MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS

(MESA)

Manual of Operations

Updated March 12, 2004

This section: 3/12/04 Version

Table of Contents

1. Overview ..... Section **1**, Page **1**

2. Identification of Possible Events ..... Section **2**, Page **1**

2.1 Events Identified by Follow-Up Phone Call ..... Section **2**, Page **1**

2.2 Events Identified by Other Methods ..... Section **2**, Page **1**

2.3 Notification of the Coordinating Center ..... Section **2**, Page **2**

3. Events Investigation ..... Section **3**, Page **1**

3.1 Initial Notification ..... Section **3**, Page **2**

3.2 Eligibility ..... Section **3**, Page **2**

3.3 Nonfatal Events ..... Section **3**, Page **4**

3.4 Fatal Events ..... Section **3**, Page **7**

3.5 Final Notification ..... Section **3**, Page **8**

4. MESA Criteria for Events ..... Section **4**, Page **1**

4.1 Criteria for Non-Fatal Events ..... Section **4**, Page **1**

5. Events Review and Classification ..... Section **5**, Page **1**

5.1 Important Definitions ..... Section **5**, Page **1**

5.2 Reporting of Event Type (by Field Center Events Staff) ..... Section **5**, Page **2**

5.3 Review Process ..... Section **5**, Page **2**

6. Quality Control ..... Section **6**, Page **1**

7. Events Data Management Software ..... Section **7**, Page **1**

APPENDIX A: ECG Reading Center Protocol ..... Appendix **A**, Page **1**

APPENDIX B: Infarct Subtype Classification ..... Appendix **B**, Page **1**

APPENDIX C: General Instructions for Administration and Completion of Events Forms ..... Appendix **C**, Page **1**

C.1 General Interviewing Instructions ..... Appendix **C,** Page **1**

C.2 General Instruction for Completing Paper Forms that will be Scanned (TELEforms) ..... Appendix **C**, Page **6**

C.3 Instructions for Online Review Forms ..... Appendix **C**, Page **11**

APPENDIX D: MESA Events Forms Instructions (Question by Question) ..... Appendix **D**, Page **1**

D.1 Follow-up Phone Call Forms ..... Appendix **D.1**, Page **1**

D.2 Initial Notification of Potential Event/Death ..... Appendix **D.2**, Page **1**

D.3 Events Eligibility ..... Appendix **D.3**, Page **1**

D.4 Events Eligibility Addendum ..... Appendix **D.4**, Page **1**

D.5 Hospital Abstraction: Cardiac/PVD ..... Appendix **D.5**, Page **1**

D.6 Hospital Abstraction Form: Stroke/TIA ..... Appendix **D.6**, Page **1**

D.7 Physician Questionnaire: Cardiac/PVD ..... Appendix **D.7**, Page **1**

D.8 Physician Questionnaire: Stroke/TIA ..... Appendix **D.8**, Page **1**

D.9 Physician Questionnaire: Cardiac Death ..... Appendix **D.9**, Page **1**
D.10 Cardiac/PVD Interview ..... Appendix **D.10**, Page **1**
D.11 Informant Interview ..... Appendix **D.11**, Page **1**
D.12 Interview for Stroke/TIA Symptoms ..... Appendix **D.12**, Page **1**
D.13 Narrative for Stroke ..... Appendix **D.13**, Page **1**
D.14 Final Notice of Event/Death Form ..... Appendix **D.14**, Page **1**
D.15 Cardiac/PVD Review ..... Appendix **D.15**, Page **1**
D.16 Stroke/TIA Review ..... Appendix **D.16**, Page **1**
D.17 Mortality Review ..... Appendix **D.17**, Page **1**
D.18 Events Contact Log ..... Appendix **D.18**, Page **1**

APPENDIX E: Sample Letters for MESA Events ..... Appendix **E**, Page **1**
E.1 Introduction ..... Appendix **E,** Page **1**
E.2 Sample MESA Events Letters ..... Appendix **E,** Page **2**

APPENDIX F: Glossary of Key Surveillance/Events Data Collection Terms ..... Appendix **F**, Page **1**

APPENDIX G: Drug Therapies: Synonyms and Equivalents ..... Appendix **G**, Page **1**

to contact the subject/family to get more information. The Field Center should retain the public notice in the subject's record. Any information that surveillance staff obtain regarding a potential event should be followed up on, regardless of source.

2.3 Notification of the Coordinating Center

When a potential event is identified, Field Center staff complete and scan an *Initial Notification of Potential Event/Death* form. Scanning the form into the database alerts the Coordinating Center of the potential event(s). This helps the Coordinating Center track event investigations that are in process, and triggers the next events collection steps for field center staff.

2.2.3 Events Identified Through Investigation of Another Potential Event

While the Field Center staff is investigating an event, they may discover another possible event. If that new event happened on the same day (for outpatient events) or during the same hospitalization (for hospitalized events) then that new event may become part of the already existing investigation. The Field Center may edit the events forms (ex/Initial Notification) to include the new information. Alternately, the Field Center may choose to open a new investigation for the newly identified event. In the case that the Field Center opens a new investigation, and the events end up being connected, they will be linked during the review process by the physician reviewers.

2.2.4 Events Identified Through a National Death Index (NDI) Search

According to its web site, "The National Death Index (NDI) is a central computerized index of death record information on file in the State vital statistics offices. Working with these State offices, NCHS established the NDI as a resource to aid epidemiologists and other health and medical investigators with their mortality ascertainment activities."

Periodically, the Coordinating Center will search the NDI for participants with whom the study has lost touch. The Field Centers will then be notified of these deaths so that additional information can be obtained and so that the death can go to physician review.

A Field Center may itself search the National Death Index (NDI) for deaths in their subject pool if the Field Center needs to use the NDI as a way to obtain death certificates. If the NDI identifies a subject as having died (previously unknown to the FC), the Field Center can immediately attempt to contact the subject/proxy to get more information. Any information obtained from the NDI should be retained in the subject's record. The Field Center must go through an application process (which involves the IRB at the Field Center's own institution) in order to begin receiving NDI information. The application and additional information can be found at the NDI web site:

National Death Index
Division of Vital Statistics
National Center for Health Statistics
3311 Toledo Road, Room 7316
Hyattsville, Maryland 20782
(301) 458-4444
email: ndi@cdc.gov
Web site: http://www.cdc.gov/nchs/r&d/ndi/ndi.htm

2.2.5 Events Identified by the Field Center through an Obituary or Other Public Notice

Periodically, a Field Center may come across an obituary or other public notice pertaining to a subject in the MESA study. The Field Center should immediately attempt

2. Identification of Possible Events

The primary means of identifying possible events in MESA is participant self-report via post-baseline contacts (Follow-up Calls) conducted by telephone. Field center staff may also learn of potential events in other ways: participants may notify the clinic when they experience an event; a MESA examination may identify a possible event; investigation of one event may identify another event; National Death Index (NDI) search could identify a death; or field center staff may learn of a participant's death through an obituary or other public notice.

2.1 Events Identified by Follow-Up Phone Call

A trained interviewer administers a standardized interview by telephone to the participant at scheduled intervals between clinic visits (see *Appendix D.1, Follow-Up Phone Call).* The interviewer asks participants if they have had any new diagnoses of MI, angina, CHF, PVD, stroke, or TIA, and whether these involved inpatient or outpatient treatment. The interviewer also asks the participants to identify all hospitalizations and initial nursing home admissions that have occurred since their last field center contact, in addition to any relevant procedures or tests. Follow-up staff refers all possible events to events surveillance staff for investigation.

During the course of follow-up, staff may also identify deaths, which are also referred to surveillance staff for investigation. As closeout for non-hospitalized deaths for which CVD is indicated as a possible primary or contributory cause, an interviewer makes a follow-up phone call to the participant's next-of-kin or other knowledgeable proxy to identify circumstances surrounding the death.

2.2 Events Identified by Other Methods

2.2.1 Events Identified by Participant Notification

Participants are asked to notify the Field Center if they are hospitalized or receive a diagnosis of CVD from their personal physician. This request is reiterated to participants during each clinic visit and follow-up phone call. In addition, newsletters sent out to participants remind them to contact the field center should they be hospitalized or diagnosed with CVD. If a participant identifies a potential event, then surveillance staff will obtain the proper information from the participant and/or the participant's proxy.

2.2.2 Events Identified Through MESA Clinic Visits

Prior to clinic visits, staff asks participants questions, similar to those asked during the interim contact interview, related to new diagnoses of CVD and hospitalizations/nursing home admissions. If the participant identifies a potential event during the field center visit, surveillance staff collects available data about that event during the clinic visit.

3.4.2 Out-of-Hospital Deaths

Eligible out-of-hospital deaths, which include deaths in the emergency room, nursing homes, dead-on-arrivals, and participants admitted without ever showing vital signs, require a different kind of investigation. For possible out-of-hospital stroke deaths (ICD-10 I60–I67 or G45–G46), surveillance staff identifies a physician to whom to send a *Physician Questionnaire: Stroke/TIA*. Events staff should also request records from the physician at this time. Staff also identifies an informant to be administered the *Stroke/TIA Narrative* form (do not administer the *Interview for Stroke/TIA Symptoms*). For possible cardiac deaths (i.e., deaths eligible for investigation per at least one non-cerebrovascular ICD-10 code), surveillance staff contacts at least one informant (e.g., spouse or next-of-kin listed on the death certificate or proxy identified on the clinic tracking form*)* to interview using the *Informant Interview* form. Staff also identifies one physician (e.g., participant's personal physician or the one certifying the death) to whom a *Physician Questionnaire: Cardiovascular Death* form is sent**. Again, request records at the same time.** If staff subsequently identifies a better informant or physician, an additional interview is conducted or an additional questionnaire is sent to this person. Staff may need to make multiple contacts to complete collection of these forms. If an eligible out-of-hospital death has an autopsy or coroner report, staff scans and transmits it to the Coordinating Center as part of the event packet.

3.5 Final Notification

After the Field Center staff has completed their investigation, they will complete and submit a *Final Notification* form. This form will tell the Coordinating Center what type of event(s) the Field Center believes are included in that investigation. There must only be one *Final Notification* form for each investigation, but multiple eligible event types (from that investigation period) may be marked. Investigations are not considered complete until all documentation for both cardiac and stroke has been submitted. Do not scan a *Final Notification* until all documentation is in the system. Once a *Final Notice* is received by the Coordinating Center, it is considered complete and ready to be sent to the M&M Physician Reviewers for classification.

NOTE: If an investigation contains both eligible and ineligible events, do not mark the "ineligible events" choice on the form. Only mark this option on the *Final Notice* if there are no eligible events.

records will be considered as part of the hospital record at large.

NOTE: Nursing stays are also considered 'outpatient' events. However, nursing home records are of limited interest. Information from nursing homes should only be obtained for limited instances such as the first admission for chronic care or death. Other nursing home records, such as stays in a rehabilitation center located in the same hospital, short-term rehabilitations after hospitalization, or long-term chronic care stays that are permanent are not of interest and do not need to be obtained.

3.4 Fatal Events

Events staff completes an *Events Eligibility* form for all participant deaths. Whenever possible, the Field Center Abstractor should be the staff member who completes the *Events Eligibility* form, although the Events Coordinator (if trained) may fill out the form if the form is then approved by the Abstractor. This includes obtaining the ICD-10 codes of the primary and any secondary causes of death listed on the death certificate. Typically, surveillance staff can obtain these from the appropriate Health Department, but, if necessary, a MESA nosologist codes the causes. Events staff should not assign codes themselves.

Using the *Events Eligibility* form, surveillance staff reviews the ICD-10 codes of all deaths to determine eligibility for further investigation. Deaths requiring investigation are all those with the following codes:

<u>Underlying Cause:</u>	
I** (except I60-I69)	Cardiovascular disease
E10-E14	Diabetes
J81	Pulmonary edema
R96,R98,R99	Ill-defined
R07	Chest pain
<u>Any Listed Cause</u>:	
I20-I23	Acute CHD
I60-I67, G45-G46	Acute stroke

3.4.1 Hospitalized Deaths

Eligible hospitalized fatal events will be eligible for hospital record abstraction (described above), in which case surveillance staff performs a hospitalization investigation as well as an investigation of the fatal event. If the in-hospital death is not eligible on the basis of the discharge ICD-9 codes but is eligible on the basis of the death certificate codes, surveillance staff still undertakes a hospital investigation. If an eligible in-hospital death has an autopsy, surveillance staff copies the autopsy report and submits it to the Coordinating Center as part of the event's case packet. The events staff may also attempt to interview the participant's proxy to obtain more information using the *Informant Interview* or *Stroke Narrative* (depending on the type of death) if the information from the hospital is insufficient. These forms are on an "if needed" basis.

is eligible on the basis of any other ICD-9 code, the Field Center Abstractor abstracts pertinent data at the field center using the *Hospital Abstraction: Cardiac/PVD* form. If a participant experiences both a cerebrovascular and cardiac event, both sets of forms must be completed. If the hospital records are unavailable or do not provide adequate information to assess the event's eligibility, a *Cardiac/PVD Interview* or *Interview for Stroke/TIA Symptoms* may need to be administered.

Screening Codes

For charts that include ICD-9 procedure code 35 or diagnosis codes 250, 390–459, 745–747, 794.3, 798-799, the abstractor reads the discharge summary looking for evidence of eligible conditions. If a possible condition is noted, the chart is also considered eligible.

If the chart is not eligible for abstraction, the abstractor simply records the ICD-9 codes on the *Events Eligibility* form, scans the form and discharge summary, and transmits this documentation to the Coordinating Center. The Field Center must also complete a *Final Notification* form indicating the reason that the event is ineligible. If the Field Center realizes early on that the event never happened (participant was never hospitalized) or is a duplicate of another investigation then they may delete the *Initial Notification* from the database. Once an *Event Eligibility* form has been submitted, however, the Field Center must continue on and submit a *Final Notice*, marking 'Not an Event' as the type.

3.3.2 Nonfatal Outpatient Events

Participants may also report outpatient diagnoses for outcomes of interest to MESA. These will most likely be in cases of angina, CHF, PVD, and TIA but are also possible in cases of MI or stroke. In addition to diagnoses, MESA wants to capture the occurrence and results of certain outpatient cardiovascular procedures. If there is an outpatient cardiac diagnosis or procedure, the Field Center will first request records (both physician notes and procedure reports). If the obtained information is not sufficient, then the Field Center will send a *Physician Questionnaire: Cardiac/PVD* to the participant's treating physician. If staff believes additional information on symptoms is needed to ascertain the cardiac outpatient event (this is rarely needed), a *Cardiac/PVD Interview* is administered with the participant or appropriate proxy. All pertinent records are noted on the *Final Notice* form. All of these records should be scanned if the case is eligible for review. If the case is not eligible for review, the procedures should be marked on the *Final Notice*, but not scanned.

If a non-fatal outpatient TIA or stroke is reported, surveillance staff requests all records and also conducts the *Interview for Stroke/TIA Symptoms* with the participant, adding the *Stroke/TIA Narrative* if needed to provide a full picture of the event. (If the requested medical records are insufficient, then the staff should also send a *Physician Questionnaire: Stroke/TIA* to the appropriate physician.) If the participant is incapacitated and thus unable to respond coherently to the *Interview*, then the staff should administer the *Stroke/TIA Narrative* (<u>not</u> the *Interview*) to an appropriate proxy or informant.

NOTE: Emergency Room visits are considered 'outpatient' for MESA unless the participant is subsequently admitted to the hospital. If the patient is admitted to the hospital through the ER, the event is considered 'hospitalized'. The ER and ambulance

Table 3.1 shows ICD-9 codes eligible for further investigation/abstraction.

Table 3.1
Eligible Hospital Abstraction Codes*[1]

	ICD-9 Code[1]	Description
Procedures	36	Operation-heart vessels
	37	Operation-heart and pericardium
	38	Operation-incision, excision, occlusion of vessels
	39	Other operation on vessels
	84.1	Leg amputation
	88.5	Cardiac catheterization
Diagnoses	402	Hypertensive heart disease
	410	Acute MI
	411	Acute CHD
	412	Old MI
	413	Angina
	414	Other CHD
	425	Cardiomyopathy
	427	Cardiac dysrhythmias
	428	Heart failure
	429	Ill-defined heart disease
	430	Subarachnoid hemorrhage
	431	Intracerebral hemorrhage
	432	Other brain hemorrhage
	433	Occlusion/stenosis of precerebral arteries
	434	Occlusion of cerebral arteries
	435	TIA
	436	Other CVA
	440	Atherosclerosis
	441	Aortic aneurysm
	443.8	PVD (specified)
	443.9	PVD (unspecified)
	518.4	Acute pulmonary edema

*Include all decimals, unless otherwise specified
[1]ICD-10 Equivalents will be incorporated when ICD-10 is implemented

NOTE: If a medical record is eligible for stroke abstraction by having an ICD-9 cerebrovascular procedure code 38–39 or diagnosis codes 430–436, surveillance staff will send the hospital record to the Central Abstractor in Minnesota. If the medical record

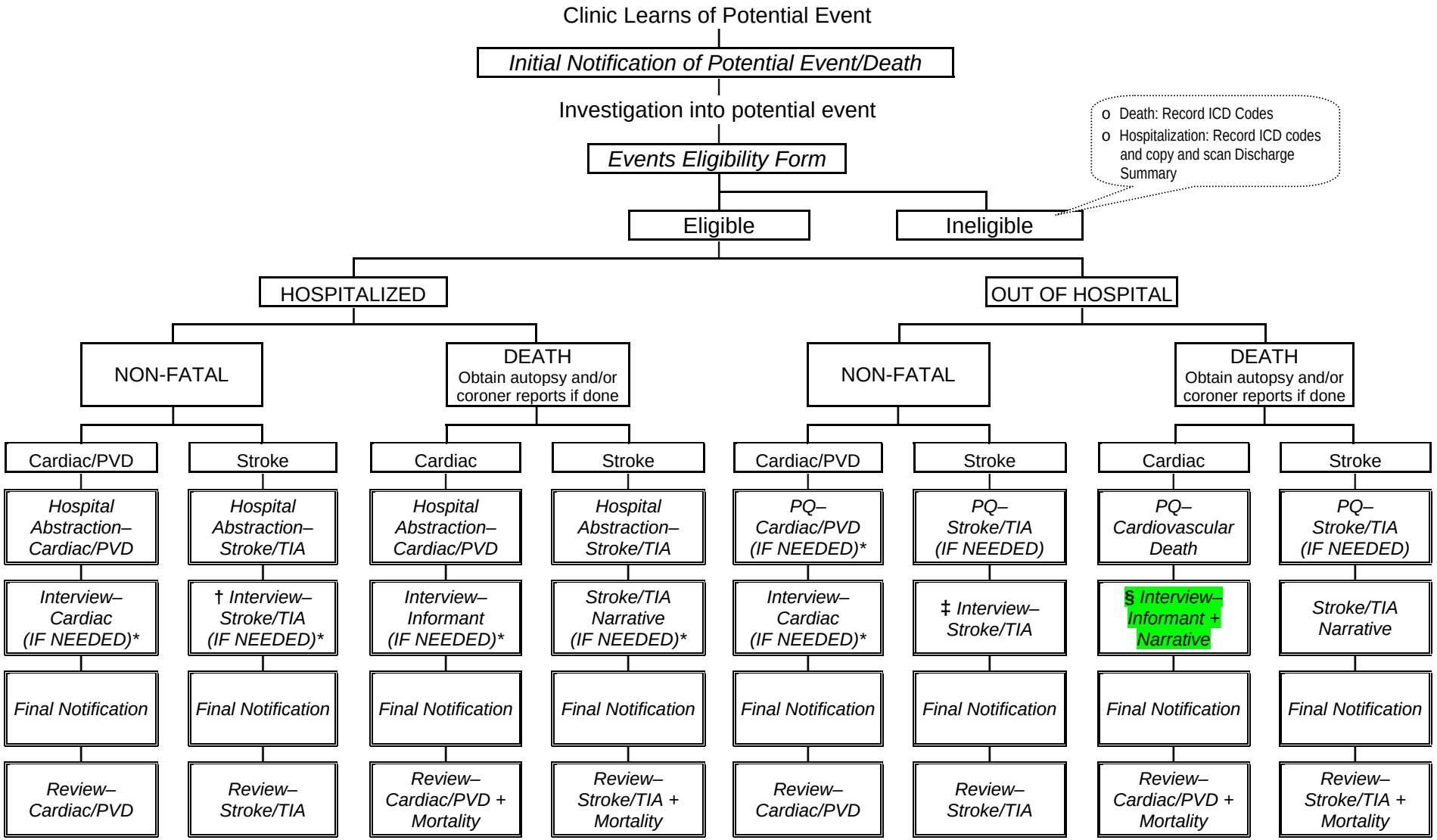
3.3 Nonfatal Events

3.3.1 Nonfatal Hospitalized

If a participant reports any hospitalization, surveillance staff requests the discharge summary, discharge diagnoses, associated ICD-9-CM codes, and any related test results and progress notes from the hospital. A recent signed consent is required by most hospitals in order to release records (see earlier in this section for more information about consents). Once the record is received, surveillance staff matches the reported hospitalization to the actual record and, if discrepancies are found, re-contacts the participant to resolve these. If the event involved a transfer to another hospital or other health-care facility, surveillance staff obtains all pertinent records from all institutions. Transfers are considered together as one potential investigation.

Surveillance staff reviews the ICD-9-CM codes and, if necessary, the discharge summary, to complete the *Events Eligibility* form, which identifies whether the hospitalization is eligible for further record abstraction. (Please see Table 3.1 for a list of eligible ICD codes.) Whenever possible, the Field Center Abstractor should be the staff member who completes the *Events Eligibility* form, although the Events Coordinator (if trained) may fill out the form if the form is then approved by the Abstractor. A computerized cross-check at the Coordinating Center of the *Events Eligibility* form, with the data collected on the Follow-Up Phone Call or the *Initial Notification of Potential Event/Death* Form, serves as a means of verifying that all reported hospitalizations have been assessed for eligibility. If the investigation is 'eligible' for cardiac, then the Field Center Abstractor must complete and submit a *Hospital Abstraction* form. If the investigation is eligible for stroke, then all collected records must be sent to the Central Stroke Abstractor at Minnesota (see Appendix D.6 for further information). Additionally, all pertinent parts of the hospital records are scanned into the database for export to the Coordinating Center. Please see Appendix E for more information on what records are scanned.

Figure 3.1 **MESA Events Forms Flow Chart**



* "IF NEEDED" does not require an override if you do not submit that form.

† *Interview* needed if hospital records inadequate; add *Narrative* if needed; do proxy *Narrative* in place of *Interview* if ppt is incapacitated.

‡ *Interview* required; add *Narrative* if needed; do proxy *Narrative* in place of *Interview* if ppt is incapacitated.

§ *Narrative* required; be sure to scan the sheet, regardless of whether it contains a narrative or not

Abstractor. If the participant was hospitalized and transferred between care facilities, the field center must complete an *Events Eligibility Addendum* form. This additional form will help determine whether this investigation is 'eligible' for review by a member of the Morbidity and Mortality (M&M) Committee. It will also ensure that all ICD codes are properly recorded. While there may be multiple *Events Eligibility Addendum* forms for any one investigation, there may be only one *Events Eligibility* form.

3.2.1 Eligible Events

If the investigation yields an eligible event, then the Field Center proceeds with the investigation. Figure 3.1 indicates which forms should be completed for each type of eligible event noted on the *Events Eligibility* form. Please see Appendix D for detailed instructions for each individual form.

3.2.2 Ineligible Events

If no events in the investigation are eligible for review, then the Field Center staff should complete a *Final Notice* form. They should mark on the *Final Notice* form all procedures/tests that were done and scan the Discharge Summary (if a Discharge Summary isn't available, please scan other summary documentation). Other materials do not need to be scanned, but any already-scanned materials do not need to be deleted. No additional forms are necessary.

blind the photocopies before they are scanned and transmitted. Please see memo dated June 16, 2003, to review the Coordinating Center's policy on blinding of medical records.

Prevalent (Pre-baseline) Disease

Although MESA participants were intended to be free of baseline cardiovascular disease, surveillance may identify events that occurred prior to baseline. These will not undergo an investigation. A Local Cardiac MD reviewer will document prevalent disease in the MESA database for all endpoints of interest (MI, angina, CHF, PVD, stroke, TIA); if the endpoint in question is stroke or TIA, the Local Cardiac MD reviewer must refer to the MESA stroke/TIA Criteria outlined in Section 4 of this manual. The Events Data Management software allows the Field Centers to enter in this information, automatically updating the participant's disease status to 'prevalent' for the relevant endpoint. Field Center staff must consult with a physician reviewer from their site prior to entering information regarding prevalent disease into the software.

Recurrent Events

MESA does review "recurrent events." These potential events should be investigated the same as incident events.

3.1 Initial Notification

The Field Center notifies the Coordinating Center about potential events by completing and scanning in an *Initial Notification of Event/Death* form. This form should be submitted immediately after the center learns of the potential event(s). The Field Center should not wait to obtain medical records before submitting this form.

This form allows the Field Center to select multiple types of events that may have occurred. Multiple events occurring during a single hospital stay belong to the same investigation and should all be reported on the same *Initial Notification*. Multiple events may be reported on the same *Initial Notification* form (thus grouping them as a single investigation) if they occurred on the same day or if they occurred within 30 days and are, in the judgment of the Abstractor, related to the same condition. It does not matter if the potential events are in or out of hospital, as long as the Abstractor feels that the incidents are clearly related. Only one *Initial Notification of an Event/Death* is to be completed for each investigation. If it is unclear whether two events should be marked on the same *Initial Notification*, you should submit two *Initial Notifications* to start two investigations or contact the Events Data Director at the Coordinating Center.

3.2 Eligibility

After the Coordinating Center has been notified of the potential events via the *Initial Notification* form, the Field Center begins to obtain the necessary information to complete the investigation. After medical records have been obtained, the Field Center must complete the *Events Eligibility* form to see if the potential event(s) contained in this investigation qualify for review. Whenever possible, the Field Center Abstractor should be the staff member who completes the *Events Eligibility* form, although the Events Coordinator (if trained) may fill out the form if the form is then approved by the

3. Events Investigation

Surveillance and Events staff may consist of coordinators, nurses, medical records technicians, and other professionals. These staff members are trained to determine a potential event's eligibility for investigation and to gather information required for its validation. A schema showing the flow of data collection and forms used is provided in Figure 3.1. For more detailed descriptions on how to complete individual forms, please see Appendix D.

Consent

During the MESA Field Center clinic visits, participants provide consent for MESA staff to access their medical records as needed in the future. However, most often this consent will only be valid for a stated period of time. If the participant's consent expires, surveillance staff must send the participant a new medical release form to obtain further permission to access medical records as needed.

Please Note:

The lifespan of participant written consents and HIPAA signatures differ. HIPAA signatures are valid in perpetuity. Therefore it is *NOT* necessary to re-obtain HIPAA signatures. On the other hand, written consents are valid for a limited duration. The length of time a signed consent form is valid varies by municipality and individual institutions. A participant written permission to release medical records must be re-obtained when consent expires. To ensure you are maintaining up-to-date medical releases for your field center's participants, be sure to familiarize yourself with any local (i.e., city, county, or state) rules governing the length of time a signed release is considered valid. Also, check with the major hospitals in your area to become aware of any specific policies they may have regarding a signed medical release form's expiration. Note that policies at individual hospitals may vary with respect to allowing Field Center staff access to the records themselves. Institutional Review Board (IRB) approval may be needed to access some records. Field Centers are encouraged to contact their institution's HIPAA official to ensure that their consent practices are appropriate.

Foreign Language Records

It is plausible that MESA participants may have medical events occurring outside of the country. If it is feasible to obtain foreign records, particularly if the record language can be easily translated (such as Spanish or Chinese), then an attempt should be made. Medical records for deaths or CVD events should definitely be sought. If foreign governments/institutions are not cooperative in providing the records, participant families should be approached to obtain the information. Field Centers should inform participants in advance to bring back medical records if they leave the country.

Methods of Data Collection

Field center staff collects most information on paper TELEforms that are scanned. However, staff must also photocopy selected parts of the medical record. These may include electrocardiograms (ECGs), catheterization reports, treadmill results, chest x-ray (CXR) reports, and other pertinent procedure and diagnostic documentation. Such records must be photocopied, scanned and then exported to the Coordinating Center electronically. If documents are photocopied, staff must use a china marker to properly