Fibroblast Growth Factor 23 and Cardiovascular Events in the Chronic Renal Insufficiency Cohort (CRIC) Study

Adjudication Supplement

Potential cardiovascular events were identified based on administrative hospital record review. Hospitalizations containing the following ICD-9/CPT codes were adjudicated:

Event type	ICD-9 Codes	CPT Codes
Myocardial Infarction	410, 411, 412, 413, 414, 36.01, 36.02, 36.05, 36.06, 36.1, 36.10, 36.11, 36.12, 36.13, 36.14, 36.15, 36.16, 36.17, 36.19, 37, 37.2, 37.21, 37.22, 37.23, 38.13, 38.14, 38.15, 38.16, 38.18, 39.22, 39.24, 39.25, 39.26, 39.28	33510, 33511, 33512, 33513, 33514, 33516, 33517, 33518, 33519, 33521, 33522, 33523, 33533, 33534, 33535, 33536, 35470, 35471, 35472, 35473, 35474, 35475, 92980, 92981, 92982, 92984, 92995, 92996
Cerebrovascular Accident	430, 431, 432, 433, 434, 435, 436, 38.10	33572
Congestive Heart Failure	398.91, 402.01, 402.11, 402.91, 425, 428, 429, 514, 518.4	92986, 92987, 92990

During adjudication, hospital records were reviewed by two independent providers. In the case of cerebrovascular accident, both providers were neurologists. Disagreement between reviewers was resolved by consensus. Reviewers were blind to study data during adjudication of hospital records. The following worksheets served as a guide for the adjudication committee in determining event status. For adjudication of myocardial infarction, electrocardiograms (ECGs) were read by a central ECG Reading Center at Wake Forest University. ECGs during the index hospitalization were compared to the closest ECG prior to the admission date, such as those obtained at a prior CRIC study visit or at a previous hospitalization. Standard scoring criteria, Minnesota Code, were performed and results provided to adjudicators.

Participant ID: **Participant Initials:**

Clinical Center: **Site:** **Visit Number:**

CRF Date: **Reviewer ID:**

Myocardial Infarction Review Form

Tracking Number: ___ ___ ___

Guidance for defining abnormality threshold for the lab using question #1. Please provide a response for each question:

1. Select the Troponin I threshold: ***(check only one)***

1 No Troponin I values available (got to Q#3)
2 Cannot determine the type of Troponin ***(go to Q#4)***
3 0.14 - No ULN available ***(go to Q#2)***
4 0.14 – Lab provides only a normal range and no indeterminate range and the ULN is ≥ 0.14. ***(go to Q#2)***
5 If the lab provides only a normal range and no indeterminate range and the ULN is < 0.14.
Specify: 2x ULN = ___.___ ___ ***(go to Q#2)***
6 If the lab provides an indeterminate category in addition to a normal range.
Specify: 2x ULN = ___.___ ___ ***(go to Q#2)***

2. Select the Troponin I Determination: ***(check only one)***

1 Two or more values (~6 hours apart) ≤ ULN and < threshold = **normal.**
2 Any value ≥ threshold = **abnormal**
3 Only one value available < ULN = **normal**
4 One or more value and all > ULN and < threshold = **equivocal**.

3. Select the Troponin T Determination: ***(check only one)***

1 Any Troponin T ≤ 0.03 = **normal**
2 Any Troponin T > 0.03 = **abnormal**
3 No Troponin T

4. Select the Indeterminate Troponin: ***(check only one)***

1 Any Troponin ≤ ULN = **normal**.
2 Any Troponin ≥ 2x ULN = **abnormal**.
3 Any Troponin >ULN < 2x ULN = **equivocal**.
99 Not Applicable

Myocardial Infarction Review Form

5. Was there evidence of muscle trauma or surgery? 1 Yes 0 No

6. Guidance for interpreting CK and LDH results: ***(check only one and go to Q#7)***

	No Muscle Trauma	Muscle Trauma
MB-ULN Available, CK-MB Measured		
CK-MB > 99th percentile of ULN or if not available, > 2x ULN	1 Abnormal	2 Equivocal
CK-MB < 99th percentile of ULN or if not available, ≤ 2x ULN	3 Normal	4 Normal
No MB ULN Available, CK-MB Measured		
CK-MB ≥ 10% CKTOT	5 Abnormal	6 Equivocal
CK-MB ≥ 5% and <10% CKTOT	7 Equivocal	8 Equivocal
CK-MB <5% CKTOT	9 Normal	10 Normal
No CK-MB measured, CKTOT and LDH measured		
CKTOT ≥ 2x ULN **and** LDH ≥ 2x ULN	11 Abnormal	12 Equivocal
[(CKTOT>ULN **and** < 2x ULN) **AND** (LDH>ULN **and** <2x ULN)]	13 Equivocal	14 Equivocal
[CKTOT>2x ULN **AND** (LDH<2x ULN **and** > ULN)]	15 Equivocal	16 Equivocal
[(CKTOT<2x ULN **and** > ULN) **AND** (LDH>2x ULN)]	17 Equivocal	18 Equivocal
[CKTOT<ULN **AND** (LDH<2x ULN **and** >ULN)]	19 Normal	20 Normal
[(CKTOT<2x ULN **and** >ULN) **AND** LDH<ULN]	21 Normal	22 Normal
CKTOT<ULN **AND** LDH<ULN	23 Normal	24 Normal
No CK-MB measured, No LDH, CKTOT measured		
CKTOT ≥ 2x ULN	25 Equivocal	26 Equivocal
CKTOT <2x ULN	27 Normal	28 Normal
No CK-MB measured, No CKTOT, LDH measured		
LDH ≥ 2x ULN	29 Equivocal	30 Equivocal
LDH <2x ULN	31 Normal	32 Normal
No CK-MB measured, No CKTOT or LDH measured		
	33 Missing	34 Missing

Myocardial Infarction Review Form

7. Was cardiac pain present? 1 Yes ***(go to Q#8)*** 0 No ***(go to Q#9)*** 88 Uncertain ***(go to Q#8)***

8. Guidance for myocardial infarction determination based on ECG data, cardiac biomarkers and **cardiac pain** documentation: ***(check only one and go to Q#10)***

	Cardiac Biomarkers Classification			
ECG Pattern	**Abnormal**	**Equivocal**	**Missing**	**Normal**
Evolving Diagnostic ECG (Evolution of major Q-wave)	1 Definite MI	2 Definite MI	3 Definite MI	4 Definite MI
Positive ECG (Evolution of ST Elevation with or without Q-wave **OR** new LBBB)	5 Definite MI	6 Probable MI	7 Probable MI	8 No MI
Non-Specific ECG (Evolution of ST-T Depression/inversion alone **OR** evolution of minor Q-waves alone)	9 Definite MI	10 Possible MI	11 No MI	12 No MI
ECG Negative for Ischemia Normal, Absent, Uncodable, or Other	13 Definite MI	14 Possible MI	15 No MI	16 No MI

9. Guidance for myocardial infarction determination based on ECG data, cardiac biomarkers and **absence of cardiac pain** documentation: ***(check only one and go to Q#10)***

	Cardiac Biomarkers Classification			
ECG Pattern	**Abnormal**	**Equivocal**	**Missing**	**Normal**
Evolving Diagnostic ECG (Evolution of major Q-wave)	1 Definite MI	2 Definite MI	3 Definite MI	4 Definite MI
Positive ECG* (Evolution of ST Elevation with or without Q-wave **OR** new LBBB)	5 Definite MI	6 Probable MI	7 Possible MI	8 No MI
Non-Specific ECG (Evolution of ST-T Depression/inversion alone **OR** evolution of minor Q-waves alone)	9 Definite MI	10 Possible MI	11 No MI	12 No MI
ECG Negative for Ischemia Normal, Absent, Uncodable, or Other	13 Definite MI	14 No MI	15 No MI	16 No MI

Myocardial Infarction Review Form

*10. What is your global impression of the final outcome using all available information in this medical record?
1 No MI 3 Probable MI 88 Can't Determine
2 Possible MI 4 Definite MI

*11. What was the participant's vital status at the discharge?
1 Alive 88 Unknown
2 Dead

*These responses must be concordant with the responses of the 2nd reviewer.

Note: If the participant's discharge status is dead, please complete a death review form.

12. Did the patient undergo coronary revascularization?
1 Yes 0 No

a. If "**Yes**": *(Check only one answer)*
1 Coronary angioplasty (including angioplasty with stenting, antherectomy)
2 Coronary artery bypass graft
98 Other (Specify):_____

Comments:

[add comments here]

Participant ID: _____ Participant Initials: _____

Clinical Center: _____ Site: _____ Visit Number: _____

CRF Date: ____ / ____ / _____ Reviewer ID: _____

EVENT CLASSIFICATION FORM

1. Tracking number: ___ ___ ___

2. Date events reviewed: ____ / ____ / _____ (*mm/dd/yyyy*)

***Please base your review on the documentation provided from this investigation. Your determination must be based on the criteria for CRIC outcome events* defined in the "Outcomes MOP".**

3. Was this a cerebrovascular event? ☐ 1 Yes ☐ 0 No (***Go to Q#5***)

   3a. According to the CRIC outcome definitions, was this event (***select only one***)
   - ☐ 1 Intraparenchymal hemorrhage (**IPH**)?
   - ☐ 2 Subarachnoid hemorrhage (**SAH**)?
   - ☐ 3 Large-vessel cerebral infarction (**LVCI**)?
   - ☐ 4 Cardioembolic cerebral infarction (**CCI**)?
   - ☐ 5 Small-vessel cerebral infarction (**SVCI**)?
   - ☐ 6 Cerebral infarction not otherwise specified (**CINOS**)?

   3a1. Please categorize probability for the cerebrovascular event?
   - ☐ 1 Definite ☐ 2 Probable
   - ☐ 3 Improbable ☐ 88 Can't Determine

4. Was there a second cerebrovascular event during this hospitalization? ☐ 1 Yes ☐ 0 No (***Go to Q#5***)
   If yes:

   4a. According to the CRIC outcome definitions, was this event (***select only one***)
   - ☐ 1 Intraparenchymal hemorrhage (**IPH**)?
   - ☐ 2 Subarachnoid hemorrhage (**SAH**)?
   - ☐ 3 Large-vessel cerebral infarction (**LVCI**)?
   - ☐ 4 Cardioembolic cerebral infarction (**CCI**)?
   - ☐ 5 Small-vessel cerebral infarction (**SVCI**)?
   - ☐ 6 Cerebral infarction not otherwise specified (**CINOS**)?

   4a1. Please categorize probability for the cerebrovascular cerebrovascular event?
   - ☐ 1 Definite ☐ 2 Probable
   - ☐ 3 Improbable ☐ 88 Can't Determine

EVENT CLASSIFICATION FORM

1. Tracking number: ___ ___ ___
2. Date events reviewed: ___ / ___ / _____ (*mm/dd/yyyy*)

5. Was the patient hospitalized? ☐ 1 Yes (go to 5a) ☐ 0 No (***STOP***)
   If yes:

   5a. What was the patient's vital status at discharge? (***select only one***)
   - ☐ 1 Alive (**STOP**)
   - ☐ 2 Dead (**STOP and complete a Death Review form**)
   - ☐ 88 Unknown (**STOP**)

Comments:

[Type comments here...]

Figure 1. Flow Chart for Initial Stroke Evaluation

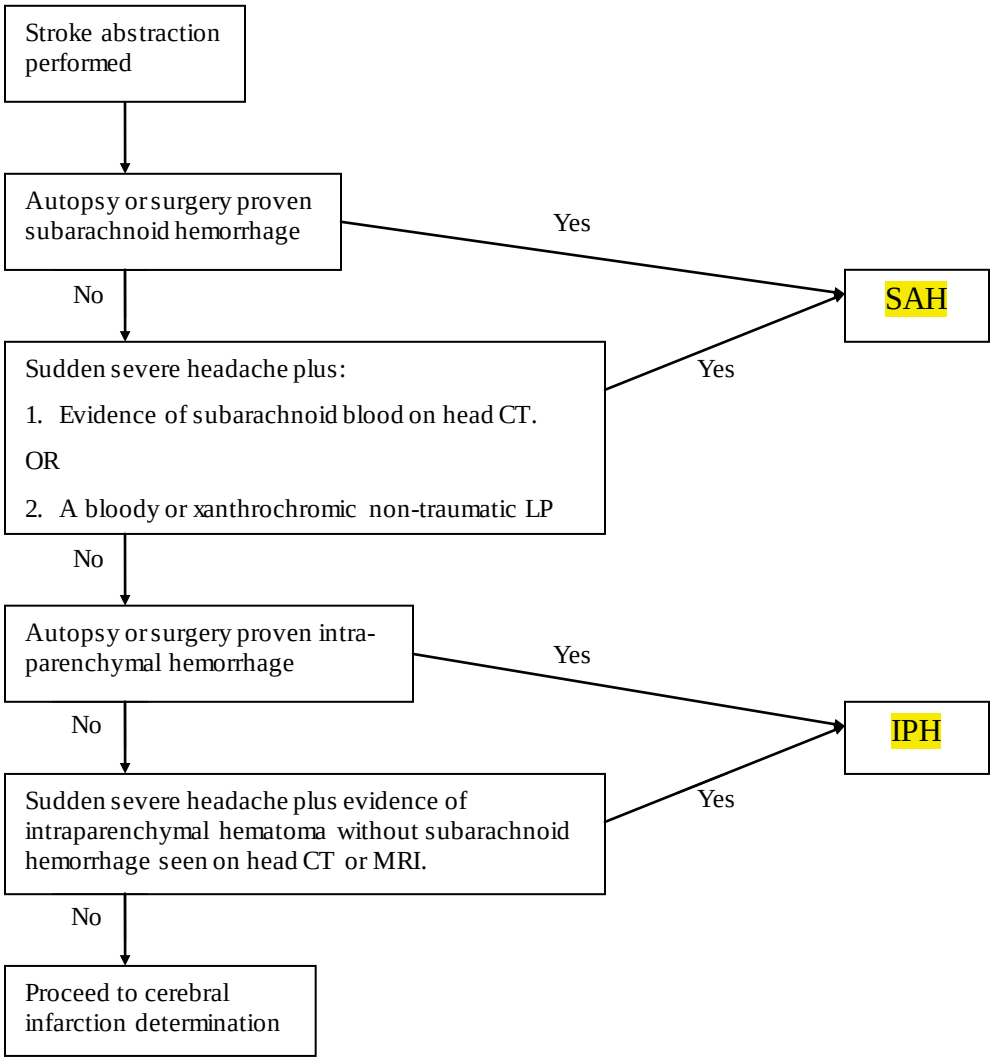


Figure 2. Flow Chart for Cerebral Infarction Determination.

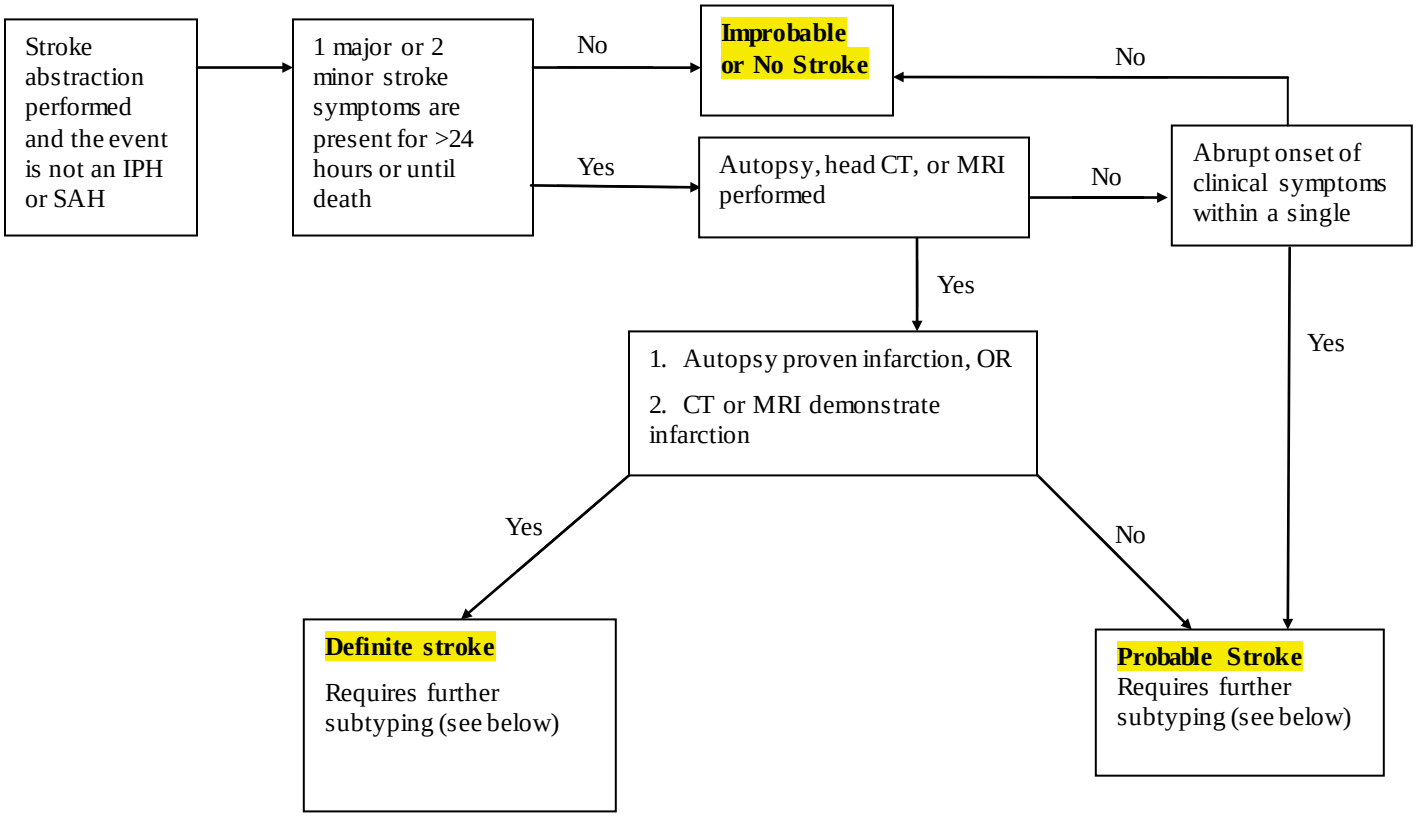
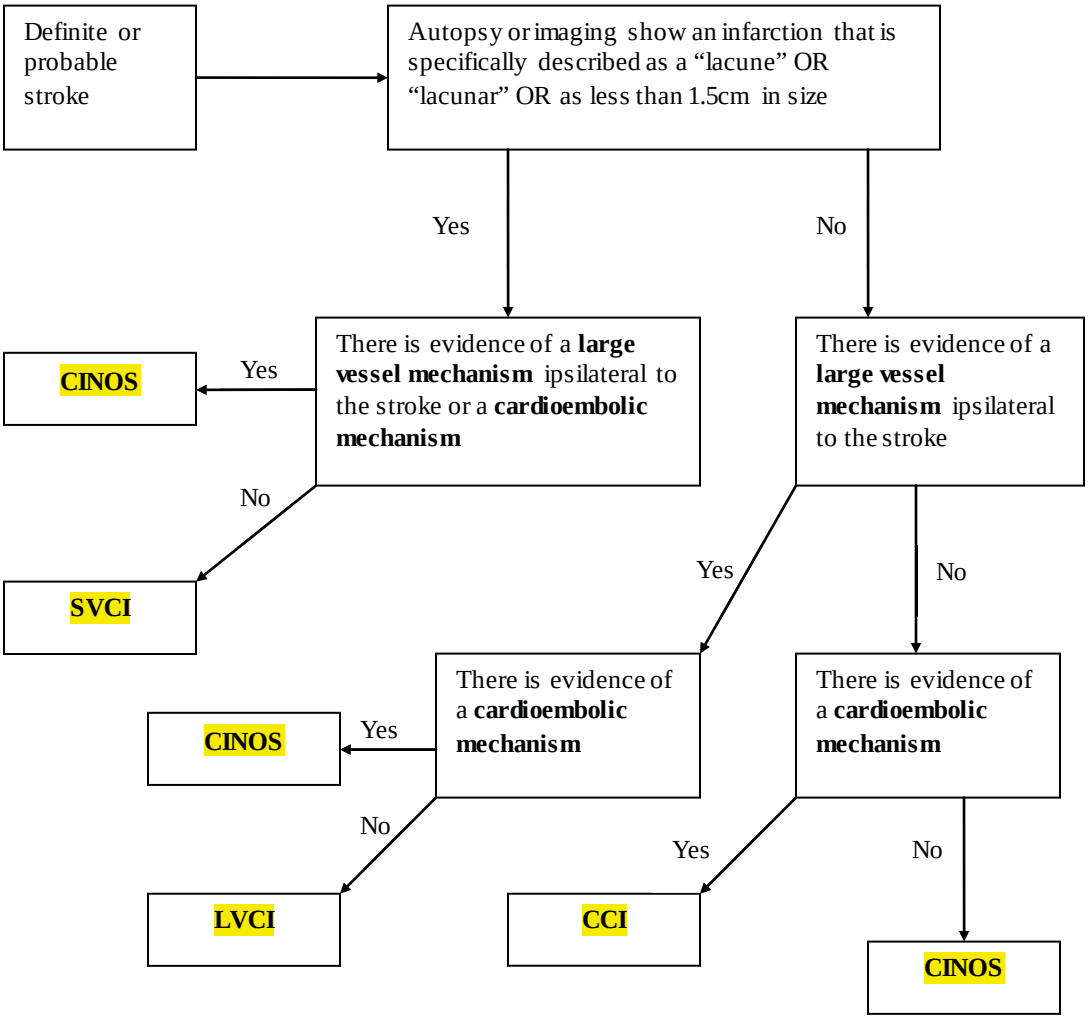


Figure 3. Flow Chart for Cerebral Infarction Subtype Determination



Participant ID: | **Participant Initials:**

Clinical Center: | **Site:** | **Visit Number:**

CRF Date: | **Reviewer ID:**

IN-PATIENT HEART FAILURE EVENT REVIEWER FORM

Instructions to Reviewers: *The data collected on this form should focus on admission and the first 48 hours of hospitalization.*

1. Tracking number: ___ ___ ___

2. Is there documentation of clinical symptoms (dyspnea on exertion or rest, paroxysmal nocturnal dyspnea, and/or orthopnea?
   ☐ 1 Yes ☐ 0 No ☐ 88 Uncertain

3. Do notes or radiology reports document radiographic evidence of pulmonary edema or pulmonary congestion?
   ☐ 1 Yes ☐ 87 Not Documented ☐ 0 No ☐ 88 Uncertain

4. Physical Exam findings to include **at least two** of the following:

   Provide one response to each item

   4a. Inspiratory crackles ("rales") involving at least 1/3 of the lower lung fields
   ☐ 1 Yes ☐ 0 No ☐ 87 Not Documented ☐ 88 Uncertain

   4b. S3 gallop on auscultation
   ☐ 1 Yes ☐ 0 No ☐ 87 Not Documented ☐ 88 Uncertain

   4c. Jugular venous distension > 5cm
   ☐ 1 Yes ☐ 0 No ☐ 87 Not Documented ☐ 88 Uncertain

   4d. Peripheral edema
   ☐ 1 Yes ☐ 0 No ☐ 87 Not Documented ☐ 88 Uncertain

Participant ID:		**Participant Initials:**	
Clinical Center:	**Site:**	**Visit Number:**	
CRF Date:		**Reviewer ID:**	

IN-PATIENT HEART FAILURE EVENT REVIEWER FORM

5. Invasive hemodynamic or echocardiogram evidence including any of the following: ***Check all that apply***

5a. Pulmonary capillary wedge pressure >18 mm Hg
- ☐ 1 Yes
- ☐ 0 No
- ☐ 87 Not Documented
- ☐ 88 Uncertain

5b. Cardiac index < 2.0 L/min/M^2
- ☐ 1 Yes
- ☐ 0 No
- ☐ 87 Not Documented
- ☐ 88 Uncertain

5c. Left ventricular ejection fraction ≤ 35%
- ☐ 1 Yes
- ☐ 0 No
- ☐ 87 Not Documented
- ☐ 88 Uncertain

6. *How would you characterize this event?
- ☐ 1 Definite Heart failure
- ☐ 2 Probable Heart Failure
- ☐ 0 Not Heart Failure

7. *What was the participant's vital status at discharge?
- ☐ 1 Alive
- ☐ 0 Dead *(Complete a death review form)*
- ☐ 88 Unknown

*These responses must be concordant with the responses of the 2nd reviewer.

8. Did the patient undergo coronary revascularization? ☐ 1 Yes ☐ 0 No
   a. If "**Yes**": *(Check only one answer)*
   - ☐ 1 Coronary angioplasty (including angioplasty with stenting, antherectomy)
   - ☐ 2 Coronary artery bypass graft
   - ☐ 98 Other (Specify):

9. Was an echocardiogram performed during this hospitalization? ☐ 1 Yes ☐ 0 No ☐ 99 Can't Determine
   a. If **"YES"**, what was the ejection fraction? ___ ___% ☐ 99 Unavailable

Participant ID:		**Participant Initials:**	
Clinical Center:	**Site:**	**Visit Number:**	
CRF Date:		**Reviewer ID:**	

IN-PATIENT HEART FAILURE EVENT REVIEWER FORM

Comments:

See Below for Heart Failure Criteria

Heart Failure Criteria

Hospitalization for clinical symptoms (dyspnea on exertion or rest, paroxysmal nocturnal dyspnea, and/or orthopnea) with at least one of the following objective findings:

1. Radiographic evidence of pulmonary edema or pulmonary congestion

OR

2. Physical Exam findings consistent with CHF to include at least two of the following:

   a) Inspiratory crackles ("rales") involving at least 1/3 of the lower lung fields
   b) S3 gallop on auscultation
   c) Jugular venous distension > 5cm
   d) Peripheral edema.

OR

3. Invasive hemodynamic or echocardiogram evidence of CHF including any of the following:

   a) Pulmonary capillary wedge pressure >18 mm Hg
   b) Cardiac index < 2.0 L/min/M^2
   c) Left ventricular ejection fraction ≤ 35%

9a. If there is more than one echo during this hospitalization, please list the ejection fraction of the first echo performed.

Peripheral vascular disease was defined by the presence of the following codes and not further adjudicated:

Event type	ICD-9 Codes	CPT Codes
Peripheral Vascular Disease	440, 441, 443, 444	24900, 25900, 25927, 26910, 27880, 33322, 33335, 33860, 33870, 35301, 35311, 35321, 35331, 35341, 35351, 35355, 35361, 35363, 35371, 35372, 35381, 35390, 35450, 35452, 35454, 35456, 35458, 35459, 35511, 35516, 35518, 35521, 35531, 35533, 35536, 35541, 35546, 35548, 35549, 35551, 35556, 35558, 35560, 35563, 35565, 35566, 35571, 35582, 35583, 35585, 35587, 35612, 35616, 35621, 35623, 35631, 35636, 35641, 35646, 35650, 35651, 35654, 35656, 35661, 35663, 35665, 35666, 35671, 35700, 35879, 75962, 75964, 75966, 75968, V49.7