CHAPTER 14

CLINICAL CENTER PROCEDURES

14.1 INTRODUCTION

The Research Coordinator plays an important role at each Clinical Center which participates in the T3 Trials. The Research Coordinator is usually the Clinical Center staff member who has the largest time commitment to the study and who is the most familiar with the study procedures and operations. Thus, with the Principal Investigator, the Research Coordinator shares responsibility for efficient, enthusiastic operation of the center, for the quality of data collected and reported to the Data Coordinating Center, and for adherence of all Clinical Center staff to the study protocol. The procedures described in this chapter are those which the Research Coordinator and Principal Investigator are responsible for implementing and maintaining. The standardization of procedures is essential so that data from all Clinical Centers can be pooled for analysis.

14.2 MATERIALS SENT FROM THE DATA COORDINATING CENTER

The Data Coordinating Center sends each Clinical Center data collection forms and identification labels to be used for recording medical data and submitting materials. The forms have been designed to standardize procedures and the flow of data.

The Patient Inventory Sheet, Transmittal List, Clinical Center Shipment Log and Shipment Receipt Card are used to document shipment of forms and materials to the Data Coordinating Center and Core Laboratories and to facilitate identification and reconstruction of lost shipments.

The Randomization Mailers are computer-generated to prevent errors in transmitting treatment assignments. The Patient Appointment Schedule is used in scheduling patient appointments and preventing loss of data because of missed follow-up contacts.

Edit queries are generated as a result of computer edit of information on the T3 data collection forms which have been processed at the Data Coordinating Center. These queries identify inconsistencies, questionable values, and unanswered items on the data collection forms and require responses from the Clinical Center staff.

14.3 DEFINITIONS

14.3.1 Military Time

Time is recorded based on a 24-hour clock and is referred to as military time. For example:

	Hours	Minutes
12 noon	12	00
12 midnight	24	00
12:01 a.m.	00	01
10:15 a.m.	10	15
2:30 p.m.	14	30

For P.M. time (other than 12 noon) add 12 to convert to 24-hour clock recording.

14.3.2 INEL Conditions

On the Screening Form any response which is marked "INEL" indicates that an exclusion criterion or contraindication of thrombolytic therapy is satisfied for the patient being evaluated. The term "INEL condition" refers to these exclusion criteria and contraindications of thrombolytic therapy which render the patient permanently ineligible to participate in the T3 Trial.

14.4 PATIENT EVALUATION, ENROLLMENT, AND FOLLOW-UP

14.4.1 Patient Evaluation and Enrollment in T3A

All patients with unstable angina or rule-out MI admitted to the hospital emergency room or other units of the hospital should be evaluated for eligibility. If the patient meets the requirements for further screening, a Screening Form (T3 Form 3A) should be completed. If a STOP or INEL is encountered, the patient does not meet the inclusion criteria, and the Form 3A should be discarded rather than completed and sent to the Data Coordinating Center. If no INEL items are checked on the Screening Form (T3 Form 3A), the patient is eligible for entry into the T3A Trial and should be asked to participate. The patient must then read and sign the informed consent form in order to be enrolled in T3A.

The Admission and Treatment Assignment Form (T3 Form 04) and Treatment Assignment Notification Form (T3 Form 5D) must be completed for all patients who are entered into the T3A Trial. T3 Form 5D should be sent to the Data Coordinating Center by telecopier or overnight courier within 24-48 hours after treatment initiation. In order that initiation of treatment not be delayed, certain sections of Form 04 may be completed after study treatment has been administered. If it is necessary to contact the patient's physician to complete the medical history portion of the Admission and Treatment Assignment Form (T3 Form 04), the patient should be asked to sign a Medical Information Release Form from the sponsoring hospital.

The patient then proceeds to the Cardiac Catheterization Laboratory for angiography to determine whether he/she is angiographically eligible to participate in T3A. If the patient is eligible, the next Randomization Mailer is opened and T3 study treatment is initiated. If the patient is determined to be angiographically ineligible, T3 Form 4A (Declaration T3A Patient Angiographically Ineligible) is completed.

For patients randomized to T3 treatment, the completed Screening Form (T3 Form 3A) and the Admission and Treatment Assignment Form (T3 Form 04) should be sent to the Data Coordinating Center. For eligible patients who do not consent to treatment, the completed Screening Form (T3 Form 3A) is sent to the Data Coordinating Center. For patients not eligible for T3 based on angiography, the completed Declaration T3A Patient Angiographically Ineligible Form (T3 Form 4A) as well as the Screening Form (T3 Form 3A) are completed and sent to the Data Coordinating Center.

If the Randomization Mailer is opened, the patient is a "randomized" patient. Although the condition of the patient may exclude him/her from study drug treatment, all tests and procedures should be completed according to the protocol unless the procedure or test is medically contraindicated. All requisite study forms on these patients should be completed and submitted to the Data Coordinating Center.

After opening the Randomization Mailer, record on T3 Form 5D the patient therapy kit number and mailer sequence number printed on the randomization mailer insert. Record the ID Number, Name Code and the date the Randomization Mailer was opened on the Randomization Mailer insert. Place the completed Randomization Mailer insert in the envelope included in the Randomization Mailer and return the Randomization Mailer to the Data Coordinating Center no more than one week after the patient was randomized. The Randomization Mailer insert can be mailed separately or with other forms and materials sent to the Data Coordinating Center.

14.4.2 Patient Evaluation and Enrollment in T3B

All patients with unstable angina or rule-out MI admitted to the hospital emergency room or other units of the hospital should be evaluated for eligibility. If the patient meets the requirements for further screening, a Screening Form (T3 Form 3B) should be completed. If a STOP or INEL is encountered, the patient does not meet the inclusion criteria, and Form 3B should be discarded rather than completed and sent to the Data Coordinating Center. If no INEL items are checked on the Screening Form (T3 Form 3B), the patient is eligible for entry into the T3B Trial and should be asked to participate. The patient must then read and sign the informed consent form in order to be enrolled in T3B.

The Admission Form (T3 Form 04) and Treatment Assignment Notification Form (T3 Form 5D) must be completed for all patients who are entered into the T3B study. T3 Form 5D should be sent to the Data Coordinating Center by telecopier or overnight courier within 24-48 hours after treatment initiation. In order that initiation of treatment not be delayed, certain sections of Form 04 may be completed after study treatment has been administered. If it is necessary to contact the patient's physician to complete the medical history portion of the Admission and Treatment Assignment Form (T3 Form 04), the patient should be asked to sign a Medical Information Release Form from the sponsoring hospital.

If the patient is eligible, the next Randomization Mailer is opened and T3 study treatment is initiated. Entry into the study is documented on the Treatment Assignment Form.

For patients randomized to T3 treatment, the completed Screening Form (T3 Form 3B) and the Admission and Treatment Assignment Form (T3 Form 04) should be sent to the Data Coordinating Center. For eligible patients who do not consent to treatment, the completed Screening Form (T3 Form 3B) is sent to the Data Coordinating Center.

If the Randomization Mailer is opened, the patient is a "randomized" patient. Although the condition of the patient may exclude him/her from study drug treatment, all tests and procedures should be completed according to the protocol unless the procedure or test is medically contraindicated. All requisite study forms on these patients should be completed and submitted to the Data Coordinating Center.

After opening the Randomization Mailer, record on T3 Form 5D the patient therapy kit number and mailer sequence number printed on the randomization mailer insert. Record the ID Number, Name Code and the date the Randomization Mailer was opened on the Randomization Mailer insert. Place the completed Randomization Mailer insert in the envelope included in the randomization mailer and return the randomization mailer to the Data Coordinating Center no more than one week after the patient was randomized. The Randomization Mailer insert can be mailed separately or with other forms and materials sent to the Data Coordinating Center.

14.4.3 Hospitalization Period

During the period of hospitalization, entries should be recorded each day to document medical history and prescribed medications. All T3 study data recorded on the standardized T3 forms should be verifiable in the medical records. Laboratory CK, CK-MB and APTT values, all episodes of ischemic pain, and selected blood data are recorded on the Laboratory Data Form (T3 Form 19). If the patient is randomized to Invasive Strategy, the catheterization, angiography, and PTCA or CABG (if medically indicated) should be performed during the 18-48 hours after study drug treatment initiation. The exercise treadmill test and thallium imaging test should be performed prior to or within five days after hospital discharge. The Hospital Discharge Form is completed on the day of discharge from the hospital or after 21 days in the hospital if the hospitalization extends beyond 21 days. A

summary of the hospital course and the patient's status at the time of discharge (or after 21 days in the hospital) are recorded on the Hospital Discharge Form. If the patient dies during his/her hospitalization, the Laboratory Data Form and Hospital Discharge Form (as well as the death forms) are completed for the time period from entry into the study until death. The Hospital Notification Form (T3 Form 32) is also completed at the time of hospital discharge (or after 21 days in the hospital) and is sent by telecopier or overnight courier within 24-48 hours after hospital discharge. The Hospitalization Discharge Form (T3 Form 10) and the Laboratory Data Form (T3 Form 19) are mailed to the Data Coordinating Center.

For patients who remain hospitalized for more than 21 days after study treatment initiation, T3 Form 33, Hospital Discharge Supplement, should be completed at the time of hospital discharge. Form 33 should contain data for events occurring during the period from the 21-day completion date of Form 10 to hospital discharge.

On the day of discharge, the patient is given an appointment for the six-week follow-up visit.

14.4.4 Follow-up

Patients entered into the T3A Trial will be contacted by telephone at six weeks after treatment for a brief interview. Patients entered into the T3B Trial are expected to return for a follow-up visit including completion of Form 13 and an ETT/persantine thallium test at six weeks after the date of entry. Six-week patient follow-up visits should occur between day 42 and day 70 after study drug treatment initiation. Occasionally it is difficult to arrange for a patient to undergo exercise testing within this time frame, for various reasons: patient convenience, physician cooperation, or medical reasons (recurrent angina, recovery from CABG, and others). However, because the primary end point in T3B requires that all patients undergo an ETT or a persantine thallium test at the six-week

visit, it is recommended that patients be contacted very early (even before 42 days) to schedule the ETT/persantine thallium test within the early part of the follow-up window. Additionally, performing the six-week ETT early within the window will help avoid the problem of patients having restenosed coronary arteries after an initial PTCA.

For patients who are physically unable to perform exercise testing (due to recovery from CABG or physical disability), it is important to schedule a persantine thallium test early within the six-week time window. For patients too ill to exercise early within the six-week time window, it is recommended that the ETT be performed as soon as possible after stabilization (but still within ten weeks of study-drug initiation). This is another reason to attempt to contact the person early because there will then be up to four weeks for the patient to stabilize and still complete the ETT/persantine thallium test on time. A standard 12-lead ECG should be obtained within 42 to 70 days, even if it is not possible to obtain the ETT/persantine thallium test. Research Coordinators are encouraged to request the assistance of their Principal Investigators and their Co-Investigators to intervene early and provide support whenever the patient and/or referring physician indicate an unwillingness to perform the ETT/persantine thallium test at six weeks. In addition, T3B patients will be contacted by telephone at one year after treatment. If at all possible, follow-up contacts and examinations should be completed within the time window specified for each follow-up. However, data collected after the follow-up window will be accepted. See Exhibits 14-1A and 14-2B for an overview of the data collection schedules for T3A and T3B.

After the Screening Form (T3 Form 3A or 3B) has been processed at the Data Coordinating Center, the Data Coordinating Center staff prepare a Patient Contact Schedule (Exhibits 14-2A and 14-2B) for the patient and mail it to the Clinical Center. The expected date of each

follow-up visit and telephone contact is determined from the patient's date of entry into T3. The first column of the Patient Contact Schedule indicates the follow-up contact period and the second column gives the expected date of the visit. The appointment should be made as close to the expected date as possible. The fourth and fifth columns designate the beginning and end of the allowable time period for the visit, that is, the earliest allowable date for the visit to be completed (fourth column) and the latest allowable date (fifth column).

If a visit is not completed within the specified time period, it is designated a "missed visit." A Missed Follow-up Form (T3 Form 12) is submitted instead of a Follow-up Form (T3 Form 13) for each missed visit when the allowable time interval for completion of the visit has passed and the Research Coordinator has not contacted the patient and obtained the information necessary to complete the Follow-up Contact Form. Both a Missed Visit Form (Form 12) and a Follow-up Contact Form (Form 13) should not be submitted for a given patient during a given follow-up period. The Form 12 should be completed only when it is determined that the protocol specified time window for follow-up contact has elapsed and follow-up contact has not been made. For example, for the six-week follow-up, Form 12 should not be completed until day 70, when it will no longer be possible to schedule that patient for a six-week follow-up visit.

The form types for Forms 12 and 13 should refer to the visit for which the forms are completed. A Form 12 or Form 13 completed in connection with the six-week follow-up visit should have a form type of MF01 OR FU01. A Form 12 or Form 13 completed in connection with the one-year follow-up visit should have a form type of MF02 or FU02.

Any ECGs, laboratory findings, hospitalization reports, or other information which have become available since the last visit are assembled for review by the clinic staff members who will examine the

patient. If necessary and appropriate, the radiographic, radionuclide and/or ETT technician are notified to schedule the required procedures.

14.4.5 Non-Performance of Protocol Procedures

If a procedure required by the T3A or T3B protocol either during the initial hospitalization or during the six-week follow-up period is not performed or is not performed in the allowable time period, the Research Coordinator should submit a Non-Performance of Protocol Procedure Form (Form 18) for each procedure not performed. The Form 18 should not be completed until the allowable time period for performance of the procedure has elapsed.

14.5 COMPLETING, REVIEWING, AND LABELING STUDY FORMS

Instructions on how each form should be completed are given on T3 form instruction page(s). Black ink should be used for completing the forms. For items which cannot be answered by a check mark (T) or an "X", print clearly all responses in the space provided. Do not use abbreviations unless necessary and then use only widely recognized abbreviations. A copy of each completed form should be retained for the Clinical Center files.

The first items to be completed on any patient data form are the Clinical Center and specific hospital number, patient's ID Number, and form type (which consists of two preprinted letters and either a preprinted 01 (for a form only completed once) or a sequence number (for a form which may be completed more than once). The sequence number is the serial count for each patient of a specific form type submitted to the Data Coordinating Center. The Patient Inventory List (T3 Forms 54A and 54B) are designed for the Coordinator's convenience in keeping track of these forms. Each additional form of a specific type is assigned the next available sequence number. Next the patient's Name Code and the date of the examination or event are

completed. The patient's ID Number and sequence number, if space is provided, are recorded in the lower right-hand corner of each page of the form. The forms are to be completed by the Research Coordinator or other T3-certified staff members and checked by the Research Coordinator before shipment.

The policy of the Data Coordinating Center is to process the information as submitted without interpretation or second guessing what the recorder had intended. The Clinical Center staff are requested to complete the forms as clearly and as legibly as possible and to follow the conventions described below in reporting certain data to minimize the possibility of errors in processing the data collection forms.

I. Responses Answered by a Check Mark (T) or an "X"

If a response is to be answered by a check mark (T)or an (X), then only a check mark or an "X" within the parenthesis is the acceptable response.

II. Numeric Responses

When a numeric response is requested, the entire response space is to be completed. Insert leading or trailing zeroes wherever required to fill all spaces.

III. Legibility

If a response is to be answered by other than a check mark (T)or an (X), then the response is to be PRINTED clearly in the spaces provided. Abbreviations are not to be used by the Clinical Center staff unless absolutely necessary and then they are to use only widely recognized abbreviations.

IV. Overwritten Responses

A. If the response has been overwritten carefully to delineate the existing mark, the response is acceptable. The tracing of the existing mark should be done in black ink.

B. If the response has been overwritten to change the response, then the response will be considered illegible unless the desired response is clearly circled and initialed by the individual making the correction. The incorrect response is to be crossed out. An incorrect numeric or alphabetic response should be completely crossed out and the correct numeric or alphabetic response written clearly above or below the original response. The correct response should be clearly circled and initialed by the individual making the correction.

V. Unsolicited Responses

Unsolicited responses should not be written within the items on the forms. This information cannot be not entered into the computer system.

The Data Entry Guidelines followed by the Data Coordinating Center data entry staff are given in Chapter 2 of Volume II of the Manual of Operations, Exhibit 2-2. These guidelines clarify the implications of the above conventions.

When a form is returned to the Research Coordinator at the end of an examination or procedure, it should be reviewed promptly, preferably while the patient is still in the Clinical Center, to assure that all required information is complete and has been recorded in a legible, unambiguous fashion. Any administrative information requested at the end of the form is to be supplied by the Research Coordinator.

Identification labels for labeling forms (Exhibit 14-3) are supplied by the Data Coordinating Center. Each Clinical Center is also supplied with labels to be used to identify ECGs, ETT ECGs, angiograms, and Holter recordings (Exhibit 14-4). The Research Coordinator is responsible for assuring that the proper labels are used and that all materials for each patient are labeled correctly.

14.6 MAILING FORMS AND OTHER MATERIALS TO THE DATA COORDINATING CENTER

The original of all data forms are mailed to the Data Coordinating Center. ECGs, coronary angiograms, Holter recordings and thallium imaging films are sent directly to the appropriate Core Laboratories. Copies of ECGs are sent to the Data Coordinating Center.

14.6.1 Frequency of Mailing

Forms and materials should be mailed to the Data Coordinating Center at least once each week.

14.6.2 Method of Shipment

Materials are usually sent to the Data Coordinating Center via first class mail. If rapid transmission of materials to the Data

Coordinating Center is required, special delivery service or Federal Express may be used. Materials should not be mailed on Friday for overnight delivery to the Data Coordinating Center. Since the Data Coordinating Center is closed on Saturday, such deliveries are frequently delayed until late Monday afternoon.

Form 5D, Treatment Assignment Notification, should be sent by telecopier or overnight courier to the Data Coordinating Center 24-48 hours after study treatment initiation. Similarly, Form 32, Hospital Discharge Notification, should be sent by telecopier or overnight courier to the Data Coordinating Center within 24-48 hours after hospital discharge. If the patient has not been discharged by 21 days after treatment initiation, the Form 32 should be completed on day 21 and should be sent to the Data Coordinating Center by day 24. The baseline forms, procedure forms and Hospital Discharge Form (Form 10) should be sent for receipt at the Data Coordinating Center within 14 days after the date of the Form 32. The only exceptions to this are the Exercise Treadmill Test Form (Form 8E), the Thallium Imaging Test Form (Form 8F) and ECG Acquisition Form (Form 09) for the hospital discharge ECG which should be sent for receipt within 21 days after the date of the Form 32 and the Blood Samples Record (Form 20) which should be sent for receipt within 42 days after the date of the Form 32.

The Follow-up Form (Form 13) and the Forms 8E (or 8F) and the Form 09 for the six-week follow-up visit should be submitted for receipt at the Data Coordinating Center within 14 days after the last day of the six-week follow-up window. The Form 13 for the one-year follow-up should be submitted for receipt within 14 days after the last day of the one-year follow-up window.

14.6.3 Transmittal List (T3 Form 51)

A Transmittal List (Exhibit 14-5) and a Shipment Receipt Card accompany each shipment of forms from the Clinical Center to the Data Coordinating Center. ECGs and/or other materials may be listed in the optional section on the Transmittal List. The Transmittal List is completed by the Research Coordinator; the original is sent to the Data Coordinating Center and a copy is retained in the Clinical Center. The information requested in the upper right-hand corner of the Transmittal List is recorded. The transmittal number is obtained by taking the next sequential number from the Clinical Center Shipment Log; the Research Coordinator records all four digits of the number in the spaces provided. The date of shipment is recorded on the Transmittal List and on the Clinical Center Shipment Log.

Each form sent to the Data Coordinating Center in a particular shipment is noted on the Transmittal List by supplying the ID Number and Name Code of the patient as recorded on the form itself; the form number and form revision number printed in the upper right-hand corner of each form; the form type; and date of the examination or event as recorded in Item 2 on the form. If more than one form is sent for a particular patient and visit, each one is listed separately. If more than ten forms are mailed in one shipment, additional sheets are used. Forms should be inserted into the package in the same order they are listed on the Transmittal List. The same transmittal number is entered on each page. The pages are numbered consecutively and the total number of pages is recorded on each one. For example, three pages are required if 21 to 30 forms are sent and the first page completed is marked "Page 1 of 3", the second "Page 2 of 3", and the third "Page 3 of 3".

14.6.4 Clinical Center Shipment Log (T3 Form 52)

The Clinical Center Shipment Log (Exhibit 14-6) is updated as each shipment is prepared and mailed. The carrier and any comments regarding contents are noted. When the Shipment Receipt Card is returned by the Data Coordinating Center to indicate that the shipment has been received, the return of the card is noted by writing the date in the right-most column. It is recommended that a separate log be maintained for shipments made to each of the central units, i.e., Data Coordinating Center, ECG Core Laboratory, Holter Core Laboratory, Qualitative Core Laboratory, Quantitative Core Laboratory, Coagulation Core Laboratory and Thallium Core Laboratory.

14.6.5 Shipment Receipt Card (T3 Form 53)

The Shipment Receipt Card (Exhibit 14-7) is completed by recording the Clinical Center number, transmittal number (from the Transmittal List), the date of shipment, and the center to which shipment is being made, e.g., Data Coordinating Center. The remaining items are completed upon receipt at the receiving center.

The Shipment Receipt Card is addressed to the center from which the shipment is being made by rubber stamping, by an address label, by typing, or by writing.

14.6.6 Patient Inventory Sheet (T3 Form 54)

To assist the Clinical Center staff in keeping a record of the status of examinations for each patient, a Patient Inventory Sheet (Exhibit 14-8) is maintained as part of the patient's T3 record and retained in the Clinical Center. The patient's name, ID Number, and Name Code are recorded at the time the patient is first considered for the study.

14.6.7 Packaging and Addressing the Shipment

Both the Transmittal List and the Shipment Receipt Card are enclosed with the forms and materials being shipped. If there are

many forms, the Transmittal List and the Shipment Receipt Card should be placed in an envelope clearly marked "Transmittal List" inside the package.

Before closing the package, the Research Coordinator should verify that a copy of the Transmittal List has been filed in the Clinical Center. If a box is not available, double envelopes and heavy duty tape at both ends of the envelopes should be used to prevent damage or loss of materials.

Mailing labels addressed to the Data Coordinating Center and the Core Laboratories are supplied to each Clinical Center and should be used routinely. Sufficient postage should be affixed to the package; the Post Office does not deliver packages to the Data Coordinating Center if postage is due.

14.6.8 Receipt of Shipment

Shipments received at the Data Coordinating Center are verified immediately by comparing the forms and materials in the package against the enclosed Transmittal List. Presence of materials which are expected to accompany certain forms is also verified.

Any discrepancy is called to the attention of the sender, usually by means of a telephone call. If any modifications to the Transmittal List are required as a consequence of discrepancies or inappropriate or missing items, a corrected copy of the Transmittal List is returned to the sender.

14.6.9 Returned Shipment Receipt Cards

When a Shipment Receipt Card is received in the Clinical Center, the Research Coordinator should complete the Clinical Center Shipment Log by completing the right-most column. If any discrepancy in the shipment is noted on the card, the Research Coordinator should call the Data Coordinating Center for clarification. The returned Shipment Receipt Card should be stapled to the corresponding Transmittal List and filed.

The Clinical Center Shipment Log should be reviewed weekly by the Research Coordinator to identify shipments which have not been acknowledged by return of the shipment receipt card. If two weeks or more have passed without notification that a shipment has been received, the intended receiver should be contacted as the first step in following up the shipment.

14.7 EDIT QUERIES

Items on the data collection forms are sometimes overlooked, information is sometimes recorded in the wrong format, or items are answered inconsistently. In order to identify such problems and other errors which may have occurred during processing in the Data Coordinating Center, all forms received at the Data Coordinating Center are subjected to computer edit to detect missing or improbable answers to every item.

Problems detected by the special computerized edit procedure trigger printed "edit messages" which are sent to the Clinical Center staff for resolution. Examples of the most frequently encountered problems and their corresponding edit messages are discussed in Section 14.7.2. Because of the need to identify a broad range of possible problems, items which have been answered correctly are sometimes identified as suspicious. An attempt has been made to provide clear, concise edit queries, but sometimes the problem is not obvious. The Data Coordinating Center staff should be contacted by

telephone or in writing to resolve any unusual problems which result in edit queries. A description of edit procedures and the routine procedures for dealing with edit messages follows.

14.7.1 Clinical Center Procedures

When edit messages are received at the Clinical Center, they should be dealt with promptly.

Responses to edit messages may be returned to the Data Coordinating Center with a shipment of forms or in a special shipment. The usual mailing procedures are followed (see Section 14.6).

Sometimes clarification of problems is required; in such cases the Data Coordinating Center staff may be contacted by telephone.

14.7.2 Samples of Edit Messages

All queries pertaining to a single form (referred to as an "edit statement") are printed on a single page; each item in question produces a query or message. The form on which the questioned data were recorded is identified at the top of each page of edit messages. The format of an edit statement is shown in Exhibit 14-9. The first column identifies the Item Number of the Form. An item description is provided in the next column. The original value of the answer to the item is printed next under the heading "OLD VALUE." The next column headed by "CORRECT VALUE" contains the appropriate number of spaces for a corrected response for the item. In the column labeled "MESSAGE" the type of error is specified.

There are basically two types of items on T3 data collection forms. Precoded items are completed by placing a check mark within the appropriate set of parentheses. The usual codes are:

1 = YES

2 = NO

3 = QUESTIONABLE OR UNCERTAIN

For items which require a written answer, the exact number of spaces needed is provided. Answers to such items requiring less than the number of spaces provided must be right justified and leading zeros must be added. For example, the answer to Item 20A (Exhibit 14-12) for a patient who had a dose of 80 mg of study drug would be 0 8 0 since three spaces were supplied.

Exhibit 14-10 is a sample edit message for a STOP item from the Screening Form which was not answered; the message "MISSING - INEL" is generated. In order to respond to this message, the correct code (either 1 for yes or 2 for no) is entered in the column headed "CORRECT VALUE."

One type of inconsistent response which results in an edit message is illustrated in Exhibit 14-11. Because Item 20 was answered "yes", a response is expected for Item 20A. If one is not given, an edit message is generated during processing because the response to either Item 20 or Item 20A is incorrect. (If Item 20 had been answered "no", no response to Item 20A would be expected and if a response for Item 20A was recorded, an edit message would be generated.) Two possible responses to this sample edit message are shown on the second page of Exhibit 14-11. If the answer to Item 20 should be "yes," a "1" is recorded for Item 20 and the correct study treatment dose is recorded for Item 20A in the "CORRECT VALUE" column. If the answer to Item 20 should be "no," a "2" is entered for Item 20 under "CORRECT VALUE" and nothing is recorded for Item 20A since the original code is correct. A similar example is given in Exhibit 14-12 except that a positive response to Item 7 is expected to be followed by responses to all parts of Items 7 (i.e., 7A - 7F). Responses to Items 7A - 7F are not appropriate if "no" is the response to Item 7. The second page of Exhibit 14-12 shows two possible responses to this sample edit message. Please note that an asterisk (*) should be recorded under the column "CORRECT VALUE" to indicate that the value

should be missing. If an item is printed on the edit message, but the response should remain the same, the correct value column should be left blank.

The sample message in Exhibit 14-13 is sometimes referred to as "extreme value" message because the recorded value is larger or smaller than usually observed for the measurement. In response to the "OUT OF RANGE" message, if a value has been recorded incorrectly, the correct value is recorded in the column marked "CORRECT VALUE." If the value printed is correctly recorded, it is repeated under "CORRECT VALUE." Although queries about correctly reported values are annoying, they are necessary to assure that recording errors have not occurred as a result of transposition of one or more digits or misplacement of decimals either during recording at the Clinical Center or during processing at the Data Coordinating Center.

The code "98" can be used on both forms and edit messages. For data entry purposes, the code "98" indicates that the data are unavailable. The T3 Form 04 is an example of how the code "98" can be used to indicate that the exact month and/or day of a prior event cannot be recalled by the patient or his family. If the year is unknown, then "unknown" should be checked and the date spaces should not be completed. When you have more than a two-digit response and you want to indicate that the data are unavailable, use as many nines as are required, but the last digit should be an "8." For example, if the patient's weight was unavailable, record "998" as the response.

14.8 MISSED VISITS

No matter how far in advance appointments are scheduled or how often patients are reminded, there are occasional instances in which a patient does not have a follow-up contact by the last possible date as indicated in the Patient Contact Schedule. If a patient is not contacted within the appropriate time window, a Missed Follow-up Form (T3 Form 12), should be submitted to the Data Coordinating Center. If

a Missed Visit Form is not submitted, the form for this follow-up contact will appear on the Delinquent Listing (Exhibit 14-14) generated every month at the Data Coordinating Center. Forms are listed as delinquent if more than two weeks have passed since the last date of the follow-up contact time window.

Even if the Research Coordinator has not been able to contact a patient within the time window, the Research Coordinator should continue his/her efforts to contact the patient. If a patient has a follow-up contact or examination after the time window, the Research Coordinator should complete a Follow-up Form (Form 13) for the patient and submit it to the Data Coordinating Center. The Form 13 will then replace the Form 12 which was previously submitted.

14.9 TRANSFER PATIENTS

If a patient moves from one T3 Clinical Center area to another T3 Clinical Center area, the Research Coordinator of the former Clinical Center should encourage the patient to continue in the trial and tell him/her whom to contact at the new Clinical Center. The Research Coordinator of the former Clinical Center should also notify the staff at the new Clinical Center and the Data Coordinating Center staff of this potential transfer patient so that the staff at the new Clinical Center can try to establish contact with this patient.

If the patient agrees to attend the new Clinical Center and an appointment for a follow-up contact is made, the Research Coordinator of the new Clinical Center informs the Research Coordinator of the patient's former Clinical Center that the patient is transferring and requests the file of T3 forms, ECGs, etc. Once the file is transferred and the staff of the new Clinical Center have made contact with the patient, the patient becomes the responsibility of the new Clinical Center and the former Clinical Center is not required to follow this patient any further. The Research Coordinator at the new Clinical Center should confirm the transfer by contacting the Data

Coordinating Center. The patient retains his/her original T3 ID Number and Name Code throughout the course of the study even though these were assigned in the former Clinical Center.

14.10 INACTIVE PATIENTS

If a patient cannot be located for follow-up contact, an intensive search should be instituted by the Research Coordinator immediately. The search should start as soon as the patient has missed one contact or any communication is returned undelivered. The Research Coordinator should use all available resources, as discussed below, to locate the patient. Since this search may be long and time-consuming, it is important that it be started as soon as any member of the Clinical Center staff is aware that there is a problem. Experience has shown that with sufficient ingenuity and effort it is almost always possible to find such patients. If all avenues have been exhausted by the Clinical Center staff and the patient has not been located, assistance can be enlisted from the Data Coordinating Center.

The Data Coordinating Center staff then assume responsibility for locating the patient and notify the Clinical Center staff if the search is successful. In the latter case it becomes the responsibility of the Clinical Center staff to see that the patient returns to the regular follow-up schedule.

If an inactive patient is persuaded to resume follow-up, the receipt by the Data Coordinating Center of a completed contact form removes this patient from the inactive category. The patient's Contact Schedule should be consulted to determine which examinations and procedures should be completed and the follow-up visit number for the contact.

If the patient moves out of the area without contacting the T3 Clinical Center and without leaving a forwarding address, a special effort is required to locate the patient. The purpose of much of the

information on the Patient Information Sheet (T3 Form 01) is to help locate such patients. The information includes the following information which may be of assistance in locating the patient:

A. Name and address of the patient's private physician or general practitioner,

B. Name and address of the patient's employer,

C. Names, addresses, and telephone numbers of two persons outside the patient's household who are likely to know the patient's whereabouts,

D. Patient's social security and driver's license numbers, and

E. Name and address of referring physician.

Other sources which may be useful in locating patients are:

A. Neighbors,

B. Neighborhood merchants,

C. Unions, professional societies,

D. Clergymen,

E. Utility companies,

F. U.S. Department of Defense Locator System,

G. U.S. Immigration Office,

H. Registers of migratory workers,

I. Employment Security Offices,

J. Health and welfare agencies,

K. Social service exchanges,

L. School boards,

M. Voter registration offices,

N. Federal and state taxing agencies,

0. Public housing and relocation authorities, and

P. Nationwide investigation agencies.

Some general information as well as specific procedures and techniques for improving follow-up may be obtained from the following

reference: Boice, J.D.: Follow-up methods to trace women treated for pulmonary tuberculosis, 1930-1954. Amer. J. Epid. 107:127, 1978.

The final responsibility for making sure that all reasonable efforts are made to persuade inactive patients to return to the study rests with the Principal Investigator. The person in the Clinical Center who had the best rapport with a particular inactive patient is usually the one best able to reestablish contact.

14.11 DECEASED PATIENTS

As soon as a member of the Clinical Center staff becomes aware that a T3 patient enrolled or followed in that Clinical Center has died, a Death Notification Form (T3 Form 15) should be completed and mailed to the Data Coordinating Center within 72 hours of Clinical Center notification. Copies of the death certificate and autopsy report, if available, are forwarded to the Data Coordinating Center with a Cause of Death Form (T3 Form 16) as soon as the Research Coordinator obtains them. The documents should be forwarded within 14 days of the death notification.

The Mortality and Morbidity Classification Committee, at the time the Committee meets to classify cause of death, may request additional documentation, e.g., a summary description of the events leading to death. The Research Coordinator is responsible for assuring that this information is supplied to the Data Coordinating Center to be forwarded to the committee.

14.12 OTHER DUTIES OF THE RESEARCH COORDINATOR

14.12.1 Supply Orders

The Research Coordinator is responsible for keeping the Clinical Center stocked with supplies of materials needed for the study.

Forms, mailing labels, shipment receipt cards, copies of manuals and reports, and identification labels are ordered from the Data Coordinating Center. A Form Requisition Sheet (T3 Form 55) is shown in Exhibit 14-15.

14.12.2 Certification of Clinical Center Staff

Certification is required for each Clinical Center staff member who performs one or more of the various tasks involved in patient examination or evaluation and data collection and handling. (See Chapter 3 of Volume II of the Manual of Operations for details of certification requirements.) When an individual is believed to have

satisfied the certification requirements for a particular task, the appropriate Request for Certification Form is submitted by the Principal Investigator to the Data Coordinating Center to document the training and experience of the individual. If the appropriate reviewer of the submitted materials recommends certification, the Data Coordinating Center staff notify the Principal Investigator in writing that the staff member is certified and assigned a certification number.

14.12.3 Procedures for Masking Patient Records

When documents are submitted to the Data Coordinating Center in conjunction with hospitalization forms or death forms, it is the responsibility of the Research Coordinator to insure that all references to the patient's name are carefully deleted and replaced with, preferably, both the patient's ID Number and Name Code or, at a minimum, the patient's ID Number. All other identifying information should be carefully deleted. The patient's ID Number and Name Code must be printed on the lower right-hand corner of each page of each document. The Research Coordinator should maintain a copy at the Clinical Center of the documents as they were received in response to his/her requests. All documents, whether they are hospital discharge summaries, ECGs, laboratory report(s), lists of medications, hospital records, death certificates, or autopsy records, must be masked to insure patients' confidentiality. All identifying information includes name, address, age, race, birth date, birth place, relative's name(s) and address(es), occupation, Social Security Number, funeral arrangements, hospital name and address, etc.

14.12.4 Other Procedures

The Data Coordinating Center should be notified promptly of changes in Clinical Center personnel, Clinical Center affiliated hospital names and addresses, or telephone numbers so that the T3

Address Directory can be maintained correctly. Changes should be reported by sending an updated copy of the Clinical Center's page in the Address Directory to the Data Coordinating Center.

It is recommended that the Research Coordinator maintain a calendar of T3 meetings and training sessions, deadlines for special projects, and record of patient payments received.

All informational memoranda from the Data Coordinating Center, National Heart, Lung and Blood Institute, and other central units should be filed for easy reference. The T3 Manual of Operations and Address Directory should be kept up-to-date by inserting revised pages as they are received from the Data Coordinating Center. A notebook which contains a reference copy of the latest revision of each T3 form is also useful. The Research Coordinator should discard all previous versions of a form whenever a new revision is received.

Information requested by the Data Coordinating Center or other groups should be provided promptly. If an immediate response is not possible, the appropriate individual should be notified. Clinical Center staff are sometimes asked to contact hotels in the vicinity of the Clinical Center to obtain information regarding meeting facilities and availability. These requests are handled promptly and the Data Coordinating Center staff are provided with the necessary information.

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