Hanford Thyroid Disease Study
Pilot Study Report: Executive Summary

EXECUTIVE SUMMARY

The Hanford Thyroid Disease Study (HTDS) was mandated by an act of Congress in 1988. The Centers For Disease Control and Prevention (CDC) was directed by Senate Bill 2889 to conduct a study of thyroid morbidity among persons who lived near the Hanford Nuclear Site between 1944 and 1957. A team of investigators at the Fred Hutchinson Cancer Research Center (FHCRC) and the University of Washington in Seattle was selected by the CDC to conduct the study, and a contract was awarded to the FHCRC on September 19, 1989.

The primary purpose of the study is to determine whether thyroid morbidity (including, but not limited to hypothyroidism, benign neoplasia, and malignant neoplasia) is increased among persons exposed to releases of radioactive iodine from the Hanford Nuclear Site between 1944 and 1957, and who received radiation doses to the thyroid as a result, relative to persons who received a very low or negligible radiation dose to the thyroid from Hanford. If an effect is detected, the study is designed to further determine in what way the increase in thyroid morbidity is related to the dose of radiation received (i.e., the characteristics of any dose-response relationship).

This study is being conducted as a follow-up prevalence study. That is, subjects are selected on the basis of presumed past exposure to radioactive iodines from Hanford, based on place and year of birth, are located, and are examined for the presence or history of thyroid disease. The primary analyses will focus on living participants who receive medical examinations to detect thyroid disease, and for whom thyroid radiation doses are estimated using the dosimetry system developed by the Hanford Environmental Dose Reconstruction (HEDR) Project. Deceased subjects and others for whom less complete information is available will be included in secondary analyses. Although the effects of primary interest are defined by three categories of thyroid disease (hypothyroidism, benign thyroid nodules, and thyroid cancer), information regarding all forms of thyroid disease is being recorded as part of the study and will be included in the overall analysis. In addition, hyperparathyroidism is being evaluated by screening individuals for hypercalcemia.

The work is being conducted in two stages. The first is a Pilot Study, the primary purpose of which is to evaluate the feasibility of the methods proposed, and to develop the specific operational procedures and data collection instruments needed for a full study. If the results of the Pilot Study indicate that it is feasible to conduct a successful full-scale epidemiologic study, the second stage will be to implement the remaining field work to complete such a study. This approach allows the accumulation of information and experience prior to initiation of a more costly full-scale study. Based on the experience gained in the Pilot Study, the design and procedures for a full study can be modified if necessary to account for the realities of the field environment.

As of this writing the pilot phase of the HTDS is essentially complete. The large majority of Pilot Study participants completed the clinical examination portion of the study by the end of December, 1994. Thus, there are now sufficient data available from the Pilot Study to adequately evaluate the specific objectives of this initial phase of the project. This report describes the primary findings from the Pilot Study.

Locating Study Subjects and Recruiting Them To Participate in the Study

The Pilot Study has demonstrated that it is feasible to locate persons using birth certificate records from the early to mid-1940s. Overall, 91% of the 1590 Pilot Study subjects identified from birth certificates have been located. Success in locating people has not differed substantially according to sex, year of birth, or geographic area of birth. The majority of Pilot Study participants subjects have been found to still reside in Washington state, and approximately three quarters live in the Pacific Northwest. The Pilot Study has also demonstrated that once located, and contacted by phone, a large proportion of individuals (85%) will agree to participate in the study. Willingness to participate does not differ substantially according to the region in which the person was born, nor according to sex or year of birth. These results indicate that the methods developed for identifying a cohort, locating individual members of the cohort, and recruiting them to participate in the study are feasible and are likely to result in relatively high levels of success.

Obtaining Information and Biological Specimens From Study Participants and Families

The Pilot Study has demonstrated that: 1) for approximately 75% of the study participants, a respondent can be identified who is willing to be interviewed by telephone regarding the participant's childhood and adolescence (to provide detailed information used to estimate a thyroid radiation dose); 2) that the participant's birth mother can serve as the telephone interview respondent in about 75% of the cases in which a respondent is identified; 3) that other immediate family members can be located and will agree to participate in most of the remaining cases; 4) that it is feasible to complete the telephone dosimetry interview for virtually all of those who agree to participate; and 5) that it is feasible to administer an expanded version of the In-Person Interview to study participants for whom a telephone respondent cannot be recruited.

Furthermore, the Pilot Study has demonstrated that it is feasible to schedule and conduct clinics in a manner that will include those identified and willing to participate, that participants will agree to participate in all components of the clinical phase of the study, including fine needle aspiration if recommended, and that participants will provide written consent to obtain prior medical records relevant to thyroid disease. It is still too early to adequately assess the success with which medical records can be obtained. Preliminary indications are that it will be possible to obtain more than 60% of the records requested.

Adequacy of Study Procedures, Forms, and Data Collection Instruments

The Pilot Study has been an on-going test of study procedures, forms, and data collection instruments. All study procedures are documented in a Procedures Manual, which is updated as changes are implemented. The operational procedures and associated forms and instruments currently in place are working well. Changes are made when specific circumstances arise that can best be addressed by instituting a procedural change. An internal Problems Form is used extensively by study staff to document problems, solutions, and any procedural changes that result. Changes will continue to be made on a continuing basis as the need arises.

Estimation of Radiation Dose Distributions and Power and Sample Size Calculations

Thus far, thyroid radiation doses have been calculated for 869 Pilot Study participants using the dosimetry system developed by the HEDR Project. The information about an individual participant's dose is actually provided as a set of 100 dose estimates, each corresponding to one realization of the integrated simulations produced by the HEDRIC computer programs. Dose distributions for the 869 Pilot Study participants are provided in this report according to year of birth (1942-1946), gender, and geographical region of birth (eight areas surrounding the Hanford Site). These results have suggested that in order to identify persons with the highest doses, further selection from the strata defined for the Pilot Study should be limited to the years 1942-1944 and to the Richland, Pasco/Kennewick, Benton County, and Franklin County strata.

Utilizing projections based on the Pilot Study dose distributions, power calculations were conducted for tests of the dose response for the endpoints thyroid neoplasia, thyroid malignancy, and ultrasound-detected abnormality. Three plans are presented for selecting potential study participants to complete a full study. Projected power functions of tests for radiation dose response functions based on these plans are presented for the three classes of endpoints listed above. The results of these calculations suggest: 1) that cohorts identified from birth records are likely to provide a sufficiently wide distribution of doses for successful completion of a full study; and 2) that the cohorts defined for the Pilot Study are likely to be inadequate to complete a full study, and that they should be augmented by the additions of 1940-41 births in Benton and Franklin Counties, and 1940-1944 births in Adams County. Such a sampling plan will, under a plausible but conservative projection, provide reasonable statistical power (>0.80) to detect an increase in the risk of thyroid neoplasia of 5.5% per Gy.

Plan For Conducting A Full Study

Based on the results available to date from the Pilot Study regarding logistical success, thyroid dose distributions, and numbers of births in the Hanford region during the early to mid-1940s, a plan was developed for completing a full epidemiologic study. The plan is based upon a number of important assumptions: 1) the thyroid dose distributions obtained thus far in the Pilot Study are reasonably representative of what will be the overall dose distribution at the

completion of a full study; 2) approximately 3200 living evaluable subjects will be required to achieve the level of power referenced above; 3) the basic study design and data collection methods will remain the same; 4) if continued, the ultrasound follow-up component of the study will be staffed and conducted separately from the main study clinic; 5) the dose calculations for study participants will be conducted by HTDS staff through remote access to the HEDR computer programs at the CDC in Atlanta; and 6) the study will be completed near the end of 1997.

The following are the key elements of a plan designed to achieve the goal of completing the study near the end of 1997 with at least 3200 living individuals evaluated.

1. Add to the sample all births from the following areas and years
    a. 1942-1944: remaining Richland, Pasco\Kennewick, and Benton County
    b. 1940-1941: all of Benton and Franklin Counties
    c. 1940-1944: all of Adams County
2. Focus on completing the tracing of study subjects quickly

    a. Hire additional staff in early Fall of 1994
    b. Complete a substantial proportion of the tracing by early 1995
    c. Complete the large majority of tracing by mid-1995
    d. Complete all tracing by mid-1996

3. Increase staff support in several areas

    a. Administration (travel, office)
    b. Recruiting and scheduling
    c. CATI interviewing (two interviewers)
    d. Clinics (one phlebotomist, one interviewer)
    e. Statistics

4. Expand clinic operations

    a. Increase the number of clinic days held per month to 6-7
    b. Increase the number of study participants at clinics to 100-120/month
    c. Conduct ultrasound follow-up clinics separately from the main clinics

In order to achieve the plan summarized above, the identification and selection of additional study subjects and accelerated tracing efforts have already begun in anticipation of conducting a full study. Tracing efforts will be conducted up to but not including the point of recruiting individuals into the study, pending final approval of this plan by the CDC. A preliminary version of this report was submitted to the National Research Council's Board of Radiation Effects Research of the Commission on Life Sciences on August 25, 1994. A report was issued from the Board on November 16, 1994 which stated, "On the basis of the written report and the presentations and in light of the unique experiences of the population around Hanford, the quality of the information obtained in the Hanford Thyroid Disease Study, and the effort expended in the Hanford Environmental Dose Reconstruction Project, the committee unanimously recommends the continuation of the Hanford Thyroid Disease Study." The Board's report and this final report will be submitted to the HTDS Federal Advisory Committee at a meeting on February 22, 1995, at which time a recommendation from the Advisory Committee regarding the continuation of the study will be made. Shortly thereafter it is anticipated that a final decision will be made by the CDC regarding the full study.

If a full study is approved, expanded operations would begin in March or April of 1995. It is expected that such a timeline would allow for the completion of the study near the end of 1997.