor for questions about entering subject data, queries, or traffic lights.

Date and Times

- Dates are in month/day/year or month/year format.
- Select the 3-letter abbreviation for the month, the 2-digit day, and the year from the drop-down box or if available, use the calendar button to the right of the date field.
- Select time from the drop-down menu using a 24-hour clock from 00:00 to 23:59.
- Provide the best estimate for unknown dates or times. Some questions provide an option to select UNK (unknown).

Signing Subject Casebooks

- The signature field is located in the Signature Completion [SIGN] form.
- Principal Investigators (PI) are required/authorized to review and sign each subject casebook. This signature is a symbol of intention to authenticate and authorize the data.
- Do not sign the casebook until instructed to do so.
- If changes occur after entering the signature, the PI must re-sign the casebook to confirm the data changes.
- PIs must access their InForm account at least once every 90 days or the account will be inactivated. To reactivate an account, contact the EDC Helpdesk at edchelp@dm.duke.edu .

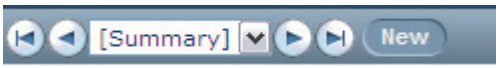
Verifying Serious Adverse Events

- The Site Delegation and Signature Log lists the Principal Investigators and designees (co-PIs or sub-PIs) authorized to verify serious adverse events (SAEs).
- All SAEs must be reviewed and verified by the PI or designee as soon as possible. However, do not delay reporting an SAE if the PI is not available for verification.
- If changes occur after entering the signature, the PI or designee must re-verify the SAE to confirm the data changes.

Form Types

- **Static (Standard) Forms:** Static forms are always present for data entry.
- **Dynamic Forms:** Dynamic forms, such as MEDS, EF, and ECG display upon submission of specific data. The Adverse Events [AE] form is an example of a dynamic form. A *Yes* response to *Did subject have any Serious Adverse Events or Safety Events of Interest?* on the CAS (cross-active study) Trigger [CASTRIG] form will dynamically create the AE form after submission of the CASTRIG form.
- **Repeating Forms:** You may create as many repeating forms as necessary to record data. For each new record, click the *New* button to create a new form. The *New* button is located at the top of the section. The [HOSP] form is an example of a repeating form.

  Select the *Summary* button in the drop-down menu to view of all of the repeating forms. To view, add, or change information, click on the underlined row number or traffic light.



- **Add Entry:** Within some forms are Add Entry buttons. The *Add Entry* option is used to collect an unlimited number of records within a form.
- **Unscheduled** follow-up visit forms may be generated as needed after therapy adjustments or hospitalizations. Select New at the bottom of the screen in a FU visit tab to create a new visit.

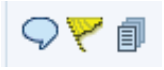
InForm Icons

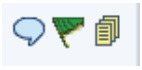
Comment No comment added  Comments added 

Audit Trail No changes  Changes made 

Comment and audit trail icons become yellow when activity occurs. They do not change back to clear/blue.

Query Flag No flag = there are no queries for the item.

Yellow = queries are present for the item. 

Green = queries have been answered. 

Lock: Seen on Time and Events Schedule or Casebook view after monitoring and resolution of queries. Data is locked for editing. 

Eraser "Reset": May be used to clear data from an item that has not been submitted or is being updated through a post-submission data change. 

Traffic Light Review

The traffic lights show the status of each module within the casebook.

Red Light → Open queries are present.

Action required: Address the query by editing the data or navigate to the query to respond after data is confirmed as correct.

Yellow Light → Missing data (required data is not present).

Action required: Enter and submit the missing information.

Green Light → Complete (all required data is present).

Action required: None.

White /No light → No data submitted.

Action required: If appropriate, navigate to form and submit data.

Data Submission

- Most text fields are limited to 200 characters. Enter concise information in text fields. InForm displays a message when the character limit has been reached and additional text cannot be entered.
- Required fields: Provide an answer for all items with an asterisk next to the item number. If a required field does not have a response, you will see a yellow background on the form, a yellow traffic light on the Time and Events Schedule, and a yellow exclamation point on the form tab.
- Avoid typing double quotes ("…") when submitting free text items or providing a reason for change.
- **Do not use special characters** (e.g., ≥ ≤ # % ") in the text fields or comment bubbles.
- Do not copy and paste formatted text from a Word document into text fields or comment bubbles. You may copy and paste *unformatted* text (eg, from Notepad).
- Do not use the *Comments* bubble to record clinical data. The appropriate use of the *Comments* bubble is to:
    - Indicate that an item is unknown, not applicable, or not done (if this option is not present on eCRF). This will allow InForm to recognize the form as complete.
    - Indicate that an entire form is not applicable or not done (if the form cannot be deleted). This will allow InForm to recognize the form as complete.
- Press *Submit* to save your data and view any automated queries. Once a form is successfully submitted, a message will appear at the top left of the form: *Form Submitted Successfully.*
- Automated queries will appear upon submission of a form (not after data entry in each field). Therefore, you will not receive query messages (eg, out of range numbers in a lab result) until **after** form submission.
- If data changes are required, update and submit the data changes first. After updating data, respond to any remaining queries.
    - Provide a reason for change when updating previously submitted data. Reason options include:
        - Transcription error
        - New information
        - Changed information (ensure all data is updated and submitted **prior to** selecting this option)
        - Other (enter only the reason for the change in the text field. Do **not** enter clinical data in this field. Ensure all data is updated and submitted prior to selecting this option) **Do not enter the new data in this field, only the reason for the change.**
- Once a form is successfully submitted, a "pop up" message will appear: "Form Submitted Successfully."
- Data submission populates the audit trail for the form. An audit trail entry remains in InForm for the life of the database.

Queries and Data Corrections

Queries – Data Entry Confirmation

A query may fire for data entered outside the expected range or inconsistent with other data in the database. For example, a query might fire for a height of 7 feet because it is outside of the expected range, but the subject really is 7 feet tall. To confirm the data is correct as entered:

1. Select the underlined red query text (a query window will appear).
2. Review the eCRF question, your response, and the query text.
3. Select Original value is correct from the drop-down box.
4. Submit the form.

A CRA must review the response to close the query.

Data Corrections – Remove or Change Data at a Variable Level

1. Select the data field item where the red query text is located.
2. Use the eraser to reset the field, or use your mouse to highlight and delete the text. Enter the corrected data value.
3. Select or describe the reason for the change. Do not enter clinical data in this location.
4. Submit the page with corrected data.
5. Confirm the data have been changed on the eCRF page.

Data Corrections – Remove or Change Data at a Form Level

1. Select “Clear CRF” at the bottom left hand side of the screen to remove the data from the form.
2. Select or describe the reason for the change. Do not enter clinical data in this location.
3. Select “Submit.”
4. Select the form level comment icon.
5. Add a form level comment and select “Submit.”
6. The form will not disappear, however the traffic light will change from yellow to green.

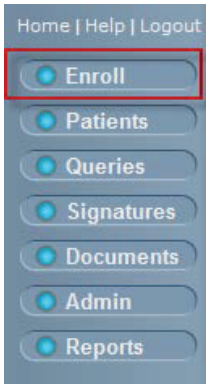
Data Corrections – Remove a Dynamic Form with an Empty Audit Trail

1. Change “Yes” to “No” on the data field item of the trigger question which dynamically created the form.
2. The form will disappear.

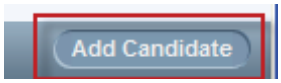
Enrolling a Subject

Access the GUIDE-IT InForm system to enroll and randomize a subject into the GUIDE-IT trial.

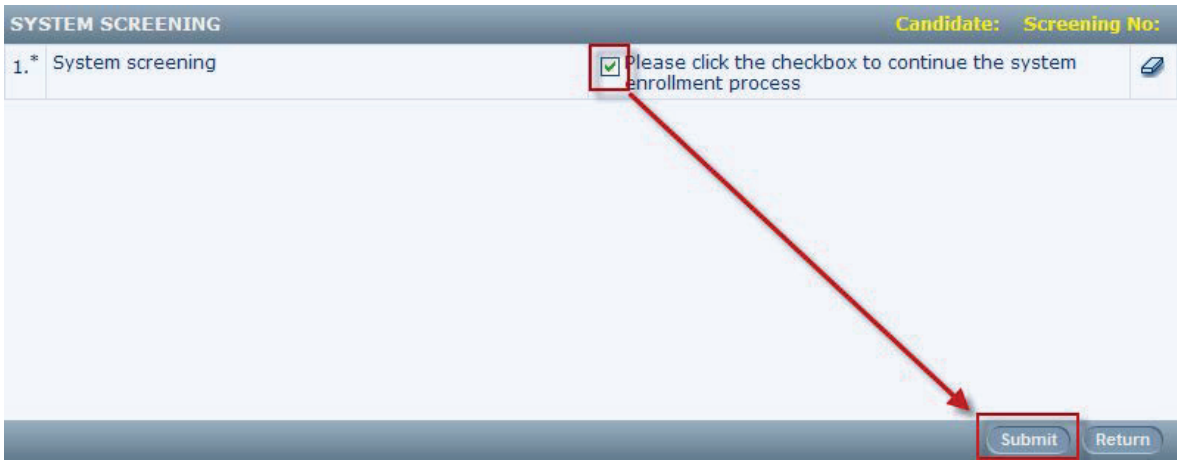
1. Confirm eligibility
2. On the left side navigation pane, select Enroll



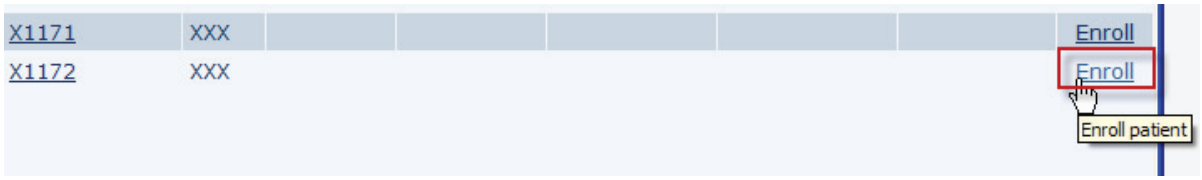
3. On the lower right corner of the screen, select Add Candidate



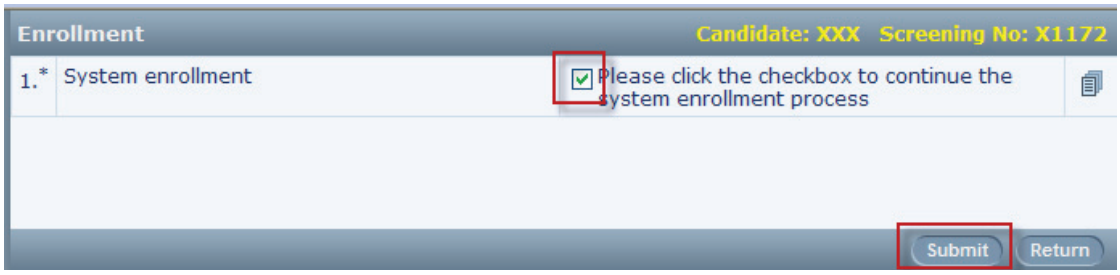
4. On the System **Screening** screen, check the box, then go to the bottom right, and click Submit.



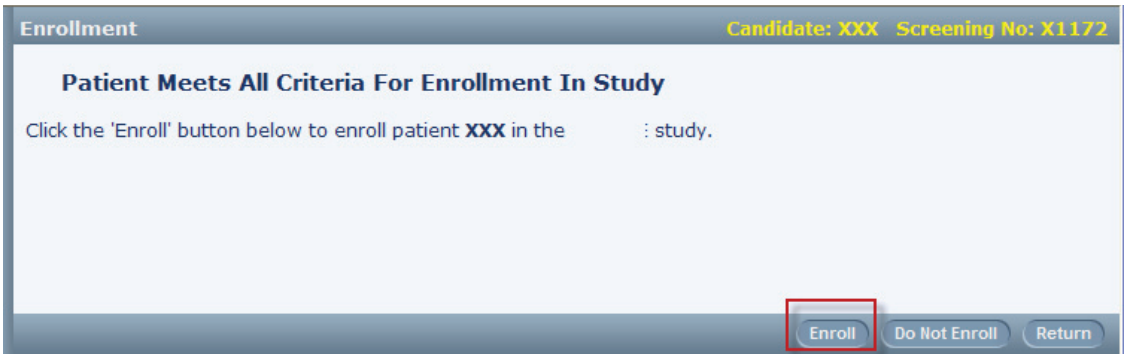
5. The next screen has a list of numbers, and on the right, an Enroll button. Click Enroll.



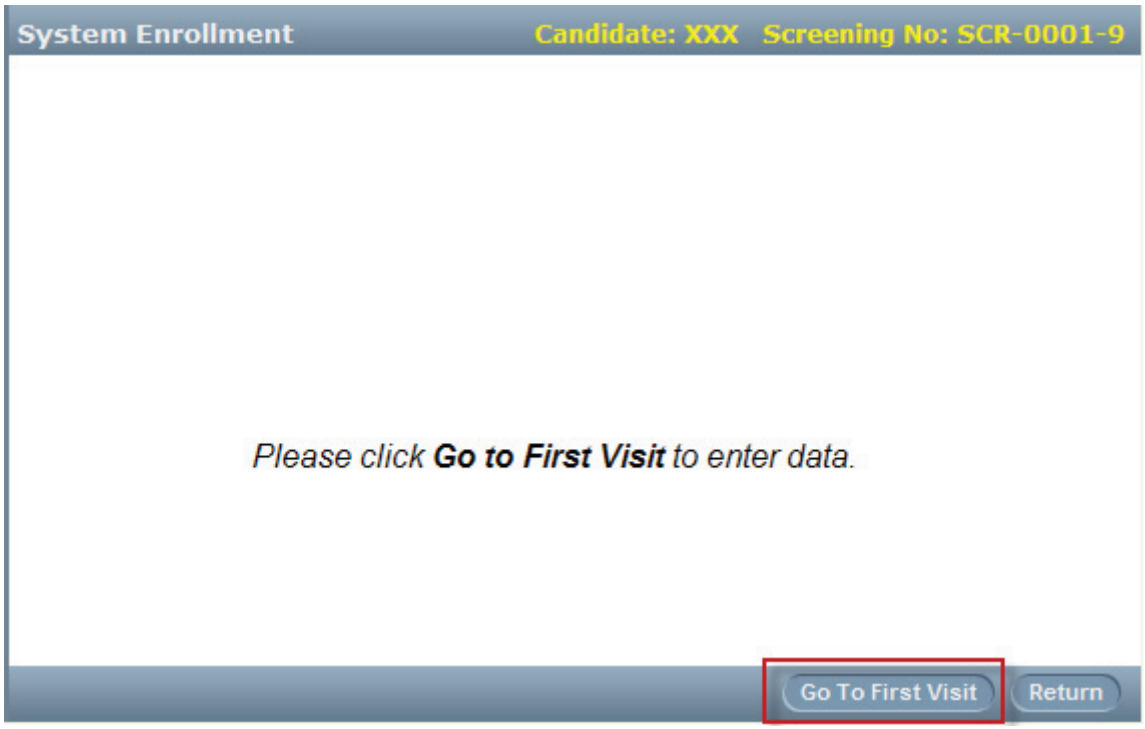
6. On the System **Enrollment** screen, check the box (if not already checked), then go to the bottom right, and click Submit.



7. On the Enrollment screen, confirm that the patient meets eligibility criteria and on the lower right side, click Enroll. A new patient is now entered into the InForm system for your site.



8. To enter information for the subject and to randomize, click Go to First Visit on the bottom right of the screen and navigate to the Baseline (BLN) visit.

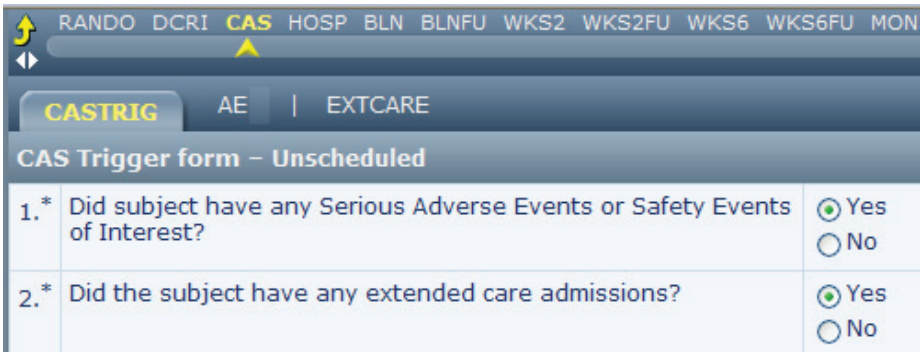


9. Continue to the RAND form to complete the randomization process.

CAS Trigger Form [CASTRIG]

- At Randomization, enter *No* to **both** questions: *Did subject have any Serious Adverse Events or Safety Events of Interest?* and *Did the subject have any extended care admissions?* This will ensure that the form is complete at the end of the trial if the subject does not have an SAE or extended care admission
- If the subject has a reportable adverse event or an extended care admission (nursing home, rehabilitation center, hospice, etc.), return to this form and change the answer to *Yes.* Completion of this form will create the adverse event and extended care forms within the CAS visit.

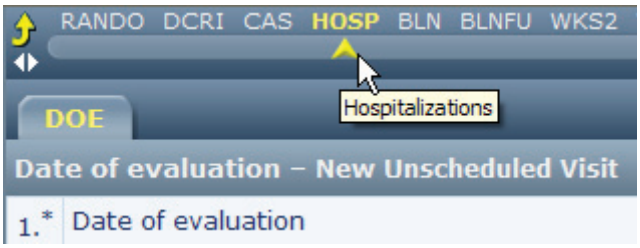
To enter a serious adverse event or extended care facility admission



Hospitalization

To Enter a Hospitalization or ED Visit

Go to the HOSP visit located on the left side of the visit ruler:



Date of evaluation: Enter the hospital admission

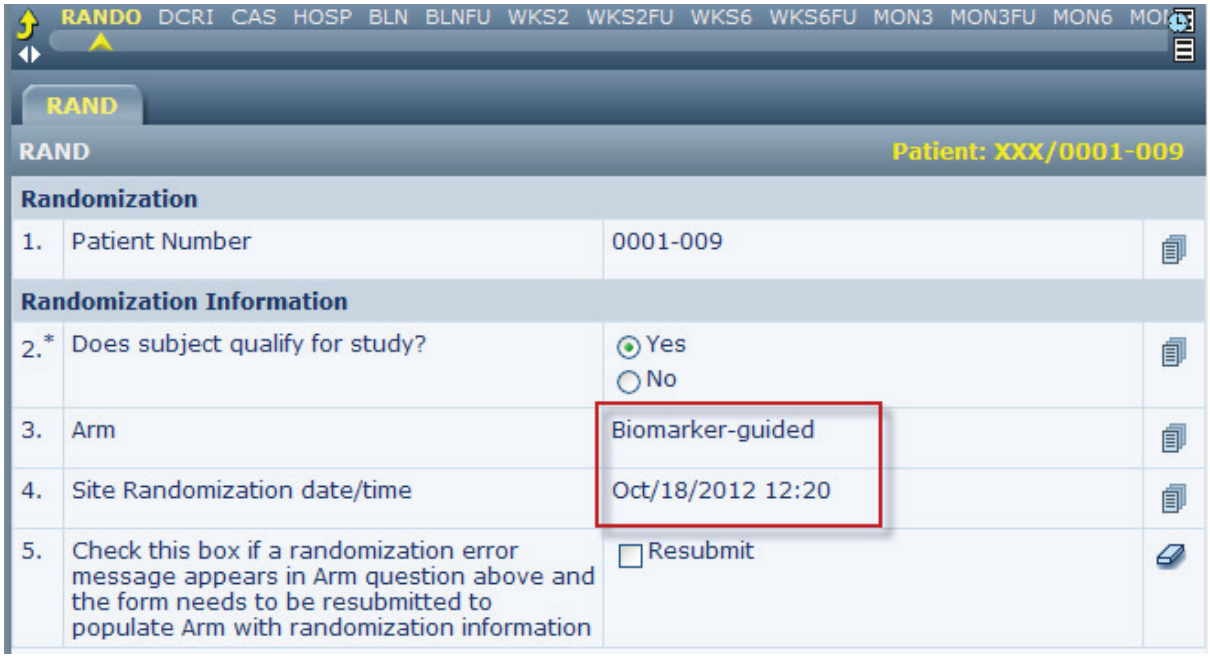
The dynamic HOSP form will appear after submission of the DOE form.

If there is more than one hospitalization or ED visit, create additional forms within the visit by selecting the New button at the bottom of the page.

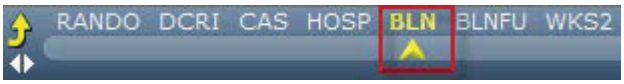
Randomization [RAND]

1 **Patient Number:** Auto-filled by the SIRE IVRS system. This field is ***read only*** and cannot be modified.

2 **Does the subject qualify for study?** Selecting *Yes* will trigger the randomization process.
The subject's assigned arm and site randomization date and time will appear on the screen.



5 **Check this box if a randomization error message appears in Arm question above and the form needs to be resubmitted to populate Arm.**
Select only if there is an error message and InForm does not display the assigned arm/randomization date and time.

Baseline [BLN] Visit 

Subject Demographics [DEM]

3. Ethnicity

Indicate if the subject is of Hispanic or Latino origin as reported by the subject.

Hispanic or Latino: A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture of origin, regardless of race.

Unknown: Select if subject prefers not to answer or is not sure.

4. Race

Select all that apply as reported by the subject or select *Unknown*. If Other Race, enter name of race.

American Indian or Alaska Native: A person having origins in any of the original peoples of North and South America (including Central America) and who maintains tribal affiliation or community attachment.

Asian: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.

Black or African American: A person having origins in any of the black racial groups of Africa.

Native Hawaiian or other Pacific Islander: A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

White/Caucasian: A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

Other Race: specify.

Unknown: Select if subject prefers not to answer or is not sure.

7. Date and time of consent: Enter the date and time the subject first signed a GUIDE-IT consent form.

Medical History [MEDHX]

Complete this section based on the subject's medical record and ensure all items have source documentation. If actual day is unknown, enter the month and year.

1. What is the primary etiology of the heart failure?

Ischemic heart disease is defined as:

- At least one major epicardial coronary artery with more than 70% obstruction by coronary angiography
- History of acute myocardial infarction associated with wall motion abnormality by echocardiography or gated blood pool imaging
- Stress testing (with or without imaging) diagnostic of coronary artery disease

If ***Non-ischemic,*** specify etiology.

If ***Other, non-ischemic,*** describe. Text space is limited to 200 characters.

Possible entries:

- Peripartum
- Drug use
- Alcohol abuse present for at least 5 years as defined by either heavy alcohol consumption (i.e., 75 g/day at least 5 days/week) or alcohol dependence
- Cocaine use
- Ephedrine use
- Temporally-related exposure to a drug or substance known to cause cardiomyopathy, including chemotherapeutic agents(s) and radiation to the chest)

3. Has the subject had any hospitalizations for heart failure (prior to index hospitalization)?

If *Yes,* enter date of most recent hospitalization and the number of hospitalizations primarily for heart failure within the past 12 months. Do not include the index (current) hospitalization. emergency department or urgent care visits.

Indicate if the subject has had a history of the following:

4. Coronary Artery Disease (CAD): Includes history of myocardial infarction (MI), angina, or revascularization procedures (PCI or CABG).

5. Prior revascularization: Includes PCI and CABG.

6. Valve surgery: *Other valve surgery* may include valve repair, valvuloplasty, or surgery on different valve.

7. Prior implantable cardioverter defibrillator (ICD)/pacemaker implantation: If *Yes,* indicate type. Biventricular refers to any type with pacing leads for the left and right ventricles.

8. Myocardial infarction (MI): determined by any of the following

- Hospital admission for acute MI
- ECG report indicating previous (old) or acute MI
- Increase in biochemical marker (creatine kinase or troponin) consistent with MI. Note that low elevation in troponin levels may be seen in patients with heart failure and should not by themselves be considered diagnostic of infarction
- Patient reports history of acute MI or heart attack

9. Prior left heart catheterization: Left heart catheterization with or without coronary angiography or ventriculography.

10. Atrial fibrillation/flutter

- **Fibrillation:** A cardiac arrhythmia arising from the atrium with an atrial rate > 300 bpm and an irregularly irregular ventricular response in the presence of conduction.
- **Flutter:** dysrhythmia with organized rhythmic atrial contractions with a rate of 200–300 beats per minute.

11. Ventricular tachycardia/fibrillation: Includes sustained and non-sustained.

12. Peripheral arterial vascular disease: May include

- Claudication, either with exertion or at rest
- Amputation for arterial vascular insufficiency
- Vascular reconstruction, bypass surgery, or percutaneous intervention to the extremities (excluding dialysis fistulas and vein stripping)
- Documented aortic aneurysm with or without repair
- Positive invasive angiogram
- Positive noninvasive test (eg, ankle brachial index 0.9 or less, ultrasound, magnetic resonance or computed
- Tomography imaging of more than 50% diameter stenosis in any peripheral artery (eg, renal, subclavian, femoral, iliac).

13. Stroke: A stroke or CVA with loss of neurological function caused by an ischemic or hemorrhagic event with residual symptoms at least 24 hours after onset or leading to death. Includes hemorrhagic and nonhemorrhagic.

14. Hypertension:

- History of hypertension diagnosed and treated with medication, diet, and/or exercise
- Blood pressure > 140 mm Hg systolic or 90 mm Hg diastolic on at least 2 occasions
- Blood pressure > 130 mm Hg systolic or 80 mm Hg diastolic on at least 2 occasions for patients with diabetes or chronic kidney disease

15. Diabetes mellitus:

- History of diabetes, regardless of duration of disease
- Need for antidiabetic agents
- Fasting blood sugar greater than 7 mmol/L or 126 mg/dL

16. Chronic respiratory disease (eg, COPD): History of chronic lung disease (eg, chronic obstructive pulmonary disease, chronic bronchitis, emphysema) or current chronic treatment with inhaled or oral pharmacological therapy (eg, beta-adrenergic agonist, anti-inflammatory agent, leukotriene receptor antagonist, or steroid).

17. Chronic liver disease: history of documented chronic liver disease, eg, chronic hepatitis, cirrhosis, gallstones, cholangitis.

18. Cancer within past 5 years, excluding skin cancer: Includes any history of solid or hematologic malignancies. Does not include non-metastatic skin cancer.

19. Cigarette smoking: Currently smoking = within 2 weeks prior to randomization.

20. Alcohol abuse: As reported by the patient or documented in the medical history; physical dependence on alcohol, characterized by excessive consumption, a loss of control, diverse personality changes, and/or social consequences.

21. Depression treated with medications: History of treated depression, or currently taking antidepressant medication for a diagnosis of depression.

22. Drug abuse: Includes use of illicit drugs or inappropriate use of prescription medications.

23. Hyperlipidemia: Documented history of hyperlipidemia diagnosed and/or treated. May include total cholesterol > 200 mg/dL (5.2 mmol/L), LDL ≥ 130 mg/dL (3.37 mmol/L), or HDL < 35 mg/dL or use of lipid-lowering therapy.

24. Sleep apnea: Refers to obstructive, central, or mixed.

25. Renal disease: A documented history of renal insufficiency including an elevation of serum creatinine > 1.5 mg/dL or 133 μmol/L.

Baseline Assessments [BASE]

Complete this form at the time of randomization—at hospital discharge or within 2 weeks of hospital discharge.

1. Date of discharge for index hospitalization: Future visit windows will be determined from this date.

2. Date of baseline assessments: Date labs obtained and 6MWT performed. If labs performed on different days, enter on an [ASMT] form in the Baseline Follow-up visit [BLNFU].

5. Was 6-minute walk performed? If Yes, enter distance walked in meters. If *No,* select the **one** best reason why the subject did not perform the walk. If more than one 6MWT was performed, enter results of the one performed closes to date of baseline assessment.

Recent Ejection Fraction [EF]

2. Value of most recent LVEF: Enter midpoint if range given. Select a descriptive term only if the medical record does not have a numeric value.

Examination [EXAM]

Performed during screening by a medically qualified person per site policy.

1. New York Heart Association Class

- **I** No limitation: Ordinary physical activity does not cause undue fatigue, dyspnea, or palpitation.
- **II** Slight limitation of physical activity: Such patients are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or angina.
- **III** Marked limitation of physical activity: Although patients are comfortable at rest, less than ordinary activity will lead to symptoms.
- **IV** Inability to carry on any physical activity without discomfort: Symptoms of congestive failure are present even at rest. With any physical activity, increased discomfort is experienced.

2. Orthopnea: Refers to number of pillows required to maintain comfort of patient in recumbent position.

6. Is the patient currently in atrial fibrillation or atrial flutter?

- **Fibrillation:** A cardiac arrhythmia arising from the atrium with an atrial rate > 300 bpm and an irregularly irregular ventricular response in the presence of conduction.
- **Flutter:** dysrhythmia with organized rhythmic atrial contractions with a rate of 200-300 beats per minute.

7. SpO2(%): Spot oxygen percent measured by pulse oximetry.

8. Jugular venous pressure: Refers to the estimated height of the mean jugular venous waveform above the right atrium in cm.

9. Rales: If *Yes*,

- < 1/3: Moist or dry rales heard in lower 1/3 of one or both lung fields that persist after cough.
- 1/3–2/3: Moist or dry rales heard throughout the lower half to 2/3 of one or both lung fields.
- 2/3: Moist or dry rales heard throughout both lung fields.

10. S3 auscultation: third (mid-diastolic) heart sound.

11. Hepatomegaly: Documentation of liver edge detectable below the right costal margin during physical examination.

12. Ascites: accumulation of serous or hemorrhagic fluid in the peritoneal cavity.

13. Peripheral edema: Increased tissue fluid indicated by perceptible indentation on lower leg or foot after palpation.

No = Complete absence of edema as determined by applying mild digital pressure in all dependent areas and failing to elicit any indentation of skin and subcutaneous tissues.

Trace: Detection of limited areas where mild digital pressure elicits an indentation of skin and subcutaneous tissues that resolves over approximately 10–15 seconds. Typically limited to only the lower extremities or only the sacrum, not both.

Moderate: Detection of moderate surface area in one or both areas (sacrum and lower extremities) where indentations of skin and subcutaneous tissues are easily created with limited pressure and these indentations disappear slowly (15–30 seconds or more).

Severe: Large areas of lower extremities (and sacrum if patient has been recumbent), often to mid-calf or higher, having easily produced and slowly resolving (more than 30 seconds) indentations. This extent of edema is sometimes associated with acute or subacute skin changes including weeping of skin and/or skin break down.

Concomitant Medications [MEDS]

This is a standard form at Baseline, and a dynamic form at follow-up visits. Entering a Date of Visit will trigger the MEDS form at scheduled visits.

- For each listed medication, select *Yes* if the patient is currently taking the medication. Provide additional information as indicated.
- For combination medications, select *Yes* for each class of active ingredient. For example, if patient is taking Lotrel, select *Yes* for both ACE inhibitor (benazepril) and calcium channel blocker.
- When requested, specify the total daily dose (amount taken in a 24-hour period).

Local NT-proBNP [PROBNP]

This is a standard form at Baseline, and a dynamic form at follow-up visits. This form will appear when question 3. *Was local NT-proBNP measured?* is answered as Yes on the [ASMT] form.

Enter date and results of local lab tests performed for all subjects at screening and subjects randomized to biomarker-guided arm at all other visits.

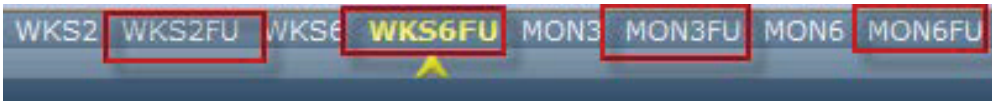
Specimen Consent [SPECCONS]

Indicate the date consent was signed for biorepository and DNA samples. If consent withdrawn at any time during the study, return to this form and enter the date of withdrawal,

Follow-up Visits

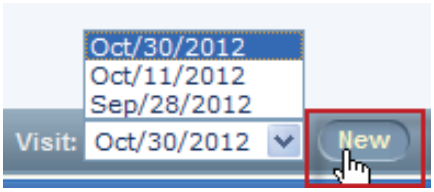
Unscheduled Visits

Each scheduled visit is listed in the visit ruler. After each scheduled visit is a follow-up visit tab for use if one or more 2-week follow-up visits are needed due to a therapy adjustment or hospitalization.



To enter the first unscheduled 2-week follow-up visit, select the appropriate FU visit tab and enter the date of evaluation. This will trigger additional dynamic forms: [EXAM] and [ASMT].

If another 2-week follow-up visit is required prior to the next scheduled visit window, return to the same FU visit tab and create a new visit: On the bottom left of the screen, select the New button next to the Visit drop-down list. To see all previous unscheduled follow-up visits associated with the scheduled visit, click on the drop-down arrow.



Date of Evaluation [DOE]

1. Date of evaluation: Enter the date of the follow-up assessment. Submission of this page will trigger additional dynamic corms.

Scheduled Follow-up Visits

Method of Contact [CONTACT]

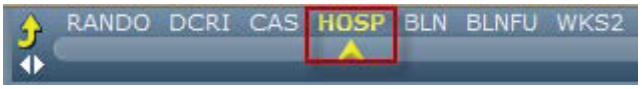
Was this visit performed? Select *Yes* and enter date if any part of the visit was performed. Submission of this form will trigger additional dynamic forms [EXAM], [ASMT], and [MEDS].

If the scheduled visit was not performed, select the one best reason to describe why.

Assessments [ASMT]

Yes responses will trigger additional dynamic forms within this visit.

4. Has the subject had an inpatient hospitalization, outpatient procedure, or emergency department visit? If Yes, complete new [HOSP] visit.



5. Was therapy adjusted? If No, indicate the **one** best reason why therapy was not adjusted at this visit. If Yes, enter details on the dynamic [ADJUST] form.

Resource Use

6. Has the subject been seen as an outpatient by a clinician since the last visit? An outpatient visit refers to any visit (elective or urgent) to an ambulatory clinical setting such as a physician's office, clinic, or urgent care facility.

If Yes, enter the total number of visits that were primarily for assessment or treatment of a cardiovascular issue, and total number for non-cardiovascular reason.

If the subject had an emergency department visit, outpatient procedure, or hospitalization, complete a new Hospitalization [HOSP] visit.

Local Labs [LABS]

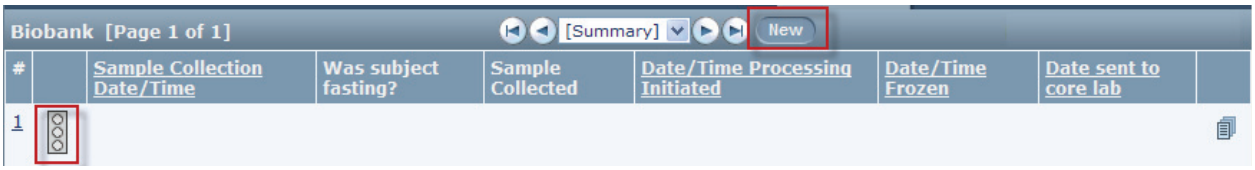
This is a dynamic form. This form will appear if *Yes* is selected on the ASMT form for question 1: *Were local labs performed?*

Protocol required labs are sodium, potassium, BUN, and serum creatinine. Enter results of other labs if performed for standard of care within 1 day of the study visit.

Value: Enter the result from the laboratory report.
Check the appropriate unit of measure for the local laboratory. If necessary, convert units from local laboratory to match listed options. See Laboratory Unit Equivalents for common conversions.

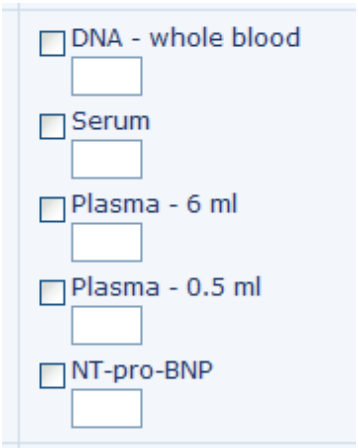
Biobank [BIOBANK]

To enter the first sample collection, select the traffic light. To enter additional samples associated with this visit, select the New button. Create a new form only if additional samples were obtained at a different time.



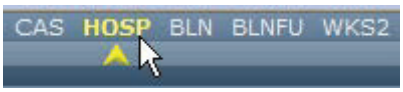
6. Date sent to core lab: Return to this form after the monthly batch shipment and enter the date of shipment.

Note: CRF may not display correct volume of cryovials. Cryovials in lab kits are 2 mL each.

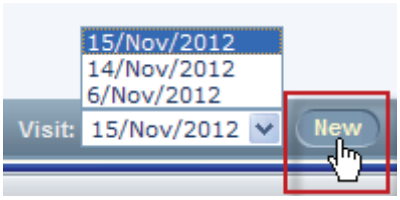


	Expected at each visit	Type
DNA – whole blood	1 or 0	EDTA tube
Serum	2	Red top cryovial
Plasma – 6 mL (EDTA)	5	Purple top cryovial
Plasma 0.5 mL (LH)	2	Green top cryovial
NT-proBNP	1	White top cryovial

Hospitalizations/Emergency Dept. Visits [HOSP]

The HOSP visit is located on the left side of the visit ruler. 

This is a repeating form. To add additional visits, select *New* at the bottom of the screen.



Create a new visit for each hospitalization/ED visit.

If a patient is transferred from one acute care facility to another (eg, from a regional hospital to a tertiary care center), enter as a new hospitalization. The discharge date of the first hospitalization should match the admission date at the transfer hospital.

If the patient is transferred to an extended care facility (nursing home, rehabilitation), go to the CAS visit and complete an extended care [EXTCARE] form. The discharge date of the hospitalization should match the admission date of the extended care facility.

1. Admission or encounter date: If an encounter begins in the ED but the subject is subsequently admitted, enter as an Inpatient visit. Enter date subject arrived at the ED as admission date.

2. Type of encounter

> **ICU:** A specialized nursing area for critically ill patients where there is the capability for invasive and noninvasive medical monitoring
>
> **CCU:** A specialized nursing area for critically ill patients where there is the capability for invasive and noninvasive cardiac monitoring
>
> **Step-down care:** A nonintensive care unit with potential for heart-rhythm monitoring and a nurse-to-patient ratio higher than a regular ward bed.
>
> **Inpatient ward:** Inpatient service of a hospital for observation, care, diagnosis, or treatment.
>
> **Observation unit:**

3. Primary reason for hospitalization: If heart failure or ACS, complete additional details on the dynamic heart failure [HF] or acute coronary syndrome [ACS] form. If *Other cardiovascular* or *Non-cardiovascular*, provide the primary medical diagnosis in the narrative.

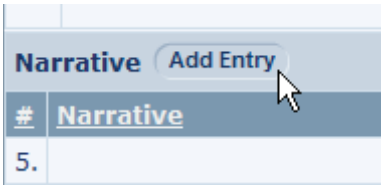
4. Were any cardiac markers drawn? If *Yes,* select all that apply and provide details.

5. Narrative: Please provide a description of the symptoms, treatment, tests/procedures, and outcome of the hospitalization. Include a description of any significant medical and/or surgical information concerning the hospitalization.

If *Other cardiovascular* or *Non-cardiovascular* is selected as primary reason for hospitalization, provide the actual primary medical diagnosis that caused the subject to be hospitalized.

Do not use quotation marks in the narrative

Text space is limited to 200 characters. If additional space is needed, select *Add Entry* as many times as necessary to provide a complete narrative.



Procedures performed

6. Was a heart catheterization performed? includes left or right heart catheterization with or without angiography or ventriculography.

7. Revascularization? Refers to cardiac revascularization. Includes CABG, PCI (with or without stent/angioplasty).

11. VAD: Refers to ventricular assist device.

14. PVD interventions: refers to amputation for arterial insufficiency; vascular reconstruction, bypass surgery, or PCI to the extremities; AAA repair or stent.

15. Mechanical ventilation: does not include standard intubation for a surgical procedure or hand-ventilation during CPR.

16. Ultrafiltration: refers to peritoneal dialysis.

17. Dialysis (acute): refers to hemodialysis.

18. IV Inotropes: refers to medications such as dobutamine (Dobutrex), dopamine (Intropin), norepinephrine (Levophed), and epinephrine.

Facility details

Enter complete information for the hospital/facility. This is required by the EQOL group to obtain billing information

21. Was the subject discharged? If the patient is transferred to an extended care facility (nursing home, rehabilitation), go to the CAS visit and complete an extended care [EXTCARE] form. The discharge date of the hospitalization should match the admission date of the extended care facility.

Heart Failure [HF]

This is a dynamic form. This form will appear if heart failure is selected as the primary reason for hospitalization on a HOSP form.

1. Indicate clinical symptoms of heart failure (select all that apply)

Dyspnea: Shortness of breath

Orthopnea: additional pillows required to ease shortness of breath

Paroxysmal nocturnal dyspnea: awakening suddenly from sleep with uncomfortable awareness of breathing, or with general distress relieved by the upright position lasting greater than 5 minutes.

Acute Coronary Syndrome [ACS]

This is a dynamic form. This form will appear if acute coronary syndrome is selected as the primary reason for hospitalization on a HOSP form.

1. Date and time of onset of ischemic symptoms… In the event of stuttering symptoms, ACS symptom onset is the time at which symptoms became constant in quality or intensity.

4. Longest duration of ischemic symptoms: duration in minutes of the single longest episode of ischemia.

7. Was there hemodynamic instability related to this event? Refers to ischemic pulmonary edema, sustained hypotension with a SBP ≤ to 80 mm Hg for ≥ to 20 minutes, or ischemic symptoms requiring use of intra-aortic balloon pump (IABP) or vasopressors.

8. Was there heart failure complicating this event? Select *Yes* if, in the investigator's opinion, the subject's heart failure contributed to the ACS event.

9. Imaging evidence of new loss of viable myocardium? If *Yes,* indicate imaging method:

ECHO: May include two-dimensional or three-dimensional echocardiography with or without Doppler imaging.

SPECT/PET:

CMR: cardiac magnetic resonance imaging

Extended Care [EXTCARE]

This form is located in the CAS visit. Select the traffic light to enter the first extended care admission. Select the New button to enter additional admissions.

2. Type of extended stay facility

Skilled nursing: A nursing facility with the staff and equipment to give skilled nursing care and, in most cases, skilled rehabilitative services and other related health services.

Rehabilitation: A specialized, nonacute, inpatient medical facility with the primary goal of increasing the subject's independence in performing activities of daily living.

End of life facility: Hospice care

Nursing home (non-skilled): Specialized residential nursing care facility for chronically ill patients who are unable to care for themselves.

3. Was the subject discharged? If the subject was discharged to another extended care facility, create a new Extended Care form and complete the details. If transferred to a hospital, create a new HOSP visit.

Therapy Adjustment [ADJUST]

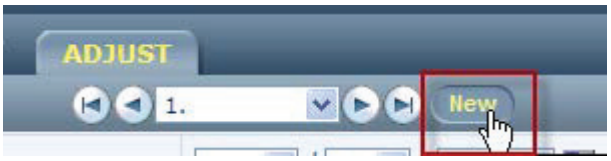
This is a dynamic and repeating form created when *Yes* is selected for *Was therapy adjusted?* on the ASMT form.

Create a new form for each date when a subject's therapy is adjusted (medication started, stopped, increased, decreased, changed frequency, changed to different class, resynchronization therapy, exercise training or cardiac rehab, HR education).

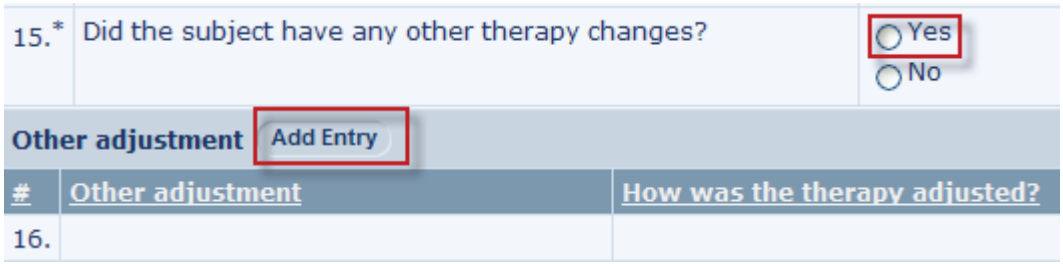
You may record details for multiple therapies on one form.

Select *Yes* for each therapy adjusted on this date and provide additional details.

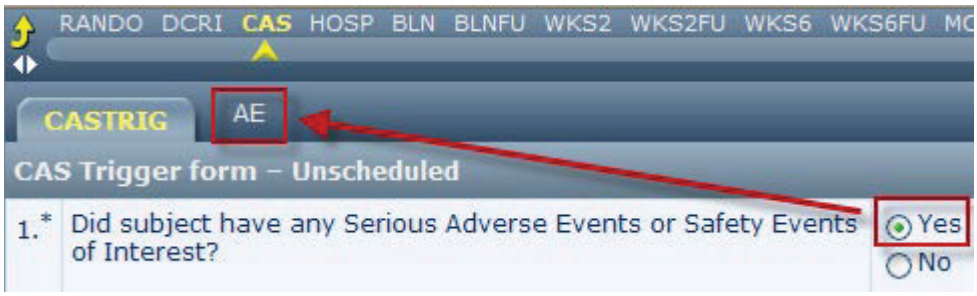
If a change in therapy is on a different date, but not associated with different unscheduled or scheduled visit, select the New button to create an additional [ADJUST] form within this visit. For example, if an additional adjustement is made after assessment of laboratory results.



If therapy is not listed, Select *Yes* for *Did the subject have any other therapy changes?* and select *Add Entry* to enter details for the other adjustment(s). Use the *Add Entry* button to add as many other therapies as needed.



Adverse Events [AE]



This is a dynamic and repeating form located in the CAS visit. Selecting *Yes* for question 1 on the [CASTRIG] form will create the AE form after submitting the [CASTRIG] form.

Non-serious AEs will not be collected in this trial.

SAEs will be collected from time of randomization through the completion of the follow-up period.

The investigator will follow all SAEs until resolution, stabilization, or the event is otherwise explained.

Safety events of interest
The following AEs of interest, which may or may not meet serious criteria, will be collected from randomization through the completion of the follow-up period.

- Symptomatic hypotension
- Symptomatic bradycardia
- Hyperkalemia (potassium > 6.0 meq/dL or requiring change in therapy)
- Worsening renal function (increase in creatinine by 0.5 g/dL from last visit or requiring change in therapy)

The following trial endpoints will not be captured separately as SAEs. These events will be monitored at regular intervals, and will be adjudicated by the Clinical Events Committee (CEC) and reviewed by the DSMB:

- All deaths
- All hospitalizations

In this trial, a serious adverse event (SAE) is any untoward medical occurrence that may result in any of the following outcomes:

- Is life-threatening
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Important medical event that may not result in death, be life-threatening, or require hospitalization may be considered a SAE when, based upon appropriate medical judgment, it may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed above

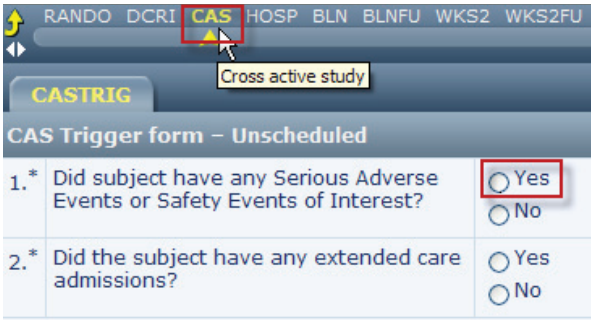
Special Scenarios

- If an AE associated with a hospitalization, capture the AE on the HOSP form.
- If an AE occurs during a hospitalization, capture the AE on the AE form.
- If a subject was hospitalized for the event that led to a death, complete the HOSP form and the DEATH form.

To Enter an SAE

Go to the CAS visit

Select Yes for question 1.



Select the traffic light on the AE form.

For subsequent SAEs, select the New button on the AE form.

1. Onset date and time: Enter the date the initial symptoms of the adverse event started or laboratory assessment drawn. If the event is the worsening of a pre-existing condition, enter the date the condition changed or worsened. Unknown is an option for month, day, and time.

3. End date: Select *Continuing* until one of the following:

- Event resolves or resolves with sequelae
- Subject dies
- Subject is lost to follow-up and end date will never be known

If *Continuing*, select Ongoing as final outcome in question 4. If subject died, enter the date of death.

4. Final Outcome:

- Select one that best describes the outcome of the event at the time of assessment.
- Update your selection if the outcome changes.
- *Ongoing* and *Unknown* are not considered final outcomes and must be updated before the event can be considered complete.
- If reporting an event with a change in severity, select an outcome of *Resolved with sequelae* and an end date for the original event.

- When the AE/SAE completely resolves the final AE/SAE should have an outcome of *Resolved.*

Resolved: Select if the patient has recovered.

Resolved with sequelae: Select if the subject has not returned to baseline status. Describe the sequelae in the narrative section of the eCRF. Note: Use this status for an AE/SAE when the Severity worsens or improves to a new level.

Ongoing: Select if event has not resolved at the time of the assessment.

Death: Select if the patient has died. Enter the date of death as the End date. If this event is not the primary cause of death, the narrative description must contain a statement that the patient died, but this event is not considered the primary cause of death.

Unknown: Select only if you are unable to determine the outcome at the time of assessment.

Onset date: If the event: If the event is the worsening or improving of a pre-existing condition, enter the date the condition changed or worsened. The new AE/SAE should have an onset date equal to the end date of the previous AE/SAE.

End date Enter the date the event resolved, resolved with sequelae, changed in intensity, or select *Ongoing*.

5. Severity: Select one to indicate the intensity at the time of the report as determined by the investigator. If severity increases or decreases to a new level (eg, from mild to moderate, from severe to mild), return to this form and update the selection

Mild: events which are usually transient, requiring no special treatment, and do not interfere with the patient's daily activities;

Moderate: events which introduce a low level of inconvenience or concern to the patient and may interfere with daily activities, but are usually ameliorated by simple therapeutic measures;

Severe: events which interrupt the patient's usual daily activity and traditionally require systemic drug therapy or other treatment.

6. Was this adverse event serious? Answer should be Yes.

7. Please specify a primary cause of the event: Select one and describe. Text space is limited to 200 characters.

8. Are there any laboratory/diagnostic tests? Provide diagnostic procedures/tests used to identify and treat the event: Enter details of each test by selecting *Add Entry.*

10. Concomitant medications: List only relevant concomitant medications. Enter details of each medication by selecting *Add Entry.* You may use brand or generic names for medications. Medications on this form may duplicate information entered on the MEDS form.

12. SAE narratives Provide a description of any significant medical and/or surgical information concerning the SAE from the onset of the SAE until the outcome is resolved including—

- The subject's course in the hospital (if applicable)
- Any significant laboratory values or medications used to treat the event
- Any significant medical or surgical procedures and/or tests/medications used to treat the subject

Do not use quotation marks in the narrative. Text space is limited to 200 characters. To add additional narrative, select the *Add Entry* button. You may add as many entries as needed to report all relevant information.

13. Primary Investigator SAE Electronic Verification Principal Investigators and authorized designees are required/authorized to sign each serious adverse event (SAE). The dated signature confirms that the investigator has personally examined all of the SAE data for completeness and accuracy and all information entered is confirmed as correct to the best of the investigator's knowledge. If changes are made after the signature, the SAE must be re-signed.

End of Study Participation [EOS]

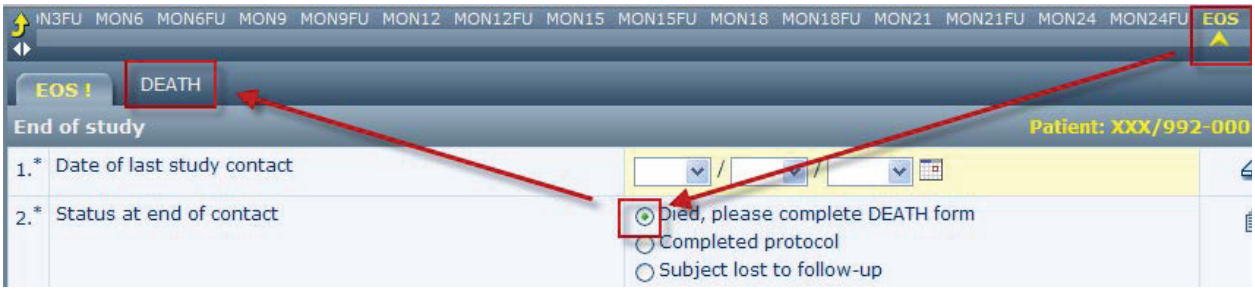
Complete this form when the subject completes participation in the trial.

1. Date of last study contact: Enter the date the subject finished participation in the study, the last study visit (clinic or phone), or if lost to follow-up, the date of last contact with the patient. If the patient died, enter the date of death as the end of study date.

2. Status at end of contact: If subject died, complete the dynamic [DEATH] form.

Death [DEATH]

This is a dynamic form in the EOS visit, located on the far right of the visit ruler. Selecting "Died" for question *2. Status at end of contact* will create the [DEATH] form after submission of the [EOS] form.



1. Date and time of death: Year is required.

3. Was the death witnessed? Indicate if anyone was with the subject at the time of death.

5. Primary cause of death: Select one, as documented in the medical record or on the death certificate.

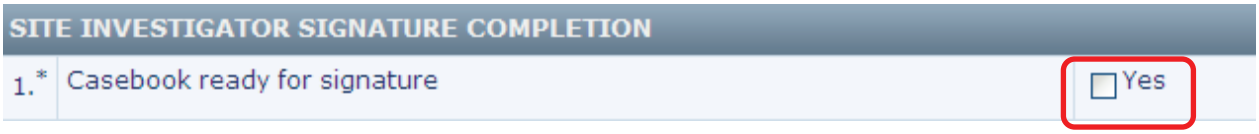
6. Narrative: Complete the narrative using concise medical terminology. Text space is limited to 200 characters.

- Please ensure that all information in the narrative is consistent with data entered into the eCRF.
- Enter a brief chronologic summary of the event including presenting symptoms, evaluation (diagnostic procedures such as x-ray should include a summary of findings), treatment, hospitalization dates, etc. Please include in the clinical narrative details of hemodynamics (SBP, DBP, MAP, CO, PCWP), echocardiography, FiO2, O2 saturations etc., both before and during the event in order to provide a clinical picture of the event as it occurred.
- Text space in narrative field is limited to 200 characters. Do not use quotation marks.
- If the subject was in an extended care facility at the time of death, return to the [EXTCARE] form in the CAS visit and update the discharge disposition.
- If subject dies in a hospital and a HOSP form has not been completed, create a new HOSP form associated with the subject's death.

Signature Completion [SIGN]

- Do not sign the casebook until your Clinical Research Associate (CRA) has confirmed that all the data in the casebook are clean.
- The **Principal investigator** is required to sign each subject's casebook by entering his or her username and password.
- The **Principal Investigator** can designate on the Site Staff Delegation and Signature Log a Sub-Investigator who may complete casebook signature.
- Signing the casebook indicates the following:
    - I confirm that I personally conducted or supervised the investigation and ensured that my designees were informed about their obligations in meeting study commitments.
    - I accept responsibility for the accuracy and completeness of the data in this Case Report Book.
    - By supplying my password and clicking the button marked Submit below, I confirm that all the data entered by me, or by the appropriately qualified persons to whom I delegated study-related duties, is complete and accurate to the best of my knowledge.
- **If changes occur after the signature, the casebook must be re-signed.**

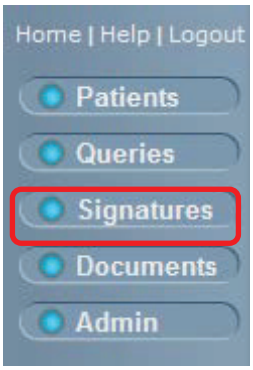
Casebook ready for signature: Select if, after the review of all data in the casebook, the data is clean and ready for the site investigator signature.



Principal Investigator instructions:

To sign a Casebook:

1. Select the Signatures button in the navigation pane to see a list of all Casebooks at your site that are ready for review and signature.
2. To review the Casebook click on the traffic light. All traffic lights should be green prior to signature. To review the details click Sign.
3. Click on Sign or Sign Book in the Signatures column.
   Sign Book = signing the final complete CRF for the subject.
4. Enter your username and password to sign the Casebook.



Form Properties

Form	Visit	Static	Dynamic, created if…	Repeating
Randomization [RAND]	RANDO	✓		
Signature Completion [SIGN]	SIGN	✓		
CAS Trigger form [CASTRIG]	CAS	✓		
Adverse Events [AE]	CAS		✓Did subject have any Serious Adverse Events or Safety Events of Interest? answered as Yes on CASTRIG form.	✓
Extended Care [EXTCARE]	CAS		✓	✓
Hospitalizations [HOSP]	HOSP	✓		✓
Acute Coronary Syndrome [ACS]	HOSP		✓ ACS selected as primary reason for hospitalization on the HOSP form	
Hospitalization for Heart Failure [HF]	HOSP		✓ HF selected as primary reason for hospitalization on the HOSP form	
End of Study [EOS]	EOS	✓		
Death [DEATH]	EOS		✓ Death selected as Status at end of contact on the EOS form	
Date of Evaluation [DOE]	Unscheduled visits, HOSP	✓		
Method of Contact [CONTACT]	Scheduled visits			
Subject Demographics [DEM]	BLN	✓		
Medical History [MEDHX]	BLN	✓		
Baseline Assessments [BASE]	BLN	✓		
Recent Ejection Fraction [EF]	BLN	✓		
Examination [EXAM]	BLN, Scheduled & Unscheduled visits		✓ Date entered on DOE or CONTACT form	
Assessments [ASMT]	BLN, Scheduled & Unscheduled visits		✓ Date entered on DOE or CONTACT form	

Form	Visit	Static	Dynamic, created if…	Repeating
Concomitant Medications [MEDS]	BLN, Scheduled Visits		✓ Date entered on CONTACT form	
Local NT-pro-BNP [PROBNP]	BLN (static), Scheduled & Unscheduled visits	✓	✓ Was local NT-proBNP measured? answered as Yes on [ASMT] form	
Local Labs [LABS]	BLN (static), Scheduled & Unscheduled visits	✓	✓ Were local labs performed? answered as Yes on [ASMT] form	
Therapy Adjustment [ADJUST]	Scheduled & Unscheduled visits	✓	✓ Was therapy adjusted? answered as Yes on [ASMT] form	✓
Biobank [BIOBANK]	Scheduled & Unscheduled visits	✓	✓Were protocol required biological samples collected? answered as Yes on [ASMT] form	✓
Specimen Consent	BLN	✓		

Laboratory Units Equivalents

Test	eCRF Unit	Unit Equivalents
B-type natriuretic peptide (BNP)	ng/L	pg/mL
	pg/mL	ng/L
Hematology		
Hemoglobin	g/dL	G/dL, G/DL, g/dl, g/DL, gm/DL, gm/dl, gm/dL
	g/L	g/l, gm/L, gm/l, GM/L, G/L, G/l
	mmol/L	MMOL/L, mM/L, mMol/L, mm/L, mmol/l
Hematocrit	L/L	
	%	
Platelets	10^9/L	10^9/L, Giga/L, 10^3/mm^3, 10^3/µL, 10^3/cumm, Giga/l x10^9/L, 10^^{9}/L, 10^9/l, 10^^{9}/l
	mm^3	/cumm, /mm^3, /µL, /mcL
WBC	10^9/L	10^9/L, Giga/L, 10^3/mm^3, 10^3/µL, 10^3/cumm, Giga/l x10^9/L, 10^^{9}/L, 10^9/l, 10^^{9}/l
	mm^3	/cumm, /mm^3, /µL, /mcL
Lymphocytes	%	
Total Cholesterol	mmol/L	MMOL/L, mM/L, mMol/L, mm/L, mmol/l
	mg/dL	mg/dl, Mg/DL, MG/DL
Uric acid	mmol/L	MMOL/L, mM/L, mMol/L, mm/L, mmol/l
	mg/dL	mg/dl, Mg/DL, MG/DL
	umol/L	µmol/L, µmol/l, µM/L, µMOL/L
Chemistry		
Sodium	mmol/L	MMOL/L, mM/L, mMol/L, mm/L, mmol/l
	mEq/L	MEQ/L, mEq/L, meq/L
Potassium	mmol/L	MMOL/L, mM/L, mMol/L, mm/L, mmol/l
	mEq/L	MEQ/L, mEq/L, meq/L
BUN/Urea	mmol/L	MMOL/L, mM/L, mMol/L, mm/L, mmol/l
	mg/dL	mg/dl, Mg/DL, MG/DL
Creatinine, Serum	mg/dL	mg/dl, Mg/DL, MG/DL
	umol/L	µmol/L, µmol/l, µM/L, µMOL/L

Conversion Chart Feet to Meters

HEIGHT CONVERSION CHART

Feet	Inches	Cm	Feet	Inches	Cm
4 ft 0 in	48	122	5 ft 10 in	70	178
4 ft 1 in	49	124	5 ft 11 in	71	180
4 ft 2 in	50	127	6 ft 0 in	72	183
4 ft 3 in	51	130	6 ft 1 in	73	185
4 ft 4 in	52	132	6 ft 2 in	74	188
4 ft 5 in	53	135	6 ft 3 in	75	191
4 ft 6 in	54	137	6 ft 4 in	76	193
4 ft 7 in	55	140	6 ft 5 in	77	196
4 ft 8 in	56	142	6 ft 6 in	78	198
4 ft 9 in	57	145	6 ft 7 in	79	201
4 ft 10 in	58	147	6 ft 8 in	80	203
4 ft 11 in	59	150	6 ft 9 in	81	206
5 ft 0 in	60	152	6 ft 10 in	82	208
5 ft 1 in	61	155	6 ft 11 in	83	211
5 ft 2 in	62	157	7 ft 0 in	84	213
5 ft 3 in	63	160	7 ft 1 in	85	216
5 ft 4 in	64	163	7 ft 2 in	86	218
5 ft 5 in	65	165	7 ft 3 in	87	221
5 ft 6 in	66	168	7 ft 4 in	88	224
5 ft 7 in	67	170	7 ft 5 in	89	226
5 ft 8 in	68	173	7 ft 6 in	90	229
5 ft 9 in	69	175	7 ft 7 in	91	231