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Follow-up of Patients Receiving Diagnostic Doses of 131 Iodine During Childhood

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September 1978

FOLLOW-UP OF PATIENTS RECEIVING DIAGNOSTIC DOSES OF 131 IODINE DURING CHILDHOOD

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FOREWORD

The many benefits of our modern, developing, industrial society are accompanied by certain hazards. Careful assessment of the relative risk of existing and new man-made environmental hazards is necessary for the establishment of sound regulatory policy. These regulations serve to enhance the quality of our environment in order to promote the public health and welfare and the productive capacity of our Nation's population.

The Health Effects Research Laboratory, Research Triangle Park, conducts a coordinated environmental health research program in toxicology, epidemiology, and clinical studies using human volunteer subjects. These studies address problems in air pollution, non-ionizing radiation, environmental carcinogenesis and the toxicology of pesticides as well as other chemical pollutants. The Laboratory participates in the development and revision of air quality criteria documents on pollutants for which national ambient air quality standards exist or are proposed, provides the data for registration of new pesticides or proposed suspension of those already in use, conducts research on hazardous and toxic materials, and is primarily responsible for providing the health basis for non-ionizing radiation standards. Direct support to the regulatory function of the Agency is provided in the form of expert testimony and preparation of affidavits as well as expert advice to the Administrator to assure the adequacy of health care and surveillance of persons having suffered imminent and substantial endangerment of their health.

This research effort was initiated with the intent of estimating the dose response curve for the development of thyroid neoplasms in young adults who received low diagnostic doses of Iodine 131 as children. This report documents the data collection methodology and procedures of a follow-up survey conducted of persons under 16 years old who received diagnostic Iodine 131 for evaluation of thyroid function at nine clinical centers prior to December 31, 1960.

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ABSTRACT

This research effort was initiated with the overall objective of defining a dose-response curve for the development of thyroid neoplasms in young adults who received low doses of Iodine 131 as children. In order to accomplish this objective, a follow-up survey was conducted of persons under the age of 16 years who received diagnostic I^{131} for evaluation of thyroid function at nine participating clinical centers on or before December 31, 1960. Certain medical, demographic, and dosimetric data were abstracted from the records of participating clinical centers and physicians; information on each eligible patient's health history and status was solicited from appropriate respondents via mail questionnaires. Correspondence was conducted under the letterhead of the appropriate participating clinical center. Copies of death certificates were obtained for deceased patients.

Of 2,287 potential study subjects identified, some medical record was reviewed and abstracted for 1,999 or some 87 percent. With study activities incomplete, of 186 private physicians and other referral sources contacted for supplemental data, only three or less than two percent declined to participate; of 1,362 patients who were determined eligible and entered the survey phase, some final resolution (completed questionnaire, death certificate, or refusal) was obtained for 1,065 or some 78 percent.

This report was submitted in fulfillment of Contract No. 68-02-1213 by Research Triangle Institute under the sponsorship of the U. S. Environmental Protection Agency. This report covers a period from June 8, 1973, to May 7, 1977. A related project is continuing under the sponsorship of the U. S. Food and Drug Administration.

CONTENTS

CONTENTS (Continued)

FIGURES

FIGURES (Continued)

TABLES

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SECTION 1

INTRODUCTION

1.1 BACKGROUND

Radioactive iodine 131 has been an important medical tool in the diagnosis of thyroid disease since the late 1940's. A series of experimental studies of animals exposed to I^{131} and other forms of radiation (1-7), and epidemiological studies of human populations exposed to x-irradiation during or before adolescence in the course of treatment for benign head and neck conditions (8-22), have demonstrated various levels of thyroid pathology; Dr. L. H. Hempelmann proposed a linear dose-response relationship based on some of these studies (13,23). There have been few studies which have specifically investigated the effects on human thyroid tissue of I^{131}, and those have involved persons exposed to I^{131} as a result of nuclear explosions in Japan, the south Pacific, and the southwestern United States (24-28), and persons with diseased glands (29-35). At least one study (35) of the effects of I^{131} on the thyroid gland observed *that there is a relatively higher risk of developing malignant and benign neoplasms in patients treated with I^{131} below the age of 20 than in older age groups* (36). Based upon this scattered and inconclusive information, it would appear that a specific study of the long-term effects of exposure to low levels of I^{131} such as those utilized in diagnostic procedures would be worthwhile.

The radiosensitivity of the growing thyroid of children is of special interest because of the potential exposure of large segments of the population to radioactive iodine and other radionuclides dispersed into the environment from the potential malfunction of nuclear power plants and fallout from nuclear testing. Children who received diagnostic doses of I^{131} comprise a unique human population, one of the few irradiated human populations available for study that could provide insight into the problems of evaluating established national environmental and emission standards for radioactive materials, specifically radioactive iodine. The large range of doses involved and the long latent periods which have elapsed provide an opportunity to establish the shape of a dose-response curve for the development of thyroid neoplasms in young adults exposed to I^{131} radiation as children and thereby enable the determination or description of the relevant sectors of the dose-response curve for this radioactive substance. In view of the current unrest over the levels of safety represented by the legally acceptable limits for exposure of the population at large, and the importance of the practical decisions affecting the availability of nuclear power, study of this population can provide one basis for evaluating established national environmental and emission standards for radioactivity.

1.2 OBJECTIVES

1.2.1 Overall Project Objectives

The purpose of this research effort was to conduct a follow-back study of persons who received diagnostic doses of I^{131} during childhood in an effort to define a dose-response curve for the development of thyroid neoplasms in young adults following I^{131} exposure. It was anticipated that this effort would result in the identification of a relevant sector of the dose-response curve and aid in the establishment of the long range effects of exposure to I^{131}.

1.2.2 Research Triangle Institute (RTI) Objectives

The purpose of RTI's involvement in this research effort was to collect health history information on persons who received I^{131} prior to 1961 in a form that would enable the sponsor, the Health Effects Research Laboratory (HERL) of the U. S. Environmental Protection Agency (EPA), to define the aforementioned dose-response curve. RTI's role in this research effort was to furnish the necessary personnel, materials, services, equipment, and facilities, except as specified, and otherwise do all things necessary for, or incident to, the collection of data for the study from and through participating clinical centers. RTI was to collect necessary study data, act as a central agency for the collection of the data, and be sure that data were comparable within and between clinical centers and collected according to protocol. RTI was to abstract pertinent and necessary medical and demographic information from the records of participating clinical centers and physicians; solicit information on each eligible patient's health history from appropriate respondents primarily via mail questionnaires; and submit data to the Project Officer or his designee as collected.

1.2.3 Purpose of this Report

This report is the final report on RTI project activities conducted under Contract Number 68-02-1213 over the period 8 June 1973 - 7 May 1977. However, an RTI contract with the Bureau of Radiological Health (BRH) of the Food and Drug Administration (FDA) is continuing and expanding the study.

SECTION 2

METHODOLOGY

2.1 PERFORMANCE SITES

The study was to involve some 3,000 patients who received I^{131} for diagnostic purposes over the period 1946 through 1960. The clinical centers and sites involved in this research effort were specified by EPA and were as follow:

Cincinnati General Hospital (CGH), Cincinnati, Ohio;
University of Kansas Medical Center (KUMC), Kansas City, Kansas;
University of Colorado Medical Center (UCMC), Denver, Colorado;
University of California Hospitals and Clinics at San Francisco, California (UCSF);
Menorah Medical Center (MMC), Kansas City, Missouri;
Strong Memorial Hospital (SMH), Rochester, New York;
Shelton Medical Clinic (SMC), Los Angeles, California;
Saint Louis University Medical Center (SLU), St. Louis, Missouri; and
Columbia-Presbyterian Medical Center (CPMC), New York, New York.

2.2 DEFINITION OF STUDY GROUP

Lists of patients identified as have received I^{131} for diagnostic purposes at the various clinical centers during the study period, with appropriate identifying information, were to have been provided RTI by EPA (37). The persons under study were selected from those patients identified, based upon the following study criteria:

1. Received I^{131} for the first time before January 1, 1961;
2. Were less than 16 years of age at the time of first administration of I^{131};
3. Did not have a diagnosed thyroid lesion (malignant or benign) at the time of the diagnostic test;
4. Had not received goitrogen therapy or radioactive iodine for hyperthyroidism; and
5. Were not diagnosed as being hyperthyroid or athyrotic at the time of the test.

The objective was to obtain a study population who received diagnostic I^{131} before age 16 and prior to 1961, and who were free of thyroid lesions and not hyperthyroid or athyrotic. Restricting this study to those persons who received radioactive iodine prior to 1961 provided a sufficiently long

latent period for the development of thyroid lesions, and by relating the dose level received, a dose-response curve could theoretically be determined. These data will also allow the evaluation of the Relative Biological Effectiveness (RBE) of I^{131}.

The study was designed originally *to test Hempelmann's hypothesis that the dose-response for radiation-induced benign tumors is 38-52/rad/10^6/yr for 25 years* (23); therefore, there was considered to be no specific need for a control group. *Dr. Hempelmann has established that the normal prevalence of palpable thyroid lesions in a group of young adults (average age 22.5 years) is one percent at a maximum* (23).

2.3 DATA COLLECTION

2.3.1 Contractual Requirements

Exhibit A - Scope of Work of Contract No. 68-02-1213 (37) specified the following data collection requirements of the contractor (RTI):

The contractor shall collect data for a study designed to define a dose-response curve for the development of thyroid neoplasms in young adults who were given diagnostic doses of ^{131}I as children. The contractor shall abstract information from the records of physicians and medical centers and shall obtain questionnaires soliciting information in patients' illnesses history.

In collecting the data required, the Contractor shall use the procedures indicated and such other procedures as necessary:

1. *The Contractor shall contact the medical centers to make arrangements for the collection of data from the hospital records and contacting patients through the hospital. Items of consideration being:*
   (a) procedures for handling hospital records
   (b) utilization of hospital and contractor personnel
   (c) method and amount of payment for services
2. *The contractor shall provide for a review of medical records of each person on the list to determine his eligibility for inclusion in the study, following protocol guidelines.*
3. *For accepted patients:*
   (a) Abstract data from medical records including: Birthdate, sex, race, date of exposure to (and dose of) *Diagnostic ^{131}I administered, uptake, size of gland, reason for test, final diagnosis, and name and address of parent or guardian and/or other location information.*
   (b) Mail cover letter and questionnaire to each parent or guardian on letterhead of the medical center involved.
4. *For rejected patients, the reason for rejection shall be shown.*
5. *The Contractor shall make every effort to locate all patients accepted for the study. This may require more than one mailing and the use of other follow-up and location procedures.*

6. *Death Certificates or the data therefrom shall be obtained where the patient is deceased.*

7. *The Contractor will turn all data over to the Human Studies Laboratory, Environmental Protection Agency, Research Triangle Park, North Carolina as it is collected.*

Based upon the above listed contractual requirements and other guidelines provided by EPA (23), RTI developed the procedures presented in following sections for implementation of the study under contract to EPA. Figures 1 and 2 are flow charts which present the procedural steps graphically. At each performance site, the study has been implemented in three basic phases, Phase I consisting of initial contact and arrangements for cooperation and participation; Phase II consisting of the Hospital Data Collection (HDC) - that is, medical record abstraction; and Phase III consisting of survey operations. Figure 1 presents the implementation of the study from initiation through HDC (Phases I and II), while figure 2 presents survey and follow-up procedures (Phase III).

2.3.2 Phase I: Enlistment of Performance Sites

Although the contract stated that *the contractor shall contact the medical centers to make arrangements for the collection of data from the hospital records and contacting patients through the hospital* (37), the EPA Project Officer actually made initial contact with each clinical center, as shown in figure 1, in order to review the overall project plan with appropriate clinical center representative(s) and obtain preliminary or tentative permission to work through the clinical center during the study and use clinical center records. The EPA representative then designated particular appropriate clinical center representative(s) as contacts for the RTI data collection staff. Following this preliminary EPA contact, the RTI Project Leader visited the proposed performance site to review the detailed study protocol and procedures with appropriate clinical center representatives and make any necessary modifications according to the particular procedures of the clinical center/performance site.

Once the site representative(s) agreed to cooperate and participate in the study, arrangements were made to obtain the review medical records; obtain clinical center letterhead stationery and envelopes; arrange for the signature of the appropriate and responsible clinical center representative to affix to study correspondence for the site; make arrangements for mail pickup and delivery; agree on reimbursement for clinical center costs incurred in involvement in the study; and enlist an on-site representative to reduce the necessity and expense of RTI staff travel where possible.

Originally RTI intended to use a Post Office Box to handle all project mail; however, due to the unavailability of Post Office boxes, as well as the possibility of confusion engendered by a Post Office address different from the letterhead address, it was decided that the participating clinical centers would serve as the mail repository where volume permitted; at those sites, project mail was coded in the return address with specific identifying letters to facilitate recognition and sorting of project mail from other mail received at or returned to the site.

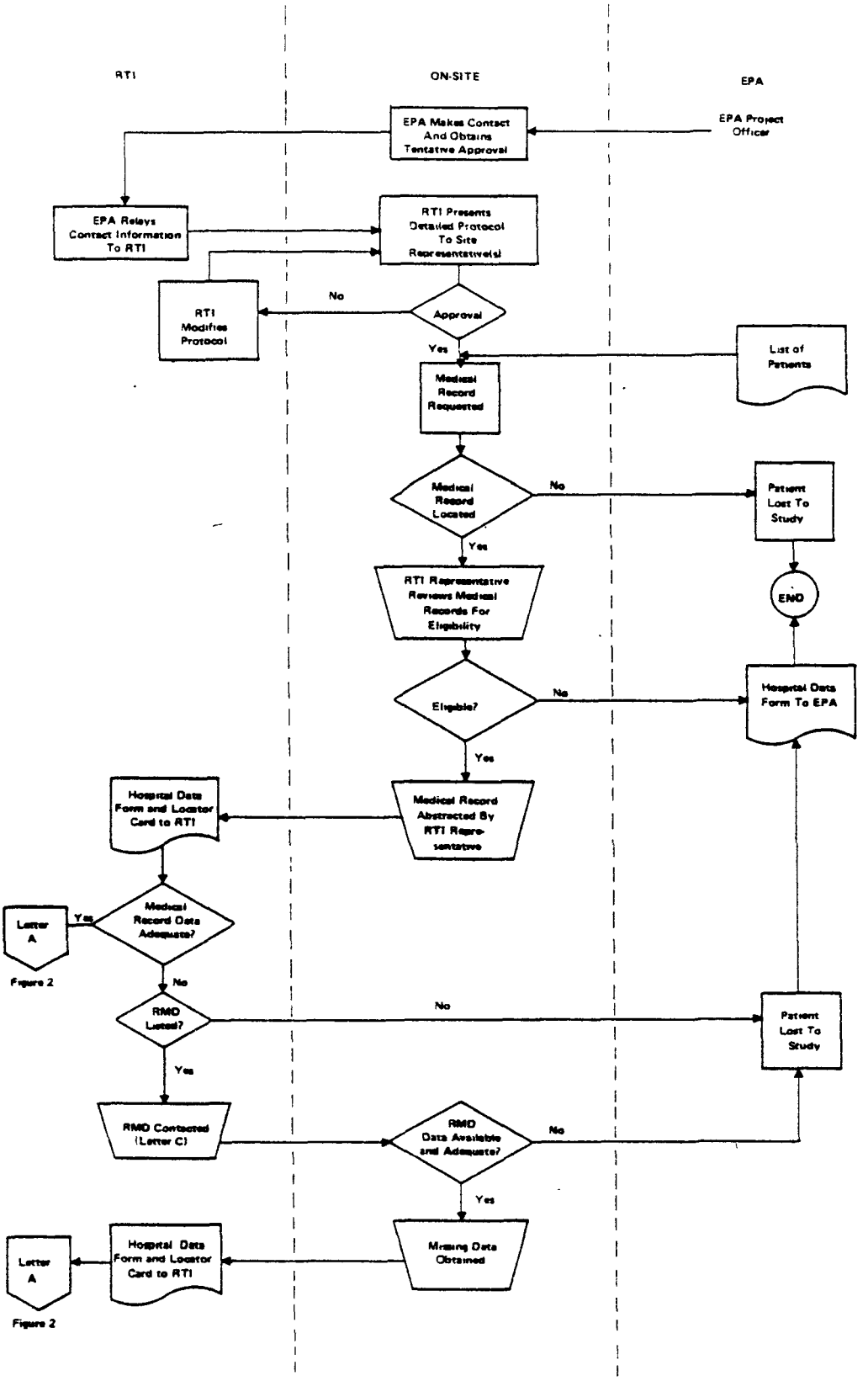

Figure 1. Diagrammatic representation of implementation of the study from contact through hospital data collection (Phases I and II).

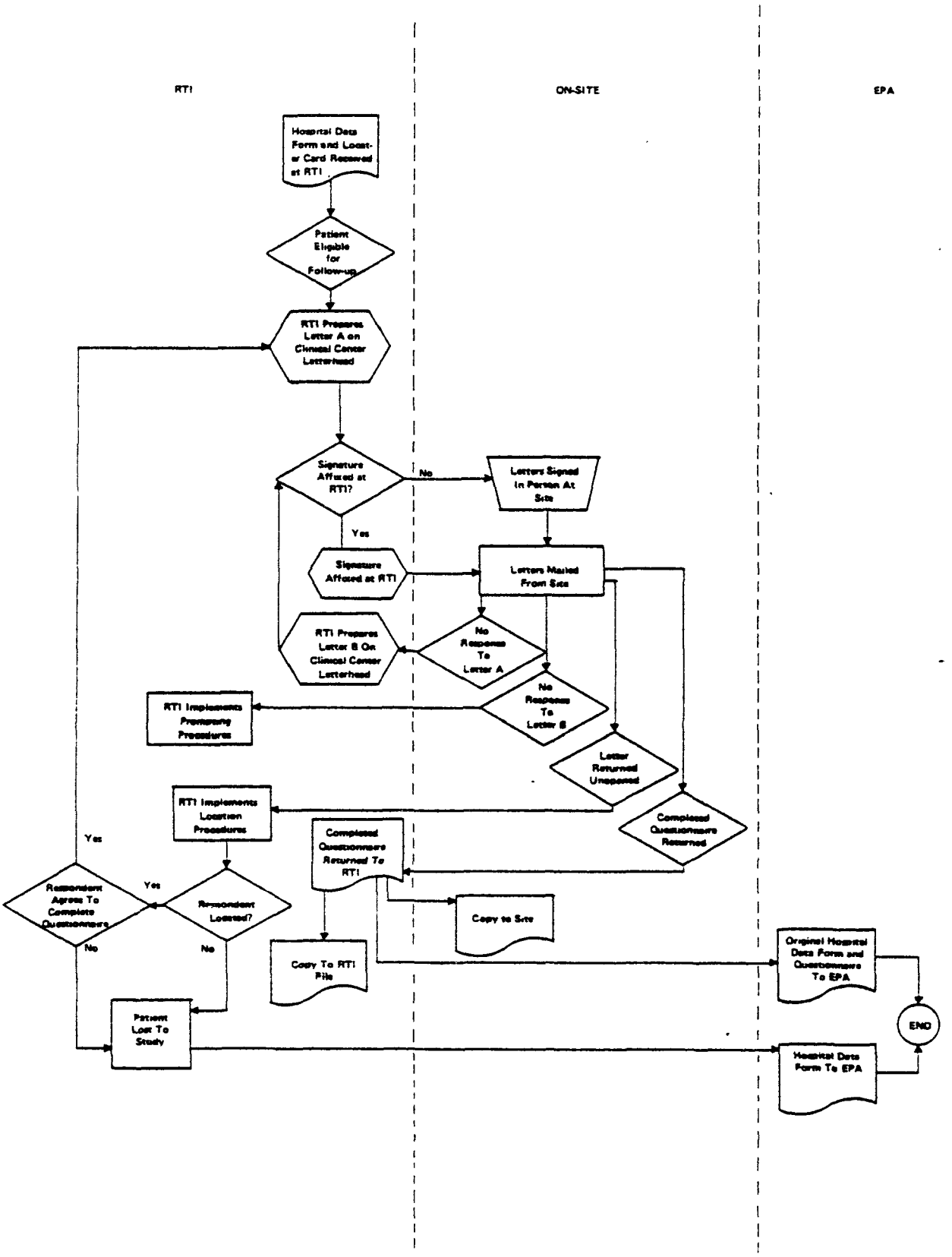

Figure 2. Diagrammatic representation of survey activities (Phase III).

Study No. _____ (1-7)

FORM APPROVED
OMB # 158-573006

HOSPITAL DATA FORM

Name _____ (8-41)

Sex: (48) ☐ 1 Male ☐ 2 Female

Race: (49) ☐ 1 White ☐ 2 Black ☐ 3 Other

Birthdate _____ mo/day/yr (42-47)

Test No. (50-51)	Date of Test mo/day/year (52-57)	Dose Administered (μc) (58-61)	Hours Uptake (62-63)	% Uptake (64-66)	Estimated Gland Size (67-70)	Pre-Test Diagnosis	Final Diagnosis	Do Not Mark In This Space (71-74)	(75-78)	(79-80)
01										02
02										03
03										04
04										05
05										06
06										07

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Figure 3. Hospital data form.

Originally, it was also planned that the site would open project mail and copy completed questionnaires for their files; however, in order to reduce the number of people handling project mail, and the amount of project work required of clinical center staff, project mail was returned to RTI where copies were made and provided the site, along with copies of related correspondence and appropriate identifying information. Some level of on-site assistance was enlisted at all sites.

2.3.3 Phase II

2.3.3.1 Hospital Data Collection

At each performance site, the medical records staff were requested to provide the medical records for the patients on the lists of individuals to be studied, in accordance with the various clinical center regulations. Staff of the various clinical centers' medical records departments physically performed the record search and retrieval.

Once the medical records were pulled by clinical center staff, they were reviewed by the RTI Project Leader in order to obtain and verify certain necessary medical and demographic information determining the eligibility of each patient according to previously outlined guidelines (see section 2.2). Each patient for whom a clinical center record was located or a private physician record anticipated was assigned a two-part, seven-digit study number: the first four digits designated the clinical center and were unique for the clinical center, having been assigned by EPA; the last three digits designated a patient within the clinical center and were assigned by RTI consecutively from 001 up. Patients were identified by the study number entered on the Hospital Data Form (HDF); this form, which was designed, prepared, and supplied by EPA, is reproduced as figure 3. Even though space was proveded on the HDF, the patient's name did not appear on that form, which was submitted to EPA, for reasons of confidentiality.

The records of each person whose name was provided were reviewed to determine the patient's eligibility for inclusion in the survey phase of the study. For inclusion in the survey phase, patients had to meet each of the criteria cited in section 2.2. Every name provided RTI was to be either accepted for the survey phase of the study (meets all of the criteria), or rejected (failure to meet one or more of the criteria), and the reason(s) for rejection noted on the HDF prepared for each patient. At the outset of the project, the plan was to hold in abeyance patients in the study population whom EPA indicated as having a final diagnosis of hyperthyroidism, thyroiditis and/or thyroid neoplasia, and some of those who did not have clinical center record numbers. However, in view of the limited number of total patients in this study, the EPA Project Officer and the RTI Project Leader decided to include in the study some of those patients held in abeyance in the event that a record might be located or that the diagnosis recorded on the EPA card might be incorrect.

For those individuals meeting the requirements for inclusion in the study survey sample, pertinent medical data necessary to define the dose-response curve, as well as information pertaining to the location of the patient's

family or guardian, was abstracted from medical records (see figure 1). The pertinent demographic and medical data entered on the HDF (figure 3) included the following information:

(1) Birthdate,
(2) Sex,
(3) Race,
(4) Date(s) of administration of diagnostic I^{131},
(5) Dose(s) of diagnostic I^{131} administered (in microcuries),
(6) Uptake with time (24 hour if available),
(7) Estimated size of gland,
(8) Pre-test diagnosis (or reason for referral), and
(9) Final diagnosis.

Pieces of data were found to be missing from the medical records and/or radioisotope (RAI) laboratory files of patients whose records were reviewed during the *Pilot Study* at CGH; this matter was discussed with the Project Officer with the decision that RTI was to proceed with the best available data, using information from the EPA cards *if other bits of information from the EPA cards could be verified from available records.*

Information collected/abstracted pertaining to the location of the patient's family or guardian included the following:

(1) Patient's name and names of parents, spouse, and any other relatives or friends provided in the medical records;
(2) The most recent and any other addresses provided for the above individuals;
(3) Information on the employment, education, and/or institutionalization of the above individuals; and
(4) Any other pertinent information available, such as Social Security numbers and indicated interest/involvement of social service agencies, physicians, and other medical care institutions.

Where possible, all information was dated in order to make it most relevant. Locator information was entered on a separate 5 by 8 inch index card, along with the patient's study number and birthdate; these cards were retained at RTI for tracing purposes.

The EPA Project Officer and the RTI Project Leader agreed that a death certificate or the information therefrom was adequate without soliciting interim medical history from the parents or guardian of the patient, *provided* the patient died within three years of receiving the isotope for the first time. Furthermore, with regard to patients who had expired, it was decided in discussion with the Project Officer that a copy of the death certificate would not be sought if a copy of the death certificate was available for review in the patient's medical record; in many of these cases, an autopsy was also performed at the clinical center, so that a detailed pathology report, in many cases including a report of microscopic examination of the thyroid gland, was available. In actual practice, however, a death certificate copy was requested in most instances.

The components of the various participating clinical centers involved in this phase of the study were primarily the RAI Laboratories or Nuclear Medicine Departments and the Medical Records Departments. Several of the sites had maintained files of old RAI reports separate from the medical records, but the medical record was the most complete and consistent source of the medical and demographic data necessary for the execution of this study. Old I^{131} uptake reports provided valuable information on patients with no other clinical center records and/or data missing from other medical records.

Part of the necessary study information was abstracted from medical records and part from the questionnaire sent to the appropriate respondent, usually the parent. The date(s) of administration of I^{131}, the dose(s) of I^{131} administered and the percent uptake and time were usually available from the RAI report, although one or more of these elements may have been missing from the RAI report and was sought in the doctor's orders, nurses' notes, progress notes, discharge summary, or a subsequent letter to a referring physician (RMD). The birthdate, sex, and race appeared at any one of several points in the medical records, such as the admission sheet or various physicians' workups, The estimated size of the thyroid gland and the reason for the test, or pre-test diagnosis, occasionally appeared as part of the RAI report but more likely came from the physical examination and impression of the attending physician's workup on admission or preceding clinic visit. The best sources for the final diagnosis were the diagnosis sheet at the front of the medical record, where one was available, the discharge summary, diagnosis on a subsequent clinic visit, or again a letter to an RMD. Location information occurred throughout the medical record, including the admission sheet, insurance forms, and correspondence; social service workups were particularly helpful where they were available.

The majority of medical record abstraction for this study was performed by the RTI Project Leader.

2.3.3.2 Referring Physicians and Facilities

At each performance site, the medical records of some patients recorded as having received diagnostic I^{131} at the clinical center were inadequate for the purposes of the study. Where medical and/or demographic data from the medical records were inadequate for the purposes of the study, but the name of the RMD was provided in available records, every attempt was made to locate that RMD. Sources consulted included the Directory of Medical Specialists (38), the Alphabetical Physician Reference listing (39), telephone directories and directory assistance for the last known address, local medical societies, and state licensing agencies, Cooperation was excellent. RTI originally intended not to contact RMD's outside of the respective metropolitan areas, but subsequently decided to do so in the event that the patient's office records might still be in the respective metropolitan area, or the RMD might be able to provide the necessary information by mail or telephone.

For all performance sites except SMC, where contact with referring physicians was not necessary, and CPMC (see below), a letter (called letter

C in figure 1) such as that shown in figure 4 was sent to the appropriate RMD or other referral facility, explaining the project and requesting permission for the RTI Project Leader to review the patient's office records in an effort to obtain necessary medical and/or demographic data on the patient. Where private physicians or other referral facilities agreed to participate in the study and provide access to patient records, arrangements were made to access necessary medical, demographic and locator information. Due to the large number of RMDs for CPMC with only one patient each dispersed over four states (CT, NJ, NY and PA), RTI is attempting to obtain missing data via mail using a modification of the letter presented in figure 4. This modification is presented in figure 5.

Discussions between RTI and EPA technical representatives determined that potential study patients for whom no medical record or RAI file could be located, and study patients who were apparently eligible but for whom no final diagnosis or RMD was forthcoming from the HDC, would be held apart from the study. However, where a patient had no medical record or RAI file, but the RMD was indicated on the EPA card, the RMD was contacted regarding patient data.

The review of medical records of study patients in private physicians' offices was a most profitable procedure from a data standpoint, although communications with RMDs and other referral sources presented some problems. At three sites where the participating clinical center served as a referral center for laboratory services for other primary medical care facilities in the community, arrangements were made for RTI staff to access patient records at the other institution(s). In many instances only the RMD's last name was recorded in a patient's medical records requiring that several physicians with the same last name be written or called regarding the same patient(s), after eliminating unlikely (due to age, etc.) prospects by referring to physician directories (38,39).

RTI did not anticipate nonresponse from referral sources. Therefore, EPA and RTI technical representatives decided to pursue referring physicians/facilities who did not respond to initial correspondence (letter C) with reminder letters, such as that reproduced as figure 6, or by telephone.

2.3.4 Phase III: Survey Operations

In most instances, the review of the medical records provided a last known mailing address for the appropriate respondent for each patient accepted into the survey phase of the study; this address was underscored on the locator card. As indicated previously, RTI obtained clinical center letterhead stationery for use in preparing project correspondence.

There were two basic letters mailed to eligible respondents on clinical center letterhead stationery over the signature of the appropriate clinical center representative. The first letter, letter A, an example of which is reproduced as figure 7, was the initial cover letter included with the questionnaire and sent to all eligible respondents; the second letter, letter B, an example of which is reproduced as figure 8, was sent to all eligible respondents whose questionnaires or initial correspondence was not returned

within a reasonable period following the first mailing. In actual practice, two letter A's were employed during the course of the study. The letter shown in figure 7 was used predominantly for the first four participating clinical centers (CGH, UCMC, UCSF, and KUMC); this letter was expanded to the form shown in figure 9 for the remaining sites (see section 3.3.3). Various participating clinical centers made minor wording changes; in addition, transmittal and reminder letters were modified as appropriate for various respondents -- that is, whether the respondent was the patient, a parent, a sibling, a guardian, etc. All study correspondence was prepared for mailing on automatic word-processing equipment at RTI by members of the RTI staff. The questionnaire, reproduced as figure 10, was designed, prepared and supplied by EPA.

Letter A was addressed to the last known address of the patient's parent or other responsible guardian, then returned to the appropriate clinical center to be signed by the appropriate representative and mailed from the site, or the signature affixed at RTI and then returned to the site for mailing, the envelopes having been previously stamped at RTI (see figure 2). A questionnaire and letter A were mailed from the site to the last address known for each eligible respondent. There were three basic possible results to this initial mailing: questionnaires completed and returned; unopened packets returned by the U.S. Postal Service as not deliverable; and packets not returned at all (see figure 2). Letters to RMDs were handled in virtually the same manner.

The basic purpose of letter A was to request that the respondent(s) complete the questionnaire (figure 10), thereby providing a brief medical history for the patient. At the end of the questionnaire, a release statement to be signed by the appropriate person authorized further examination of medical records of the named patient, if required (see figure 10). This authorization applied to EPA personnel and did not imply that RTI staff are/were responsible for examining medical records other than as required in the initial determination of eligibility for the survey phase of the study and the collection of basic demographic, medical, and locator data at that time. In actual practice, however, RTI has written where authorized to physicians, clinics, hospitals and laboratories to complete or verify information provided by respondents regarding hospitalizations, thyroid function tests, and thyroid medication, and to obtain pathology reports for throat, neck, or thyroid surgery.

Each mailout packet included a postage-paid preaddressed return envelope for returning the completed questionnaire. RTI made arrangements for the collection of project mail at each performance site and its return to RTI for sorting, recording, and appropriate action. RTI staff visited the performance sites as appropriate during the course of the study.

Once a completed questionnaire was returned, the original was submitted to EPA along with the corresponding HDF, and a copy returned to the site for the patient's records at the clinical center. In the event of a death, a copy of the death certificate was requested from the appropriate state or local office and dispensed in the same manner.

Dear Dr. :

This hospital is presently involved in a study to determine if people suspected of thyroid disease in early life do or do not develop thyroid disease or other illnesses in later years. In reviewing our files and medical records, we have encountered the name of one of your private patients who was referred to this hospital for diagnostic procedures, but for whom there is no medical record maintained at this hospital. The name of that patient is given below:

(Patient's name)

We are writing at this time to request permission for Mr. Benjamin S. H. Harris, III, a representative of the Research Triangle Institute in Research Triangle Park, North Carolina, who is working with this hospital and the Environmental Protection Agency, under whose auspices this research effort is being undertaken, to visit your offices and review the medical record of the patient listed above in order to ascertain his eligibility for inclusion in the study sample and, if eligible, to abstract certain basic medical and demographic information in order to solicit information from the parents of this patient regarding the patient's medical history and current health status. For your information, a copy of the protocol and procedures for implementing the study is enclosed.

We would greatly appreciate your cooperation in this research effort.

Yours very truly,

Figure 4. Letter C, initial letter to referral sources.

Dear Dr. :

This hospital is presently involved in a national study to determine if people suspected of thyroid disease in early life do or do not develop thyroid disease or other illnesses in later years. In reviewing our files and medical records, we have encountered the names of several private patients who were referred to this hospital for diagnostic procedures, but for whom medical records are inadequate for purposes of the study. Furthermore, in several instances, we only have the referring physician's last name. We are writing at this time to inquire as to whether or not one or more of the patients in question were referred by you, and, if so, to request certain information necessary for our research effort but missing from the medical records and radioisotope laboratory files here.

In reviewing our files and medical records, we encountered the name of one *(Patient's name)*, who was referred by you to this hospital for care in *(year)*, at which time he received radioactive iodine for suspected thyroid disease. However, there is no definitive final diagnosis recorded relative to the *(year)* uptake test. Do you by any chance have any information in your records on *(Patient's name)* regarding a definitive final diagnosis relative to a *(year)* uptake test? A stamped, self-addressed return envelope is enclosed for your convenience. Please address your response to that address.

We would greatly appreciate any information which you could provide on this matter.

Yours very truly,

Figure 5. Letter C', revised initial letter to referral sources.

Dear Dr. :

You may recall that this hospital recently asked for your participation and assistance in a study to determine if people suspected of thyroid disease in early life do or do not develop thyroid disease or other illnesses in later years. In a previous letter, a copy of which is attached, we requested permission for Mr. Benjamin S. H. Harris, III, a representative of the Research Triangle Institute in Research Triangle Park, North Carolina, who is working with this hospital and the Environmental Protection Agency, under whose auspices this research effort is being undertaken, to visit your offices and review the records of certain of your private patients who were referred to this hospital for diagnostic procedures, but for whom there is no medical record maintained at this hospital. The purpose of Mr. Harris' visit would be to ascertain the eligibility of your patient(s) for inclusion in our study sample, and, if eligible, to abstract certain basic medical and demographic information in order to solicit information from the parents of the patient(s) regarding the patient's medical history and current health status. For your information, a copy of the protocol and procedures for implementing the study was enclosed.

As of this date, we have received no reply from you. As our study sample is somewhat circumscribed, each response and information on each patient in the study sample is of considerable importance to us. Your participation and cooperation in this research effort would be greatly appreciated.

Thank you for your consideration. We look forward to hearing from you in the very near future.

Yours very truly,

Figure 6. Reminder letter to referral sources.

Dear :

In *(year)*, your child, *(Patient's name)*, was given a test in this hospital for suspected thyroid disease. This hospital is presently involved in a study to determine if people suspected of thyroid disease in early life do or do not develop more illnesses or develop thyroid disease in later years. In order to make this determination, it is important that we receive information concerning your child.

Please answer the questions on the enclosed questionnaire and return it in the self-addressed envelope. Give the best information you can, even though you may not know the exact answers to some of the questions. All answers will be held in strict confidence and all information will be used only for statistical purposes. Your participation in this research effort is, of course, voluntary, but your cooperation would be greatly appreciated.

Yours very truly,

Figure 7. Letter A, initial letter to respondents for eligible patients.

Dear :

You may recall that this hospital recently asked for your participation in a national study to determine if people suspected of thyroid disease in early life do or do not develop more illnesses or develop thyroid disease in later years. We requested that you complete a brief questionnaire regarding the health of *(Patient's name)* for this purpose. As of this date, your reply has not been received.

The questionnaire was mailed only to a select group of people; since you are one of the select few and your response is of importance to us, we are taking the liberty of mailing you another copy of the questionnaire. Won't you please take a few minutes to answer the questions and return the completed questionnaire to us? Again, we want to assure you that your reply will be held in strictest confidence and used for research purposes only.

If you have mailed the completed questionnaire to us during the last few days, please disregard this reminder. However, if more than a few days have elapsed since you returned the questionnaire, we would greatly appreciate your completing this additional questionnaire, as your response has apparently been lost in the mail.

Thank you for your cooperation.

Sincerely,

Figure 8. Letter B, reminder letter to respondents for eligible patients.

Dear :

In *(year)*, your child, *(Patient's name)*, was given a test in this hospital that is often given to detect conditions that might be due to thyroid malfunctions. This test is relatively routine for a number of conditions, and was probably one of many tests your child received at the time. The fact that your child had a "thyroid test" at some time does not mean your child has thyroid disease.

We are presently involved in a study to determine if people suspected of thyroid-related illnesses in early life do or do not develop more illnesses or develop thyroid disease in later years. As part of this study we are reviewing the records of all young people who had a thyroid test in this Center, whether or not the gland was found to be normal at the time of the test. In order to make our determinations in this study it is important that we receive information concerning your child.

Please answer the questions on the enclosed questionnaire and return it in the self-addressed envelope. Give the best information you can, even though you may not know the exact answers to some of the questions. All answers will be held in strict confidence and all information will be used only for statistical purposes.

Due to the passage to time, some of the patients in our study are adults or have passed away. If your child is of age, you might wish to have him or her complete the questionnaire and/or sign the authorization. If your child resides at a different address we will gladly forward the questionnaire if you will provide us with the correct address. In the event that your child has passed away, we would greatly appreciate your completing the questionnaire covering the time up to passing and indicate date and place of death on the questionnaire.

Your participation in this research effort is voluntary, but your cooperation would be greatly appreciated.

If you have any questions or problems with the study or questionnaire, please note such on the back of this letter or questionnaire and return in the enclosed self-addressed envelope. Each inquiry will be handled promptly and on an individual basis.

Thank you for your cooperation.

Yours very truly,

Figure 9. Letter A', revised initial letter to eligible respondents.

FORM APPROVED
OMB #158 S73008

THYROID STUDY QUESTIONNAIRE

Study No _____ *Birthdate* _____
(Complete or correct birthdate if in error.)

1. What do you consider the current status of the health of this child? Please check one.

☐ Good ☐ Fair ☐ Poor

If you do not consider this person in good health, state briefly his or her health problem

_____

_____

2. Has this child had any illnesses other than the usual childhood diseases?_____ If yes, list illnesses and year of onset of that illness.

Illness, year of onset	Illness, year of onset
_____	_____
_____	_____

3. Has this child been hospitalized since he or she was tested in this center?_____ If yes, list place, time and reason for hospitalization.

Hospital name	City, state	Year of hospitalization	Reason for hospitalization
_____			
_____			

4. Has this person been tested for thyroid disease since he or she was seen in this center?_____ If yes, list place and time of test.

Place of test	Year of test
_____	_____
_____	_____

5. Is this person presently on or has he or she ever been on thyroid medication?_____ If yes, please state kind of medication._____

Dosage _____ Date of medication from _____ to _____
(year) *(year)*

Thank you very much for this information. Your cooperation in this effort is greatly needed and appreciated. If you have answered yes to questions 3 and 4 please sign the authorization below

---

AUTHORIZATION

For purposes of this medical survey, I authorize the personnel conducting this survey to examine the medical records of my child in both private physicians' offices and in hospitals if necessary.

Signature: _____ Date: _____

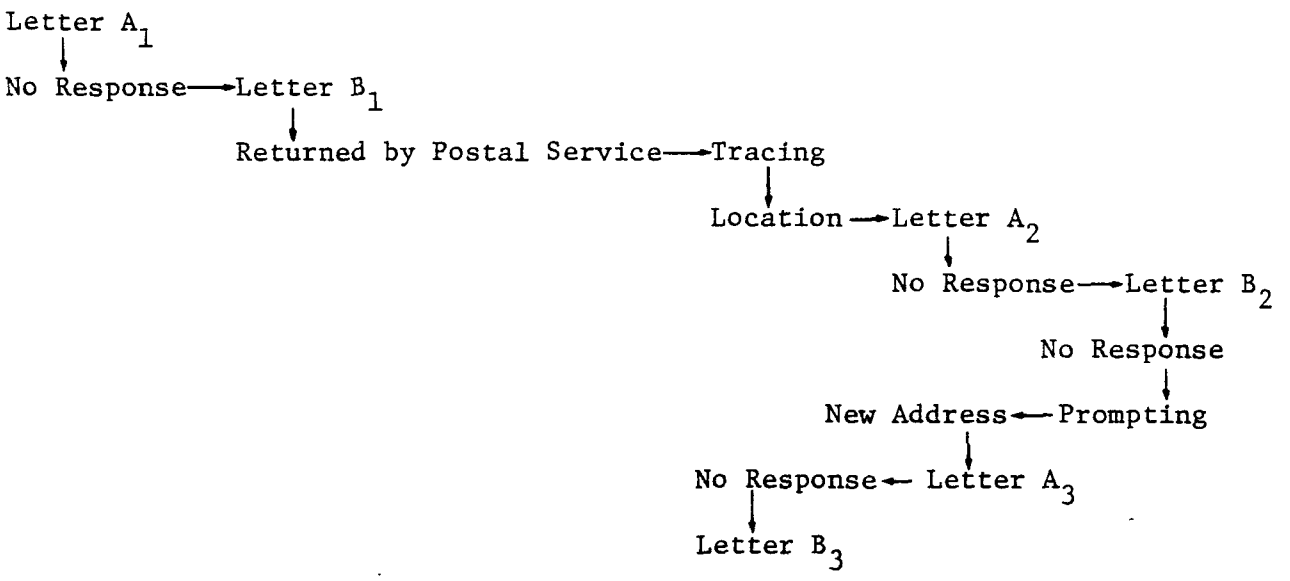
Address: _____

Figure 10. Thyroid study questionnaire.

It was anticipated that the addresses of respondents obtained from medical records may not have been updated for several years and therefore a number of the initial (and even subsequent) mailouts (letters and questionnaires) would be returned to the site by the Postal Service as not deliverable, indicating incorrect addresses, addresses unknown, moved-not forwardable, etc. Any packets thus returned unopened were returned to RTI where tracing procedures were utilized in order to locate respondents (see figure 2). RTI attempted to contact the patient, relatives, employers, schools, etc., and employ such resources as telephone and city directories, service agencies, marriage and voter registration, drivers license files, and other sources in order to locate potential respondents. The order in which these sources were utilized varied from individual to individual, depending in part on what and how much information was available in/from the medical records. Once a respondent was located, the questionnaire and letter A were sent to the correct address. Telephone tracing operations guidelines developed by RTI staff and utilized in the tracing operations are presented in an appendix. *Every effort has been made to locate and obtain a response for each eligible patient.*

For those respondents to whom the initial letter and questionnaire were assumed to have been delivered (not returned by the Postal Service), but from whom no response was received within a reasonable time after mailing, usually about four weeks, letter B (figure 8) was mailed on clinical center letterhead stationery again signed by the appropriate clinical center representative. Letter B was intended to urge the respondent to complete the questionnaire and return it to the site as soon as possible. Following this second mailing, expected responses were similar to those encountered after the first mailing; again following a reasonable period of time, usually about four weeks, nonrespondents were contacted by RTI by telephone, or personal visit if necessary, in order to resolve the case. The respondent was given the option to provide the information over the telephone if absolutely necessary. Similarly, when questionnaires were returned incomplete, every effort was made to complete these by telephone. Again, in the event of a patient's death, an attempt was made to obtain a copy of the death certificate from the appropriate office; these have been submitted as appropriate to EPA.

In many cases, multiple mailings for the same patient were required, because respondents lived out of the study area(s) and/or without telephone service or by going through the following process:



2.4 DATA PROCESSING

All data processing for this research effort was handled manually utilizing the two log sheet forms reproduced as figures 11 and 12. As study numbers were assigned, the patient was listed by name on the short form (figure 11) along with an indication as to whether the patient had an RAI file and/or a clinical center record, an HDF was completed, and the patient was eligible or ineligible for the survey phase; the clinical center medical record number, if one existed; and reasons for ineligibility or other pertinent remarks. A study number was assigned when an RAI file or a clinical center medical record was located, or when a letter was sent to an RMD. The long form (figure 12) recorded the various survey steps and the date and result of each step by study number. In essence, the short form summarized HDC (Phase II), while the long form monitored survey operations (Phase III).

2.5 REPORTS AND DATA SURRENDER

2.5.1. Reports

Technical Progress Reports outlining, and in many cases detailing, project progress, problems, and plans were submitted to the EPA Project Officer by RTI on a monthly basis from July 1973 through May 1977; copies were also provided to participating clinical centers. A detailed report of study activities at/through the CGH pilot site through January 31, 1975 was provided the EPA Project Officer on March 4, 1975; an interim report of study activities at/through all performance sites through February 28, 1975 was provided the EPA Project Officer on May 2, 1975. Dialogue between RTI and EPA technical representatives was continuous and excellent throughout the project performance.

2.5.2 Data Surrender

HDFs of ineligible patients; completed questionnaires and corresponding HDFs; and other information on patients lost to the study, deceased, and refusals were transmitted to the EPA Project Officer of his designee as received and/or as appropriate endpoints were reached (see figures 1 and 2).

Site: ____________ No. ____________

Study Number	Name	Medical Record	Record Number	RAI File	Hospital Data Form	Eligible	Ineligible	If ineligible, reason; any other pertinent remarks

Figure 11. Form used to monitor hospital data collection.

Site: _____ No. _____

Study Number	Letter A 1 Out	Letter A 1 Ret	Letter A 2 Out	Letter A 2 Ret	Letter A 3 Out	Letter A 3 Ret	Letter B 1 Out	Letter B 1 Ret	Letter B 2 Out	Letter B 2 Ret	Letter C Out	Letter C Response Yes	Letter C Response No	Letter C Followup	Trace Assignment Staff	Trace Assignment Date	Trace Success Yes	Trace Success No	Q Returned Date	Q Returned Completed Yes	Q Returned Completed No	Hospital Data Form to EPA	Q to EPA	Death Certificate Req.	Death Certificate Rec.	Death Certificate To EPA

Figure 12. Form used to monitor survey activities.

SECTION 3

PROJECT IMPLEMENTATION

3.1 INTRODUCTION

This section will discuss the implementation of the project at the various performance sites, citing the time frame(s) and specific steps taken to realize the methodology at the various sites. For the most part, the project was implemented using the previously described methodology at the various performance sites as planned.

Figure 13 presents graphically the schedule of project implementation at the various performance sites, from contract initiation in June 1973 through the termination of the technical performance period in May 1977. As indicated in section 2.3.1, the study was implemented at each performance site in three basic phases, Phase I consisting of initial contact and arrangements for cooperation and participation, Phase II consisting of medical record abstraction, and Phase III consisting of survey operations.

Figure 14 presents graphically projected and actual cumulative project expenditures by month, from project initiation in June 1973 until contract termination in May 1977. Project expenditures can be related to project activities by comparing figures 13 and 14.

3.2 PILOT STUDY

As intimated in previous sections, CGH was the specified pilot site for this research effort. Virtually all project procedures and activities were tested at CGH before implementation at other sites. Modifications were minimal.

The pilot study did result in the refinement and detailed documentation of study procedures. EPA had provided a general study protocol (23) and RTI had proposed certain general procedures to implement that protocol which outlined the methodology presented in section 2 of this report. In August 1973, RTI developed a detailed description of the procedures which would be utilized to implement the study and execute the EPA protocol, including the draft questionnaire and transmittal letter designed and revised by HERL/EPA.

3.3 PROBLEMS

Significant problems during the conduct of this research effort were few; non were insurmountable. Problems were related primarily to delays in

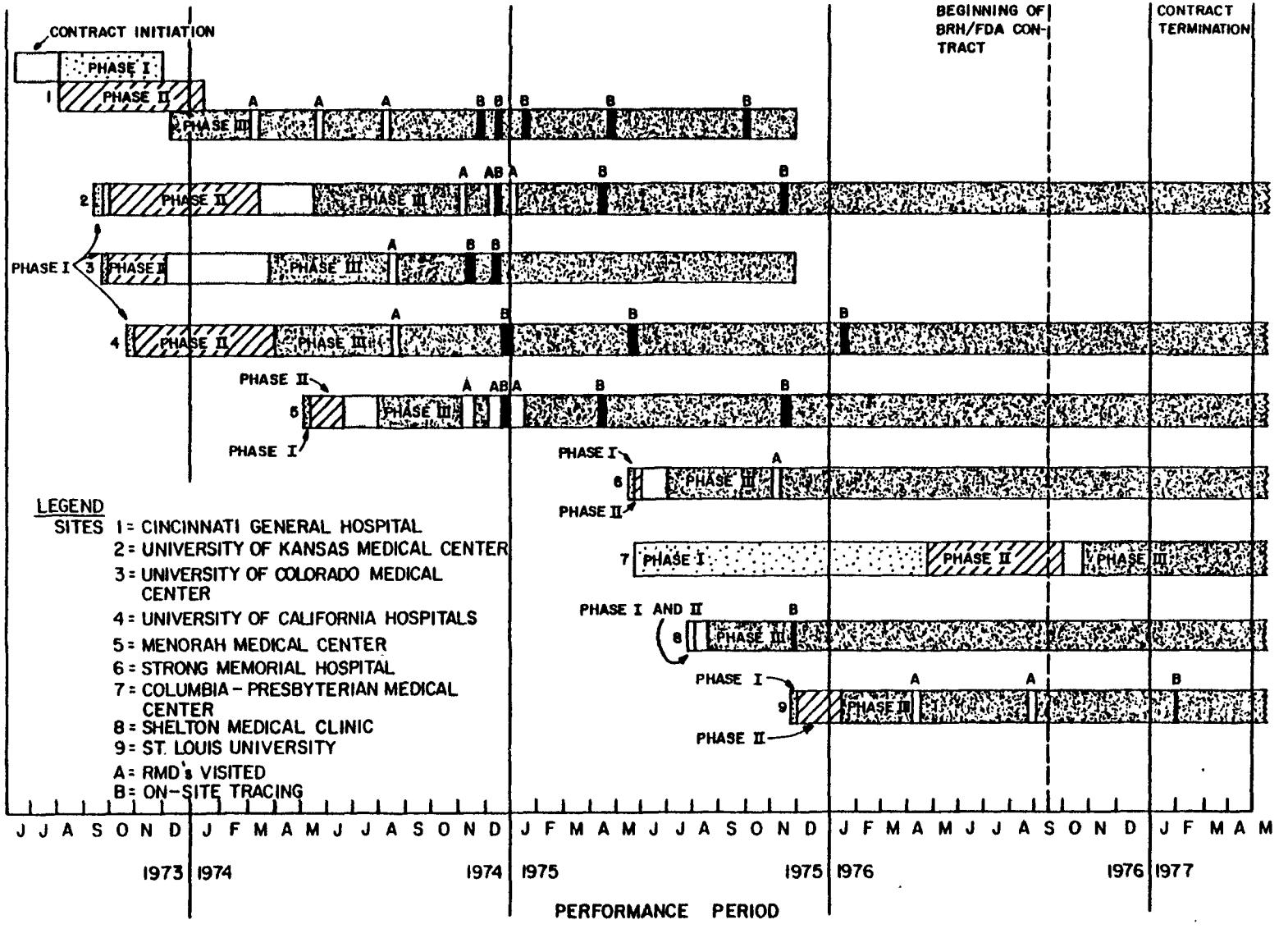


Figure 13. Schedule of project timetable, activities, and milestones.

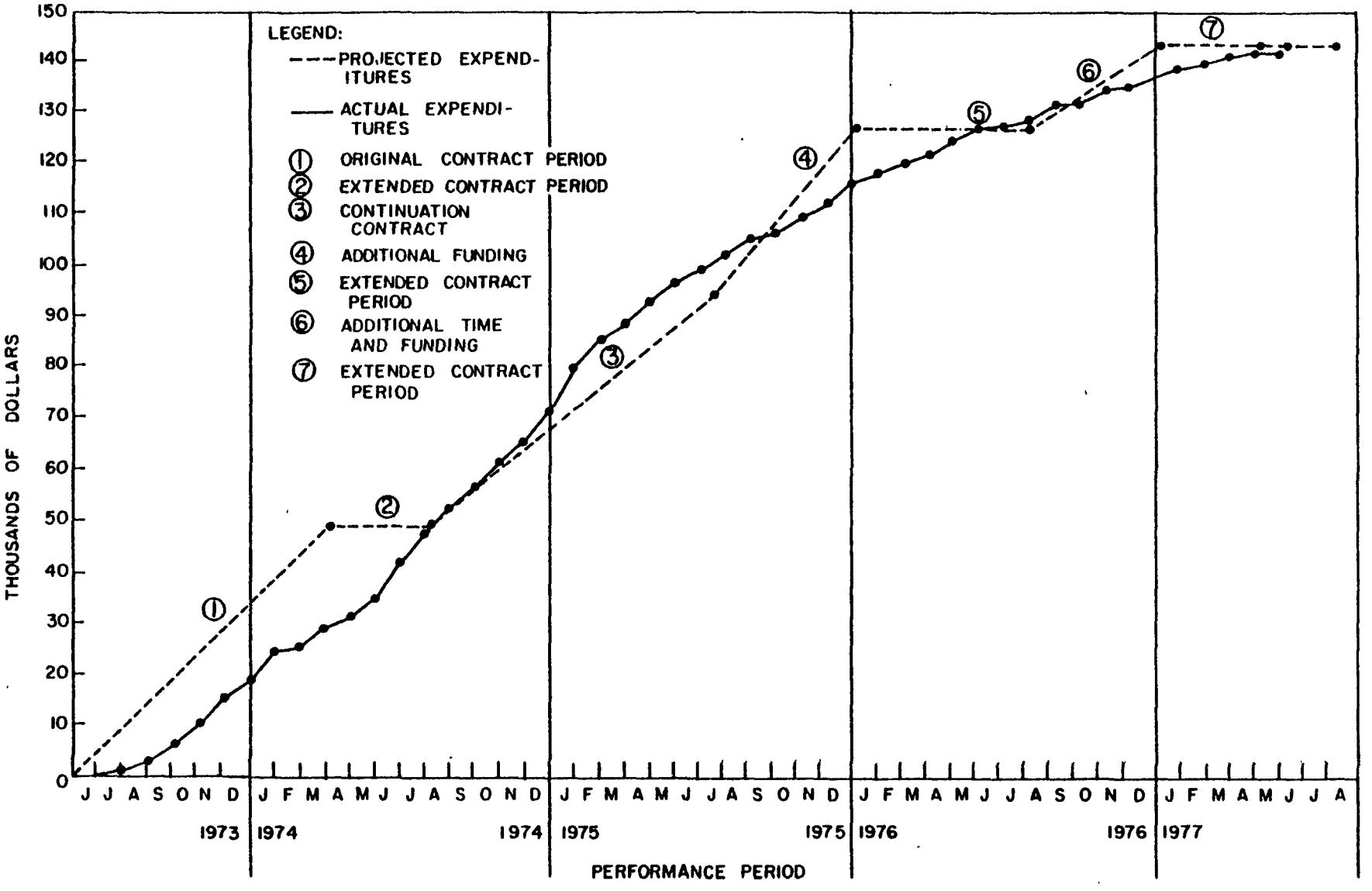


Figure 14. Cumulative project expenditures by month, June 1973 - May 1977.

gaining approval at some clinical centers, variations in recordkeeping systems, and respondent overreaction.

3.3.1 Approval Delays

As reflected in figure 13, approval delays were particularly marked at two performance sites where 4 and 11 months respectively elapsed between the first RTI contact and initiation of HDC. These delays were promulgated by requirements at the individual clinical centers that the study be reviewed by an internal committee. At the other sites, approval was virtually immediate. The presence during initial discussions of representatives of all involved clinical center disciplines - administration, nuclear medicine, and medical records - seemed expeditious.

The delays did require extensions in the technical performance period of the contract. In spite of these delays, however, RTI attempted to make the most effective and efficient use of project time and funds in the meantime so that the study could proceed with all deliberate speed once activities reached an appropriate point. The various delays undoubtedly resulted in more precise data collection instruments and a more efficient outline of procedures for implementing the study by both EPA and RTI.

3.3.2 Record Systems

The variability in record systems between participating clinical centers was marked. The passage of time had resulted in the loss of a number of records. The RAI laboratories and RMDs had taken advantage of a statute which only requires them to retain records for five years. Of the nine participating clinical centers, only two had complete RAI laboratory files and three had no RAI files at all other than what existed in the patient's medical record.

At all nine participating clinical centers, there were some patients for whom no medical record could be located even though these patients ostensibly had record numbers. At one clinical center, of 21 patients for whom there was no medical record number provided by EPA or the RAI laboratory files, none of these patients apparently had a clinical center medical record, *even though one of the patients was known to have died at the clinical center* according to the death certificate.

Of the female patients for whom no medical record could be located, RTI speculated that records on many of these patients were not located due to last names changed through marriage and not all facilities maintaining records cross-referenced by maiden and married names. RTI attempted to determine the names of at least some of these patients through marriage records, but this process met with limited success; for example, marriage records in Denver cannot be located without the approximate date of the marriage.

The record problem at the clinical centers was complicated somewhat by problems with misspelled patient names and other errors on the cards and lists provided by EPA. In several cases, RTI staff documented that the error was transcribed from a typographical error in the RAI files, but where RAI files

did not exist, the EPA information was frequently the only guide. For example, on one list prepared and supplied by EPA, one patient was listed under two first names, only one of which was correct, and another was listed under two last names, neither of which was correct; in both cases, the two listings represented separate isotope administrations for the same patient.

3.3.3 Respondent Reaction

In early November 1974, one of the clinical center physicians whose signature was affixed to study correspondence indicated that he no longer wished to have his signature so affixed due to problems which he was encountering mostly in the form of telephone calls from curious and concerned respondents. After discussions with RTI and EPA technical representatives, the physician agreed to the continued use of his signature, but requested that RTI implement a revised letter A for the clinical center's private patient population. Prompted by comments received in writing from Dr. Robinson of KUMC and verbally from Drs. Saenger of CGH and Price of UCSF, and experience gained in the survey operations, the EPA Project Officer and the RTI Project Leader had already discussed revisions in the initial transmittal letter which would facilitate survey operations at future performance sites. As stated by Dr. Robinson, *the public...is grossly uninformed generally about medical practices, and...undue concern has been generated in some of the families because of the survey.* In addition, RTI and EPA technical representatives felt that followup with respondents could be reduced. As a result, a revised letter A was developed for future initial correspondence; an example of the revised letter A is reproduced as figure 9. The revised letter required approximately twice the time to play back on automatic word processing equipment than the initial letter used for the first four performance sites; on the other hand, the revised letter required two pages and since the second page did not change from respondent to respondent, it could be printed, including the signature, thereby eliminating the time required to affix the signature.

During the course of this study, two television programs produced some reaction from respondents and/or participating clinical centers. In early 1975, an episode of the television series *Marcus Welby, M.D.* involved a research firm conducting a survey of individuals who had received radioactive iodine for thyroid disorders. The RTI telephone tracing operators reported some comment by persons contacted in the course of tracing and prompting operations immediately following the episode, but there was no written reference to the *Marcus Welby* episode by a respondent. In early 1977, *60 Minutes* aired a segment dealing with the effects of *therapeutic* application of radioactive iodine. The participating clinical centers were deluged with calls from persons who received therapeutic and diagnostic doses of I^{131}; in some instances, the patient lists for this study were the most readily available source of quickly identifying those persons who had received diagnostic doses. These episodes may have had some immeasureable effect on the study response rate.

SECTION 4

RESULTS

4.1 GENERAL REMARKS

This section presents a summary of results of study activities as related to HDC and survey operations. As reflected in figure 13, all procedural study steps were completed or were in some stage of implementation at/through all nine clinical centers participating in this research effort as of the contract termination date, May 7, 1977. As shown in figure 13, study activities at the CGH pilot site and UCMC were terminated in November 1975, while study activities at the other seven clinical centers continued. RTI continued to attempt to resolve unresolved cases as possible and appropriate within the limits of cost-effectiveness as long as funds were available in order to attempt to obtain a response for every eligible study subject.

At the time of contract termination in May 1977, study activities were virtually complete for all sites except SLU and CPMC, where Phase III survey activities were not initiated until 1976 (see figure 13). In the tabulations in subsequent sections, data will be presented for the participating clinical centers in three groups - the CGH pilot site alone; UCMC, KUMC, MMC, SMC, SMH, and UCSF grouped together as Group I since study activities at those six participating clinical centers were virtually complete at the time of contract termination in May 1977; and SLU and CPMC grouped together as Group II where study activities were still ongoing at the time of contract termination in May 1977. Although the contract terminated on May 7, 1977, tabulations for this report were not prepared until August to permit outstanding mail to reach RTI from the various performance sites.

4.2 HOSPITAL DATA COLLECTION

As shown in table 1, which summarizes medical record abstraction, RTI was provided with 2,287 potential study patient names for the nine participating clinical centers, for whom some medical record (clinical center record, RAI file, and/or RMD office record) was reviewed and abstracted for 1,999 or some 87 percent. Of those potential patients *for whom some medical record was reviewed and abstracted*, 1,085 or some 54 percent had a central clinical center medical record only, 305 or some 15 percent had an RAI file only, and 538 or some 27 percent had both a central clinical center medical record and RAI file. In addition, 71 patients or some 4 percent of the potential study population for whom some medical record was abstracted had an RMD office record *only* (see table 1 and section 4.3.1 below). These figures do not include clinical center records reviewed for incorrect patients with similar

TABLE 1. SUMMARY OF HOSPITAL DATA COLLECTION ACTIVITIES

Type of records reviewed and abstracted	Patient population by clinical center(s)						Total all sites	
	CGH pilot study		Group I facilities*		Group II facilities**			
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Total potential patient population	144	100.0	1,533	100.0	610	100.0	2,287	100.0
Clinical center record only	3	2.1	701	45.7	381	62.5	1,085	47.4
RAI file only	20	13.9	253	16.5	32	5.3	305	13.3
Clinical center and RAI file	119	82.6	325	21.2	94	15.4	538	23.5
RMD office record only	1	0.7	70	4.6	--	--	71	3.1
Total records reviewed and abstracted	143	99.3	1,349	88.0	507	83.2	1,999	87.3

* UCMC, UCSF, KUMC, MMC, SMH, SMC; study activities virtually complete.

** SLU and CPMC; study activities incomplete.

names and ages as potential study patients, or reflect patients having clinical center records *and* RMD office records reviewed and abstracted or an estimate of the variability in record volume and time required to review and abstract.

As shown in table 1, clinical center medical records have been available on 1,623 patients or some 71 percent of the potential population, with a range of 23-94 percent among the nine performance sites, while RAI files have been available on 843 patients, or some 37 percent of the potential population, with the range among the nine clinical centers being 0-97 percent.

Table 2 presents a summary of the results of medical records abstraction at the nine clinical centers which participated in this research effort. As shown in table 2, of the 2,287 potential study population patients whose names were provided to RTI, 1,362 or some 60 percent were determined to be eligible for inclusion in the survey sample (see section 4.3.2 below); 309 or some 14 percent were determined to be ineligible for inclusion in the survey sample based on study guidelines; 29 or some one percent were determined from HDC to have expired within three years of the first administration of the isotope, thereby obviating further followup beyond procurement of a copy of the death certificate or the data therefrom; 554 or some 24 percent of the potential total have apparently been lost to the study due to insufficient medical data available in/from medical records or the refusal of a private physician to provide missing data (see section 4.3.1); and the status of 33 or some one percent were undetermined as of the date of the tabulation (August 1977).

In order to include a study patient in the survey sample, it was essential that at least one item of the RAI data be verified (at the very least, it was necessary to verify that the medical record in hand was indeed that of the patient in question), and that there be some resolution of a final diagnosis for at least one of the isotope administrations. As indicated in previous sections, RTI initiated additional efforts to locate records for patients lost to the survey phase due to insufficient medical data through marriage records, provided appropriate information could be located. For the Interim Report in February 1975, a cursory review of the 335 patients lost to the study due to insufficient medical data at the five performance sites covered by that report (CGH, UCMC, UCSF, KUMC, MMC) revealed that some 57 percent were female and some 42 percent were male. At Cincinnati, marriage records were searched as far back as 1946 for 16 study patients (male and female) who were apparently lost to the study due to insufficient medical data or failure to locate through mail, telephone, and other on-site tracing activities. Information gleaned from the marriage records search provided possible leads on four patients, some 25 percent of those for whom information was sought. Subsequently, marriage records were searched only for female patients.

As shown in table 2 and cited in a preceding paragraph, 309 patients or some 14 percent of the total potential patient population were determined upon review of their medical records to be ineligible for inclusion in the survey sample - that is, they failed to satisfy one or more of the criteria for inclusion cited in section 2.2 of this report. The ineligible

TABLE 2. SUMMARY OF HOSPITAL DATA COLLECTION RESULTS

Result	Patient population by clinical center(s)						Total all sites	
	CGH pilot study		Group I facilities*		Group II facilities**			
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Total potential patient population	144	100.0	1,533	100.0	610	100.0	2,287	100.0
Lost to study$^{\theta}$	6	4.2	407	26.5	141	23.1	554	24.2
Expired within 3 years	3	2.1	12	0.8	14	2.3	29	1.3
Ineligible for survey$^{\pi}$	29	20.1	236	15.4	44	7.2	309	13.5
Eligible for survey‡	106	73.6	878	57.3	378	62.0	1,362	59.6
Status undetermined§	—	—	—	—	33	5.4	33	1.4

* UCMC, KUMC, UCSF, MMC, SMH, SMC; study activities virtually complete.

** SLU and CPMC; study activities incomplete.

θ Due to insufficient data in medical records.

π Due to having received isotope for the first time after 12/31/60, age 16 or over, or diagnosis of hyperthyroidism, toxic or nodular goiter, athyreosis, thyroiditis, or thyroid neoplasm; see table 3.

$\ddagger$ All these patients were involved in the survey phase; see table 5.

§ The ultimate status of these patients depends on the results of responses from non-respondent RMDs and further searches for medical records.

patients for the nine performance sites are broken down according to reasons for ineligibility in table 3. As shown in table 3, the most common reason for ineligibility was having received the isotope for the first time after December 31, 1960; 174 or some 56 percent of the ineligible patients fell into that category. Thirteen patients were excluded from the survey sample for having been over 16 years of age at the time of first isotope administration; 87 patients were ineligible due to a final diagnosis of hyperthyroidism or toxic or nodular goiter, 14 due to a final diagnosis of athyreosis, 14 due to a final diagnosis of thyroiditis, and 27 due to a final diagnosis of thyroid neoplasia; and five received I^{131} for reasons other than thyroid uptakes (see table 3). Several patients have been ineligible for more than one reason; therefore, the breakdown of ineligibles in table 3 totals more than 309, or 100 percent. For example, a patient may have received the isotope for the first time after 12/31/60 and also been diagnosed as hyperthyroid.

4.3 SURVEY OPERATIONS

4.3.1. Referral Sources

As mentioned in preceding sections, referral sources were contacted in an attempt to complete medical data on patients for whom clinical center records were inadequate for the purposes of the study. In most instances, the data item(s) sought were dosimetric data and/or the final diagnosis. Table 4 summarizes the results of contacts with referral sources through each and all performance sites. In table 4, *physicians* (or referral sources) refers to the number of RMD's or other referral sources in each category; *primary RMD* refers to the referring physician or facility cited in the clinical center record and/or EPA card, and *secondary care sources* refers to physicians or facilities to whom the primary RMD referred the study as currently caring for the patient(s) in question or holding the necessary records. The numerous physicians who were contacted in the course of tracing operations are not considered here.

As shown in table 4, RTI contacted 170 primary referral sources through eight of the participating clinical centers (no RMDs were contacted for data through SMC, but then SMC is a private group medical practice and not an inpatient facility), as a result of information in the clinical center records and/or on the EPA cards, in attempts to complete necessary medical data on patients for whom records maintained at the various participating clinical centers were inadequate for the purposes for the study - that is, to determine eligibility and include the person in the survey sample. As indicated in table 4, there were four basic responses by referral sources - they could agree to participate in the study, in which case they may or may not have had records on all the patients in question; they could refer the study to another source of care; records on the patient(s) may have been lost or destroyed; or the physician or facility could decline to participate in the study. In addition, the RMD could have expired with the disposition of the records unknown, or be a *nonrespondent*. An RMD could be a nonrespondent one of three ways: as indicated in a preceding section, in many cases only the RMD's last name was provided in the patient's medical record or on the EPA card, resulting in several possible physicians with the same last name being contacted regarding data on the same patient(s); if the requisite data were

TABLE 3. SUMMARY OF HOSPITAL DATA COLLECTION: REASONS FOR INELIGIBILITY

Reasons for ineligibility	Patient population by clinical center(s)						Total all sites	
	CCH pilot study		Group I facilities*		Group II facilities**			
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Total patients determined ineligible for survey phase θ	29	100.0	236	100.0	44	100.0	309	100.0
Received isotope after 12/31/60π	16	55.2	157	66.5	1	2.3	174	56.3
Over 16 years of age	--	--	7	3.0	6	13.6	13	4.2
Final diagnosis of:								
Hyperthyroidism, toxic or nodular goiter	8	27.6	60	25.4	19	43.2	87	28.2
Athyreosis	4	13.8	4	1.7	6	13.6	14	4.5
Thyroiditis	--	--	11	4.7	3	6.8	14	4.5
Thyroid neoplasm	5	17.2	17	7.2	5	11.4	27	8.7
Other†	--	--	1	0.4	4	9.1	5	1.6

* UCMC, UCSF, KUMC, MMC, SMH; study activities virtually complete; SMC had no ineligible patients.

** SLU and CPMC; study activities incomplete.

θ A patient can be ineligible for more than one reason; therefore, percentages add up to more than 100 percent.

π Many of these patients will be eligible for inclusion in the BRH/FDA continuation of this study.

† Received I^{131} for diagnostic purposes other than thyroid uptake (leg scans, red cell volume, etc.).

TABLE 4. SUMMARY OF RESULTS OF CONTACTS WITH REFERRAL SOURCES

Result	Performance site						Total all sites	
	CGH pilot study		Group I facilities*		Group II facilities**			
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Primary referral sources, total	7	100.0	72	100.0	91	100.0	170	100.0
Agreed to participate	4	57.1	34	47.2	11	12.1	49	28.8
Referred to secondary source	1	14.3	11	15.3	7	7.7	19	11.2
No records	1	14.3	18	25.0	20	22.0	39	22.9
Declined to participate	—	—	3	4.2	—	—	3	1.8
RMD deceased	1	14.3	6	8.3	2	2.2	9	5.3
No response or lost	—	—	—	—	51‡	56.0	51	30.0
Secondary care sources, total	3	100.0	6	100.0	7	100.0	16	100.0
Agreed to participate	—	—	6	100.0	1	14.3	7	43.8
Referred to another MD	1θ	33.3	—	—	—	—	1	6.2
No records	2	66.7	—	—	6	85.7	8	50.0

* UCMC, UCSF, KUMC, MMC, and SMH; study activities virtually complete. No referral sources were contacted for SMC and no secondary sources were contacted for UCMC or UCSF.

** SLU and CPMC; study activities incomplete.

θ Referred to MD already in survey.

‡ 46 of these are CPMC physicians to whom letters were sent just after contract termination; the remaining five are SLU physicians of whom two were lost - unable to locate and three were physician with the same last name as another contacted who had records on the patient and were therefore not pursued.

obtained, outstanding or nonrespondent physicians for the patient(s) were not pursued further. A few physicians could not be located despite extensive tracing activities, and many of the CPMC physicians have not been pursued yet beyond the initial letter.

As shown in table 4, 49 of the 170 primary referral sources contacted (or some 29 percent) agreed to participate in the study; 19 or some 11 percent referred the study to secondary sources; 39 or some 23 percent indicated a lack of records; 9 RMDs had expired, representing some five percent; and no response had been received from 51 referral sources at the time of this tabulation. Most of these nonrespondents represented RMDs for CPMC for whom letters went out after the contract terminated. Of the 16 secondary care sources contacted, one referred the study to one of the other secondary sources; eight indicated a lack of records; and seven agreed to participate in the study.

Three referral sources representing less than two percent of the total referral sources contacted refused to participate in the study by refusing to provide information from or access to patients' records; one refusal was from a juvenile court referral center while another was from a physician with terminal cancer. One referring physician provided the necessary medical and demographic data to complete the HDF, but requested that the study not contact the patient or his family. One RMD agreed to participate in the study but required patient authorization to release information from office records; RTI is seeking the required authorization.

4.3.2 Eligible Respondents

Table 5 presents a summarization of project survey operations for the nine participating clinical centers, including the status of all eligible respondents as of August 1977. In table 5, the Group I facilities are further subdivided into two subgroups in that the short version of the initial transmittal letter A (figure 7) was used predominantly at UCMC, UCSF and KUMC, while the longer version of the initial transmittal letter A (figure 9) was used predominantly at MMC, SMH and SMC. In terms of overall response rate, as reflected in the total cases resolved shown in table 5, the difference in the letters does not appear to have had a significant impact.

As shown in table 5, of the 1,362 patients eligible for the survey phase of this study, 1,065 cases or some 78 percent were successfully resolved as of August 1977 - completed questionnaires were obtained on 1,010 patients or some 74 percent of the eligible survey population; 17 patients representing some one percent of the eligible survey population were determined from survey activities to have died within three years of the initial isotope administration and a copy of the death certificate obtained; and 38 respondents representing less than three percent of the eligible survey population refused to participate in the study. Many respondents provided considerable information beyond that requested by the questionnaire; some even went so far as to write separate letters or notes.

Of the 297 cases unresolved as of August 1977, as shown in table 5, 176 or some 59 percent are from CPMC where the survey phase of the study was not initiated until November 1976 (see figure 13). Of the 297 unresolved cases

shown in table 5, 216 or some 73 percent reflect active correspondence or tracing activities; only 81 cases or some 27 percent had been relegated to some inactive category such as nonrespondent or unable to locate. Of the total patient population eligible for the survey phase, these 81 cases represent only six percent.

As an example of the study mail survey activities, table 6 summarizes such activities at the CGH pilot site as of September 1975, two months before study activities were suspended at CGH. In table 6, letter A_1 refers to the initial letter A sent to eligible respondents (see figure 1); $A_{n>1}$ refers to letter A's sent to eligible respondents whose letter A_1 was returned by the U. S. Postal Service as not deliverable and who were then traced and located, or some subsequent letter A in accordance with some response to a letter A or B or a tracing or prompting call (see figure 2); B_1 refers to letter B sent to eligible respondents whose letter A was not returned by the Postal Service and from whom no response was received (see figure 2); $B_{n>1}$ refers to subsequent reminder letter(s).

As shown in table 6, all 106 eligible CGH respondents (see tables 2 and 5) were sent letter A to the last address available from clinical center and/or RMD records. From this initial mailing, 18 or some 17 percent of the eligible respondents returned a completed questionnaire, one respondent (less than one percent of the eligible respondents) provided information short of a completed questionnaire, 48 or some 45 percent of the initial letter A's were returned by the Postal Service as not deliverable, and 39 or some 37 percent of the initial letters remained outstanding. As a result of supplemental information regarding the location of eligible respondents obtained by mail and/or telephone and/or on-site tracing (see below), 59 eligible respondents were sent a second letter A (letter A_2 - see table 6), of whom 23 or some 39 percent returned a completed questionnaire and two or some three percent responded in some other fashion; three or some five percent of these second letter A's were returned by the Postal Service as not deliverable, and 31 or some 53 percent remained outstanding. A third letter A (letter A_3) was sent to 17 eligible respondents, while one case required a fourth letter A (letter A_4); results of these mailings are shown in table 6.

As further shown in table 6, 65 eligible respondents were sent an initial reminder letter (letter B_1), in response to which 24 respondents or some 37 percent of the total returned a questionnaire, one or some two percent refused to participate in the study, and two or some three percent provided some other response; only six or some nine percent of these initial reminder letters were returned by the Postal Service as not deliverable, while 32 or some 49 percent remained outstanding. A second reminder letter (letter B_2) was sent to 28 eligible respondents, of whom 12 or some 43 percent returned a questionnaire, and three or some 11 percent refused to participate in the study; one of these second reminder letters, or some four percent of the total sent, was returned by the Postal Service as not deliverable, and 12 or some 43 percent remained outstanding. Eleven respondents required a third reminder letter (letter B_3), nine a fourth reminder letter (letter B_4), and two a fifth reminder letter (letter B_5); results of these mailing are shown in table 6. Two respondents each returned two questionnaires.

TABLE 5. SUMMARY OF PROJECT SURVEY OPERATIONS

Status	Patient population by clinical center(s)								Total all sites	
	CGH pilot study		Group IA facilities*		Group IB facilities**		Group II facilitiesθ			
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Total population eligible for survey phase	106	100.0	419	100.0	459	100.0	378	100.0	1,362	100.0
Total cases resolved	97	91.5	373	89.0	415	90.4	180	47.6	1,065	78.2
Questionnaire received	91	85.9	347	82.8	400	87.1	172	45.5	1,010	74.2
Expired within 3 years	1	0.9	10	2.4	1	0.2	5	1.3	17	1.2
Refused to participate	5	4.7	16	3.8	14	3.1	3	0.8	38	2.8
Total cases unresolved	9	8.5	46	11.0	44	9.6	198	52.4	297	21.8
Outstanding letter A	--	--	--	--	--	--	36	9.5	36	2.6
Outstanding letter B	--	--	1	0.2	8	1.7	87	23.0	96	7.0
In tracing	--	--	1	0.2	9	1.9	74	19.6	84	6.2
Lost to study - unable to locate	8	7.6	44	10.5	27	6.0	1	0.3	80	5.9
Nonrespondent	1	0.9	--	--	--	--	--	--	1	0.1

* UCMC, UCSF, and KUMC; study activities virtually complete; short version of initial letter (appendix C) used predominantly.

** MMC, SMH, and SMC; study activities virtually complete; longer version of initial letter (appendix E) used predominantly.

θ SLU and CPMC; study activities incomplete.

As might be expected, the best response rates were in response to letters $A_{n>1}$ and reminder letters B; letters A_1 resulted in the most returned as not deliverable, but were necessary in order to establish a baseline based upon the last known address; letter $A_{n>1}$ and reminder letters B accounted for the most letters presumed or verified delivered with no response; and reminder letters ultimately resulted in the most refusals. The CGH pilot study required approximately three letters per respondent. The figures in table 6 do not fully reflect correspondence conducted in the course of tracing activities.

Figure 15 presents graphically the progress of study survey operations at each of the nine participating clinical centers in terms of percentage of eligible respondents who returned a completed questionnaire since the initiation of survey operations at the site, shown against the study performance period. Figure 15 may be compared with figures 13 and 14 to determine the relationships and overlaps of survey operations with other project activities and phases. The decrease in the response rates for KUMC and MMC in January 1975 represented the entrance of additional eligible respondents into the survey phase. Figure 16 presents graphically those same rates shown in figure 15 at which the study survey operations progressed, in terms of percentages of eligible respondents *from whom a completed questionnaire was received,* but plotted as though the survey phase were initiated simultaneously at all sites. Despite variations in the timing of various survey activities at the different sites, the response curves in figure 16 are quite similar, with less than five percentage points separating the response rates for all sites except SLU and CPMC during the fourteenth month of activity.

Those study patients who entered the survey phase only after the acquisition of certain medical data from private physicians formed a special subpopulation, although for MMC the 330 patients who entered the survey phase after the acquisition of such data from RMD's represented some 82 percent of the MMC survey patient population; furthermore, those 330 MMC private patients represented more than the combined eligible survey patient populations for CGH, UCMC, and UCSF. The private patients also presented other variables; in many cases, additional demographic information, including addresses more current than those in clinical center records, were obtained. For MMC private patients, the revised longer letter A (figure 9) was used and one group of MMC private patient letter A's were inadvertantly mailed from RTI rather than Kansas City and demonstrated a shorter turnaround time from mail to return. Table 7 presents the response rates and status for the CGH private patients as an example.

As shown in table 8, which summarizes study telephone survey activities for the CGH pilot study, 15 eligible respondents were prompted at least once following nonresponse to letter B's while 71 eligible respondents were referred to RTI telephone tracing operators for location following the return of correspondence by the Postal Service. Although ten of the prompted respondents are shown in table 8 as ultimately submitting a completed questionnaire, several of these were actually completed by personal visit or telephone, following nonresponse to the prompting call(s). Of those 15 respondents prompted, two or some 13 percent were determined to have expired within three years of the first isotope administration and a copy of the death

TABLE 6. SUMMARY OF MAIL SURVEY ACTIVITIES: CINCINNATI PILOT STUDY

Input/output result	Instrument/activity																	
	Letter A_1		Letter A_2		Letter A_3		Letter A_4		Letter B_1		Letter B_2		Letter B_3		Letter B_4		Letter B_5	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Total letters sent	106	100.0	59	100.0	17	100.0	1	100.0	65	100.0	28	100.0	11	100.0	9	100.0	2	100.0
Questionnaire obtained*	18	17.0	23	39.0	5	29.4	1	100.0	24	36.9	12	42.9	1	9.1	5	55.6	1	50.0
Refusal to participate	--	--	--	--	--	--	--	--	1	1.6	3	10.7	--	--	--	--	--	--
Other response	1	0.9	2	3.4	2	11.8	--	--	2	3.1	--	--	1	9.1	--	--	--	--
Letter returned as not deliverable	48	45.3	3	5.1	1	5.9	--	--	6	9.2	1	3.5	1	9.1	--	--	--	--
No response or end result	39	36.8	31	52.5	9	52.9	--	--	32	49.2	12	42.9	8	72.7	4	44.4	1	50.0

* Two respondents each returned two questionnaires.

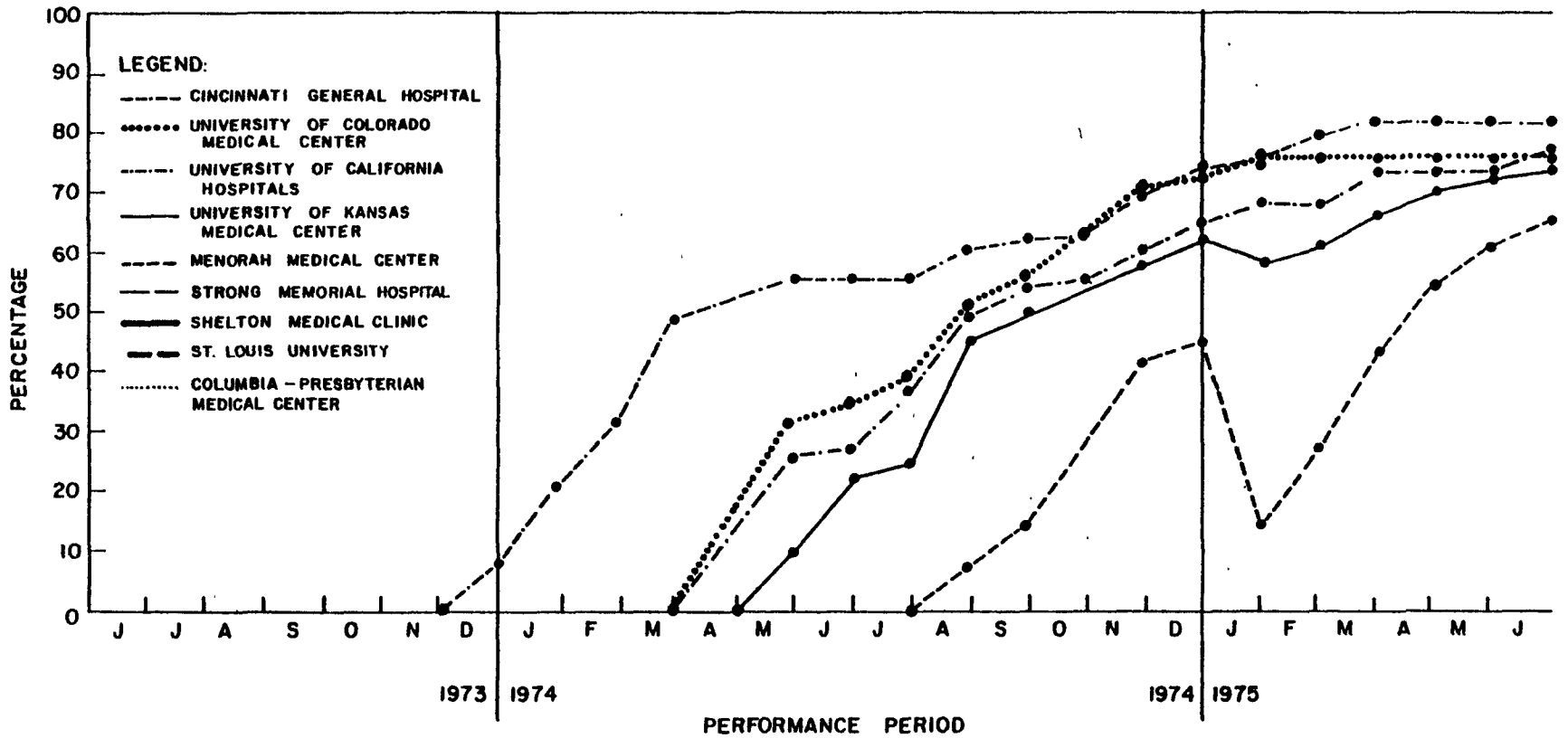


Figure 15. Progress of study survey operations (in terms of percentages of eligible respondents who returned a completed questionnaire since the initiation of survey operations at the site) at each of the participating clinical centers, shown against the study performance period.

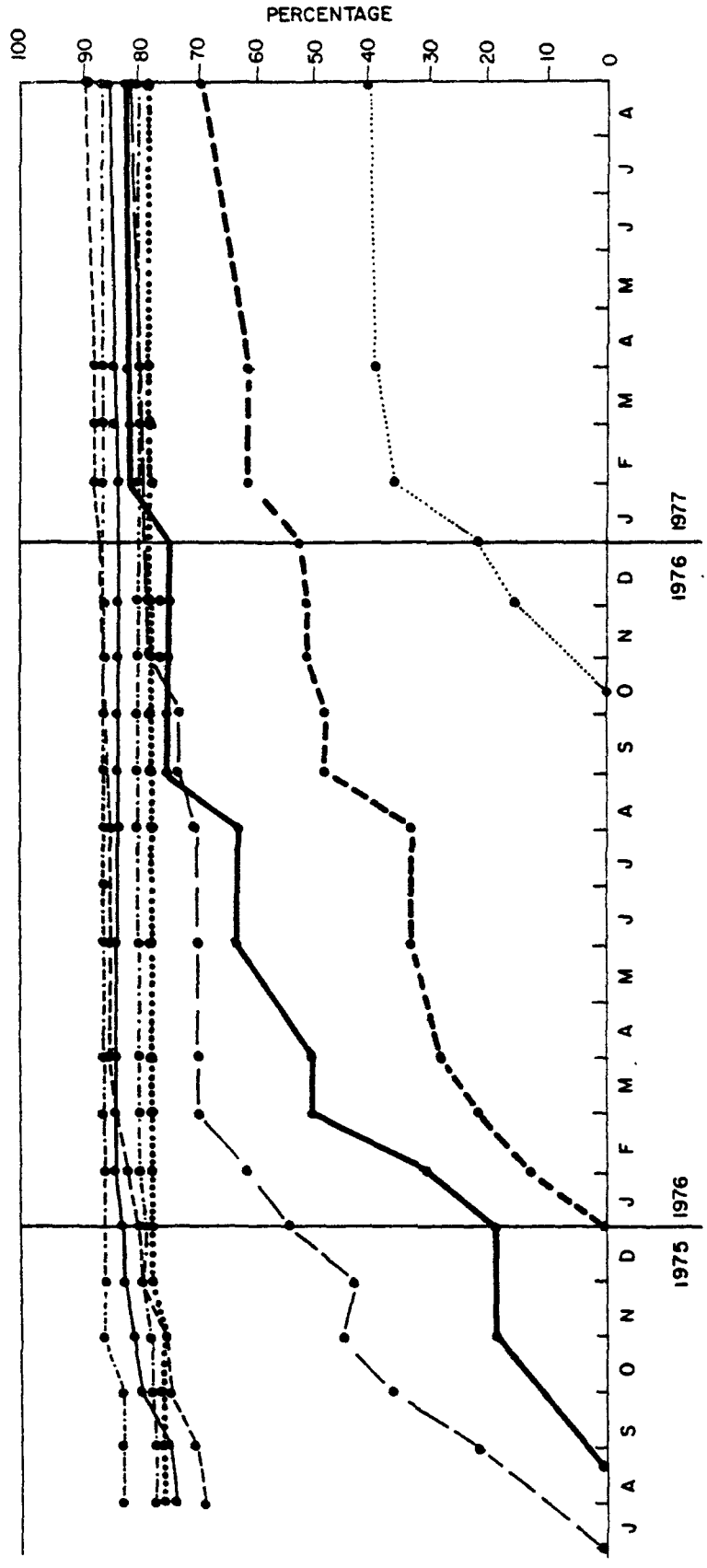


Figure 15. (Continued).

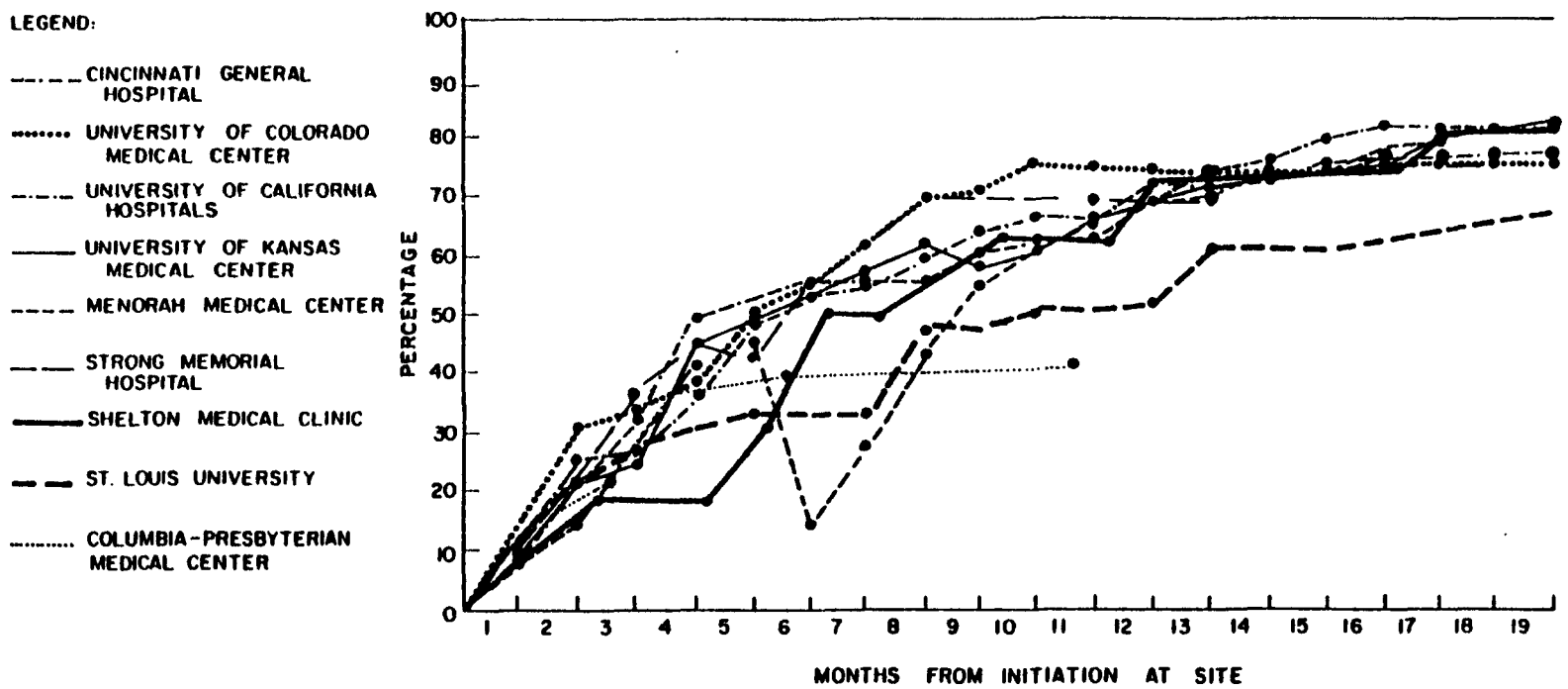


Figure 16. Progress of study survey operations (in terms of percentages of eligible respondents who returned a completed questionnaire since the initiation of survey operations at the site) for each of the participating clinical centers, plotted as though survey operations were initiated simultaneously at all sites.

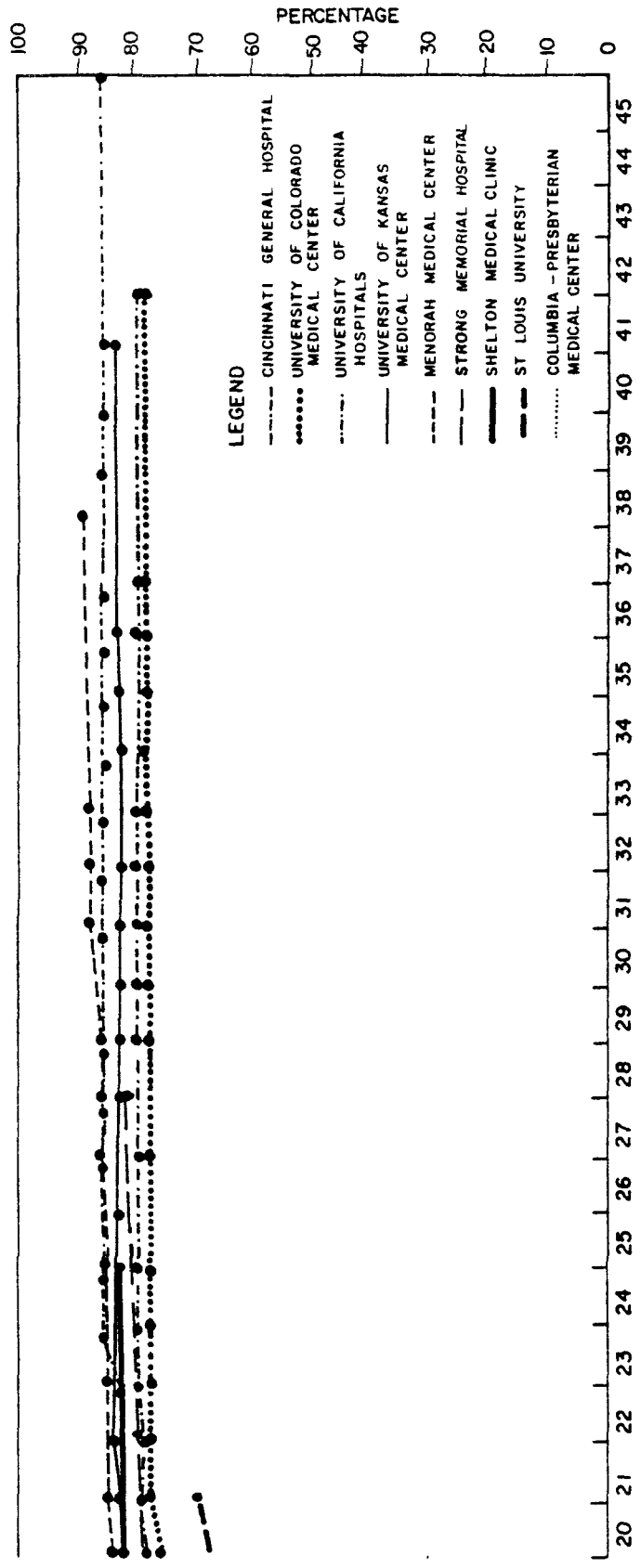


Figure 16. (Continued).

TABLE 7. SUMMARY OF SURVEY ACTIVITIES: CINCINNATI PRIVATE PATIENT STATUS AND RESPONSE RATE

Status	Number	Percent
Total patients	15	100.0
Questionnaire received	12	80.0
Refused to participate	2	13.3
Lost-unable to locate	1	6.7

TABLE 8. SUMMARY OF TELEPHONE SURVEY ACTIVITIES: CINCINNATI

Result	Prompting		Tracing	
	Number	Percent	Number	Percent
Total respondents referred	15	100.0	71	100.0
Questionnaire obtained or respondent located	10	66.7	62	87.3
Expired within 3 years	2	13.3	--	--
Refused to participate	2	13.3	1	1.4
Other response	1	6.7	--	--
Respondents not located	--	--	8	11.3

certificate obtained, two of some 13 percent refused to participate in the study, and one or some seven percent provided information which resulted in additional correspondence. Of the 71 respondents referred to the telephone tracing operators for location, 62 or some 87 percent were ultimately located by some combination of telephone, mail, and/or personal followup on-site, while extensive tracing activities failed to locate eight respondents/patients, or some 11 percent of the total referred to tracing. As shown in table 8, one respondent refused to participate in the study during the course of telephone tracing contact, less than two percent of the total referred. Tracing activities were most effective among the CGH study patient population, some 89 percent of those respondents referred to tracing having ultimately been located. Just as some respondents required more than one reminder letter, several required more than one prompting call and/or were traced more than once, but these are not double-counted in table 8.

As indicated in figure 13, on-site tracing activities were instituted at all sites except the two New York sites to retrieve questionnaires from respondents who had not returned them and make one last effort on-site to locate respondents who had not been located by telephone and mail tracing activities. Table 9 presents a summarization of on-site tracing activities for the CGH pilot study, indicating the disposition of all cases so traced. As shown in table 9, of the 25 respondents and/or patients who were traced on-site, completed questionnaires were obtained from 16 or 64 percent by administering the questionnaire in person or by phone, or mail followup to the personal visit; one patient was determined to have died within three years of initial isotope administration and a copy of the death certificate obtained; and on-site tracing and subsequent mail and telephone followup were unable to locate eight respondents. As shown in table 9, tracing at Cincinnati resulted ultimately in the successful resolution of 68 percent of the cases traced on-site; however, in most instances, successful on-site tracing required visits to more than one address in greater Cincinnati or more than one visit to the most current address.

TABLE 9. SUMMARY OF SURVEY ACTIVITIES: ON-SITE TRACING, CINCINNATI

Status/Disposition	Number	Percent
Total cases traced	25	100.0
Questionnaire received	16	64.0
Expired within 3 years	1	4.0
Refused to participate	--	--
Lost-unable to locate	8	32.0

SECTION 5

CONCLUSIONS

The purpose of this study was to locate and obtain pertinent medical information on approximately 2,300 patients who as children received I^{131} for diagnostic purposes over the period 1946 - 1960 at nine clinical centers. Of 2,287 potential study subjects identified, some medical record was reviewed and abstracted for 1,999 or some 87 percent. With study activities incomplete, of 186 private physicians and other referral sources contacted for supplemental data, only three or less than two percent declined to participate; of 1.362 patients who were determined eligible and entered the survey phase, some final resolution (completed questionnaire, death certificate, or refusal) was obtained for 1,065 or some 78 percent.

A pilot study was conducted, the primary objective of which was to test, and refine as necessary, the data collection scheme for this project, a goal which was achieved relatively early. Furthermore, the pilot site experience contributed greatly to project implementation at the other sites. In particular, the pilot site experience accelerated project approval and implementation at the other performance sites by involving representatives of all concerned disciplines at each site thereby abbreviating Phase I at seven of the eight subsequent sites (see figure 13), and in part accelerated and facilitated HDC and survey operations at the other sites. At least some of this acceleration was due to improved efficiency resulting from the pilot study experience.

RTI's original techncal proposal (40) stated that *RTI will instigate a series of tracing procedures designed to locate 90 percent of the families of the patients* in the study population, and, *based upon previous experience cited by* [EPA] *staff, RTI anticipates a very high response by patients who are located in this study.* For the two clinical center patient populations for whom study activities were suspended in November 1975 (CGH and UCMC), RTI located respondents for over 90 percent of the patients who were eligible for inclusion in the survey phase of the study, and obtained a response (completed questionnaire, refusal, or evidence that the patient died within three years of receiving the isotope for the first time) from over 99 percent of those located. For the seven sites (CGH, UCMC, UCSF, KUMC, MMC, SMH and SMC) where study activities were completed or virtually complete, the response rate in August 1977 in terms of completed questionnaires was some 85 percent while the percentage of resolved cases in terms of completed questionnaires, death certificates, and refusals was some 90 percent.

The successful acquisition of these data provide a unique opportunity to assess the chronic effect of low dose I^{131} exposures.

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APPENDIX

TELEPHONE TRACING OPERATIONS

I. Background Information

RTI is under contract to the Environmental Protection Agency (EPA) to collect data about patients who received diagnostic doses of Iodine 131 during their childhood. From several medical centers in the U. S., records have been abstracted to select a sample of patients who received I^{131} during the period January 1, 1946 - December 31, 1960; all patients selected were younger than 16 years of age at the time of the procedure.

The objective of the research effort is to provide data for the definition of a dose-response curve for the development of thyroid neoplasms in the patients exposed to I^{131} radiation. Data are being collected via short questionnaires directed to the patients' parents.

II. Tracing Objective and Procedures

The objective of telephone tracing for this project is to obtain a current mailing address for the parents of a specific patient so that the Thyroid Study Questionnaire can be mailed to them.

For each tracing case, the operator will be provided with a data card on the patient, which gives the following information:

- study number (a seven digit number)
- patient's name
- patient's birthdate
- parents' name
- all known previous addresses
- various types of information such as employment data for parents, evidence of involvement with public agencies (welfare, housing, etc.), and other data that might aid in locating the parents.

In addition, the envelope in which the initial correspondence was mailed will be attached to the patient data card.

Several problems are obvious from the onset of tracing: the patient may be as old as 43 or as young as 13; the address(es) shown on the patient data card may be out-of-date; the patient's parents (or guardian) may be dead, in which case you must attempt to secure a current mailing address for the patient.

Specific procedures for tracing are as follow:

1. Study the patient data card; have names of patient and parents firmly in mind; compute the patient's age from his birthdate so that you can evaluate his "usefulness" for tracing (i.e., is he old enough to have a phone listed in his own name, etc.).
2. Begin tracing by consulting Directory Assistance (DA) in the town where the patient/parents last lived; in cases of unusual last names or in small towns, secure listings for persons with same surname. Area phone books will be available for your use--consult them, where applicable.
3. In cases where telephone numbers are shown on the patient data card, call the most current one. If the number is no longer assigned to the patient/parents, try to find out how long the party with whom you are speaking has had the number.
4. City Directory Service is available through many public libraries. These listings also cover many smaller suburban areas. Be specific in the items for which you are requesting information.
5. In cases where employment data for patient/parent is less than five years old, call the last known employer.
6. In some cases, the names of physicians who have treated the patient are given on the patient data card. We may contact these offices for addresses if all other sources fail.
7. Where patients/parents may have been clients of public agencies (welfare, housing, etc.), attempt to secure any address data the agency may have on file. These sources, however, may not be productive since many of their records are confidential.

As in all tracing cases, document fully your efforts and your findings on the Control Sheet (figure A-1). Make certain the operator name, hospital and patient number have been entered on the Control Sheet. Indicate if the case was completed by marking the yes/no box. If the case is pending, write "pending" in this box.

The source of address should be specified, especially in the "other" category.

Parent/patient names should be shown on the Control Sheet as they are on the patient data card. Do not substitute initials for names. Include in the updated address the proper ZIP Code. Do not abbreviate any element of the address.

In general, complete all areas of the Control Sheet before returning it to Lil Smith.

Before a patient is considered "unable to locate," glean the patient data card for pertinent information and leads. Other sources should be pursued as indicated. All should be exhausted before pronouncing the patient lost. When it has been determined that the patient cannot be located, complete the Unable To Locate Check Sheet (figure A-2) and attach it to the Control Sheet.

TELEPHONE TRACING
PROJECT 25U-874

CASE NUMBER: _____

OPERATOR: _____

	Date	Time	To	Result	Phone Number
Call 1					
Call 2					
Call 3					
Call 4					
Call 5					
Call 6					
Call 7					
Call 8					
Call 9					
Call 10					

Case Completed?

☐ Yes ☐ No

Source of address data

☐ Patient ☐ Parent

☐ Other _____

Reason for unable to locate:

Mail Questionnaire to:

☐ Parent ☐ Patient

Parent Name: _____ Patient Name: _____

St. Address: _____ St. Address: _____

City, State, Zip: _____ City, State, Zip: _____

Comments:

Approved by: _____

Date: _____

Figure A-1. Telephone tracing control sheet.

TRACING CHECK SHEET UNABLE TO CONTACT

SOURCES CONTACTED/USED

Locator Card

City Directory

Chamber of Commerce

Board of Election

DMV

Figure A-2. Unable to locate check sheet.

III. Script Outline

In this study, there are strict requirements regarding how we represent ourselves to individuals and organizations by phone. There are to be no exceptions to these requirements. Specifically, RTI and EPA are not to be mentioned in conjunction with this study; all references to sponsorship of the study are to be made as though the M.D. at the specific hospital were the project sponsor. For example, when you are talking to a patient or his parents from the Cincinnati population, you would introduce yourself as follows:

> "Hello. My name is Sue Smith and I am working with Dr. Eugene Saenger of Cincinnati General Hospital."

Do not indicate that you are calling from RTI or from North Carolina. If you are queried about who you are and who you represent, repeat that you are working with Dr. Saenger of Cincinnati General Hospital.

In general, do not get involved with medical terms which you cannot explain. Your description of the study should be brief and concise, based on the suggested narrative below:

> "Your son/daughter *(Patient's name)* was tested at *(appropriate participating clinical center)* for suspected thyroid disease. The hospital is presently conducting a study to determine if people suspected of having thyroid disease in childhood are inclined to have more illnesses or tend to develop thyroid disease in later years. Your son/daughter was chosen from a number of patients. We have tried to mail you a brief questionnaire concerning your son/daughter's general health, but the questionnaire was returned to us by the Postal Service. Could I have your current mailing address so that we can mail you another questionnaire?"
>
> "Thank you very much. You will be getting the questionnaire within a few days. We would appreciate your filling it out and returning it as soon as possible. Thank you again."

If a parent or patient asks detailed questions, do not attempt to answer them. Instead, refer them to Ben Harris. If someone wants to know how the information will be used, explain that this is a statistical study and that all information obtained will be held in strict confidence. Furthermore, we are following up all persons who had the test, whether or not the test was abnormal.

IV. General Information

All calls are to be dailed direct station-to-station. Do not, under any circumstances, leave a message for a patient/parent to call back collect here. We will initiate all calls.

When you complete a case, give it to Lil Smith for review and approval. Questions concerning tracing procedures or conversations with patient/parent should be referred to Lil Smith or Ben Harris.

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO.	2.	3. RECIPIENT'S ACCESSION NO.
EPA-600/1-78-059		

4. TITLE AND SUBTITLE
Follow-up of Patients Receiving Diagnostic Doses of 131 Iodine During Childhood

5. REPORT DATE
September 1978

6. PERFORMING ORGANIZATION CODE

7. AUTHOR(S)
Benjamin S. H. Harris, III, Martha L. Smith, Mildred I. Holt

8. PERFORMING ORGANIZATION REPORT NO.

9. PERFORMING ORGANIZATION NAME AND ADDRESS
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Research Triangle Park, N. C. 27709

10. PROGRAM ELEMENT NO.
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U.S. Environmental Protection Agency
Research Triangle Park, North Carolina 27711

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Final report covering 6/73-5/7

14. SPONSORING AGENCY CODE
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15. SUPPLEMENTARY NOTES

16. ABSTRACT

This report documents the data collection methodology and procedures of a follow-up survey conducted of persons under 16 years old who received diagnostic Iodine 131 for evaluation of thyroid function at nine clinical centers prior to December 31, 1960. The intent of this data collection effort is to estimate the dose response curve for the development of thyroid neoplasms in young adults who received low diagnostic doses of Iodine 131 as children.

Of 2,287 potential study subjects identified, some medical record was reviewed and abstracted for 1,999 or some 87 percent. With study activities incomplete, of 186 private physicians and other referral sources contacted for supplemental data, only three or less than two percent declined to participate; of 1,362 patients who were determined eligible and entered the survey phase, some final resolution (completed questionnaire, death certificate, or refusal) was obtained for 1,065 or some 78 percent.

The statistical analysis of these data will be performed under a related project sponsored by the U. S. Food and Drug Administration.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
thyroid iodine diagnostic dose follow-up	Follow-up study	

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