Research on human disease or human physiology has long required the examination of human tissue from multiple research subjects. Tissues from both affected patients and normal controls are necessary for comparison studies to ascertain the etiology and pathology of a particular disease. By studying diseased tissue, researchers can delineate the normal pathway and understand the mechanisms underlying growth, development, and function. Thus, an advantage exists in obtaining tissue from affected persons for scientific study.

In a world where time and money are scarce, it is extremely costly for researchers who require tissue samples from a select group to wait for these persons to enter their hospitals or clinics. Often, different research projects may require the same set of tissue samples. This chapter briefly describes several research studies that have already collected or are continuing to collect human tissue samples. Depending on how these tissues were obtained, they may be available for other research studies.

LONGITUDINAL STUDIES

Longitudinal studies, in which the same group of individuals is studied at intervals over a prolonged period, often collect large numbers of specimens that can be used for both retrospective and prospective research. Several well-known longitudinal studies have been conducted over the years, including the Physicians’ Health Study, the Nurses’ Health Study, and the Framingham Heart Study. Other large longitudinal studies include the Women’s Health Initiative, the Health Professionals Follow-Up Study, the MRFIT study, and the National Health and Nutrition Examination Surveys. Several longitudinal studies are described below.
The National Institutes of Health Women's Health Initiative

The NIH Women's Health Initiative (WHI), established in 1991, is the largest preventive study of women's health in the United States. The WHI is a 15-year research program, concluding in 2005, that focuses on the major causes of death, disability, and impaired quality of life in postmenopausal women. The overall goal of WHI is to reduce coronary heart disease, breast and colorectal cancer, and osteoporosis in postmenopausal women through prevention, intervention, and risk factor identification.

The WHI will involve more than 168,000 women of all races and socioeconomic backgrounds aged 50–79. Recruitment began in September 1993 and concluded in January 1998. The WHI conducts three studies: a randomized clinical trial, an observation study, and a community prevention study. Almost 70,000 women are enrolled in the randomized clinical trial that consists of three study groups: hormone replacement therapy, dietary modification, and calcium and vitamin D supplementation. Eligible women could choose to be in one, two, or all three of the study groups. The observational study will track the medical history and health habits of approximately 100,000 women to examine the relationship between lifestyle, health and risk factors, and disease. The clinical trial and observational study are conducted at 40 clinical centers nationwide. The Fred Hutchinson Cancer Research Center in Seattle, Washington, is the WHI Clinical Coordinating Center for data collection, management, and analysis.

The 168,000 women enrolled in both the clinical trial and the observational study will be followed for eight to 12 years and will provide multiple blood samples throughout the course of the study. Participants sign a consent form that states that the collection of blood samples is for use in future research, which may include genetic research, and participants will not be informed of any test results. Participants may opt out of having their samples used for genetic research if they so desire. The clinical trial participants provide a blood sample at their initial visit and at their one-year visit, and a subset of participants have samples drawn at three, six, and nine years. Blood samples are also collected from participants in the observational trial at their initial visit, and then again at their three-year visit. Blood samples are divided into serum, plasma, and buffy coat and are stored at a central facility in Rockville, Maryland. Participants' charts contain identifying information, including name, Social Security number, and address and telephone number, which are bar-coded. Blood samples are labeled with matching bar codes to link them to the charts. Approximately 27,000 women will be enrolled in the hormone replacement therapy trial, some of whom will also undergo an endometrial biopsy to
rule out endometrial hyperplasia or cancer.\textsuperscript{1} These biopsies are stored at the individual clinical centers within the pathology departments and are labeled with a pathology accession number. In cases where abnormalities are detected, slides of the biopsy are bar-coded and sent to a central laboratory at NIH. Participants and their physicians are informed of any abnormalities found in the endometrial biopsy. All study records will be kept indefinitely for analysis and follow-up.

The third component of the WHI, the community prevention study, is a five-year collaborative effort with the Centers for Disease Control and Prevention (CDC) to study community approaches to developing healthy behaviors. This study will include women of all races and socioeconomic backgrounds, aged 40 and over. Eight university-based prevention centers will conduct and evaluate health programs that encourage women to adopt improved diet, nutritional supplementation, smoking cessation, exercise, and early detection of treatable health problems, among other healthy behaviors.

**Baltimore Longitudinal Study of Aging**

The Longitudinal Studies Branch of the NIA is responsible for the operation and management of the Baltimore Longitudinal Study of Aging. The Baltimore Longitudinal Study was initiated in 1958, enrolling only men until 1978, when women were included. The Longitudinal Studies Branch has a research program based primarily on the Baltimore Longitudinal Study because it offers a unique opportunity to study a number of aging-related diseases and disabilities, including frailty, Alzheimer’s disease, cardiovascular disease, cancer, osteoporosis, and menopause.

Storage of blood samples and blood fractions began in 1963 and has been systematically continued since. Serum, plasma, lyophilized erythrocytes and whole-blood plasma (including leukocytes), and aliquots of 24-hour urine collections have all been stored. Over the years, samples have been used for various approved protocols. For example, a longitudinal study of prostate-specific antigen (PSA) was retrospectively performed and demonstrated that continued monitoring of PSA levels could detect prostatic cancer many years earlier than usual clinical measures could.

\textsuperscript{1}It is estimated that approximately one-third of the women enrolled in the hormone replacement therapy trial will have had a hysterectomy and therefore will not undergo the endometrial biopsy.
The Nun Study

The Nun Study is a longitudinal study of aging and Alzheimer’s disease funded by the NIA. The Nun Study is based at the University of Kentucky, Sanders-Brown Center on Aging. A total of 678 women between the ages of 75 and 103 were drawn from the School Sisters of Notre Dame religious congregation. Each participant is annually assessed on her cognitive and physical function, and a brief medical exam is performed and a blood sample taken. Investigators have full access to each participant’s archival and medical records. Each study participant has also agreed to donate her brain at death for further scientific study.

Bogalusa Heart Study

The Bogalusa Heart Study, ongoing since 1972, is the longest and most detailed study of children in the world. The Bogalusa Heart Study is an NIH-sponsored Specialized Center of Research (SCOR) at Louisiana State University Medical Center, run by a multidisciplinary team of anthropologists, biochemists, cardiologists, epidemiologists, geneticists, nurses, nutritionists, psychologists, sociologists, and statisticians. The study seeks to understand the environmental and hereditary aspects of early coronary artery disease, essential hypertension and cardiovascular risk factors in African-American and Caucasian children in the semirural community of Bogalusa, Louisiana. In addition, 160 substudies have been conducted, including special studies on socioeconomic evaluations, blood pressure, lipid levels, genetics, exercise, heart murmurs, and pathology. Knowledge gained in the Bogalusa Heart Study has been applied to develop, test, and evaluate methods for cardiovascular risk intervention.

The Bogalusa Heart Study has conducted cross-sectional and longitudinal observations on more than 14,000 children and young adults. For example, a post–high school study currently follows subjects until 38 years of age. Blood samples have been sent to Boston, Baltimore, Sweden, and Finland for special analysis. More than 632 publications, three textbooks, and numerous monographs have been produced using samples and data from the Bogalusa Heart Study.

National Health and Nutrition Examination Survey

Since 1960, the National Center for Health Statistics (NCHS) of the CDC has conducted seven health examination surveys of the population of the United States: the National Health Examination Surveys (NHES) Cycles 1, 2 and 3, the National Health and Nutrition Examination Surveys (NHANES) I, II and III, and the Hispanic Health and Nutrition Examination Survey (HHANES). The surveys
are designed to assess the health and nutritional status of children and adults in the United States periodically through interviews and direct physical examinations. The surveys employ interviews to answer questions about demographics, socioeconomic status, dietary habits, health-related issues, and physical and dental examinations, which include physiologic assessments and laboratory tests. Blood samples are collected as part of the physiologic assessments and placed in storage banks after laboratory tests are completed.

Cumulatively, the health examination surveys have analyzed and banked samples from more than 85,000 participants. The most recent survey, NHANES III, conducted between 1988 and 1994, performed laboratory tests on approximately 30,000 people of all races aged 2 months and older from 81 counties in 26 states. Some of the 30 topics investigated in the NHANES III included high blood pressure, high cholesterol, obesity, secondhand smoking, lung disease, osteoporosis, HIV/AIDS, hepatitis, helicobacter pylori, immunization status, diabetes, allergies, growth and development, anemia, dietary intake (including fats), antioxidants, and nutritional blood measures. The NHANES I analyzed blood and urine samples from 23,808 study participants, and NHANES II analyzed 20,322 samples. The HHANES was a one-time survey conducted from 1982 to 1984 that provided data on 11,653 people of Hispanic origin.

National Institute of Allergy and Infectious Disease—Division of AIDS

The Division of the Acquired Immunodeficiency Syndrome (DAIDS) was formed in 1986 to address the national needs of the cause and spread of HIV/AIDS. The mission of DAIDS is to increase basic knowledge of the pathogenesis, natural history, and transmission of HIV disease and to promote research in the detection, treatment, and prevention of the disease. DAIDS supports a number of longitudinal as well as clinical trials programs in the epidemiologic, therapeutic, and vaccine/prevention research as described below and in Chapter Two.

Individually and collectively, these studies have amassed a wealth of data that provides detailed information on the natural history and clinical and laboratory course of HIV disease in various populations. Specific fluids and tissues collected from the various studies include peripheral blood, mononuclear cells, serum, plasma, semen, saliva, vaginal washings, urine, placenta, and autopsy samples. These samples together with the huge database to which they are linked provide a rich resource for multidisciplinary investigations to scientists.

The Multicenter AIDS Cohort Study and the San Francisco Men’s Health Study. The Multicenter AIDS Cohort Study (MACS) and the San Francisco Men’s Health Study, awarded in 1983 by DAIDS, is a longitudinal study of HIV infection in approximately 5,000 homosexual and bisexual men. The goals of
the study are to provide an appropriate epidemiological basis for laboratory-based studies of HIV pathogenesis; to study the changing natural history of HIV infection; to define subgroups of HIV-infected individuals with unique HIV-related outcomes; and to identify individuals who remain HIV seronegative despite ongoing or prior high-risk sexual activity. Clinical specimens are collected on a regular basis (every six months) and include cells, serum, plasma, and tissue (including lymph node tissue and tissue collected at autopsy).

**The Women and Infants Transmission Study.** The Women and Infants Transmission Study (WITS) is a collaborative, multisite, longitudinal study of U.S. women with HIV infection and their offspring. As of September 1995, more than 1,200 women and almost 1,000 infants have been enrolled in the study. The goals of the study are to determine maternal cofactors related to maternal-infant HIV transmissions; to ascertain the timing of perinatal transmission and the risk factors for ante- versus intrapartum transmission; to evaluate HIV disease progression among both pregnant and nonpregnant HIV-positive women; to assess the natural history of infants born to HIV-positive women and determine factors affecting disease progression; and to establish effective means for early diagnosis of HIV infection in infants. Adult specimens collected during the study include blood, urine, and genital samples. Pediatric specimens include blood and urine.

**The Women's Interagency HIV Study.** The Women's Interagency HIV Study (WIHS), awarded in 1993, is a collaborative, multisite, longitudinal study established to investigate the impact of HIV infection on U.S. women. As of September 1995, more than 2,300 women were enrolled. The goals of the study are to describe the spectrum and course of clinical manifestations of HIV infection in women; to describe the pattern of immune markers in HIV-infected women; to investigate factors that may delay or accelerate HIV-induced immune dysfunction and specific HIV-related conditions; and to study the length of survival and quality of life of women living with HIV infection. Specimens routinely collected from study participants include blood, oral/pharyngeal swabs, urine, vaginal and cervical swabs, and cervicovaginal lavage fluids.

**Framingham Heart Study**

Since 1948, the federal government has followed a representative sample of 5,209 adults in Framingham, Massachusetts. These people have been tracked using standardized biennial cardiovascular examinations, daily surveillance of hospital admissions, death information, and information from physicians and other sources outside the clinic. The goal has been to study the epidemiology of cardiovascular diseases and to learn the circumstances under which they arise, evolve, and terminate fatally in the general population. The study is also
designed to differentiate those who develop cardiovascular diseases from those who remain disease-free over a longer period of time.

**Physicians' Health Study**

The Physicians' Health Study, conducted at Brigham and Women's Hospital in Massachusetts since 1982, is a randomized, double-blind, placebo-controlled trial studying the role of aspirin and beta-carotene in decreasing risks of cardiovascular disease and cancer. The study has been conducted entirely by mail among 22,701 U.S. male physicians between the ages of 40 and 84 years of age. In addition, blood specimens have been collected from each participant.

The Physicians’ Health Study II will evaluate the effects of beta-carotene, vitamin E, vitamin C, and multivitamin supplements on the prevention of cancer, especially prostate cancer in a randomized, double-blind, placebo-controlled trial. Fifteen thousand U.S. male physicians will be enrolled in this study.

**Nurses’ Health Study**

The Nurses’ Health Study began in 1976 at the Harvard School of Public Health. Since then, 117,000 nurses have entered the study. The study was designed to serve as a prospective follow-up study to examine a possible relationship between oral contraceptive use and breast cancer. Follow-up questionnaires have been mailed to participants every two years, and blood specimens were collected at the time of enrollment. Extensive details of lifestyle practices have been collected for each participant. The Nurses’ Health Study has been a part of many studies investigating the relation between use of hormones, diet, exercise, and other lifestyle practices as related to the development of various illnesses, including diabetes, breast cancer, and colon cancer.

**Health Professionals Follow-Up Study**

The Health Professionals Follow-Up Study was initiated in 1986 at Harvard University. More than 51,000 male health professionals aged 40 to 75 years were followed, and blood specimens were obtained from each of the participants. This study has been the basis for several prospective studies investigating factors that are potentially important in the development of prostate cancer, colon cancer, colorectal adenoma, cardiovascular disease, chronic dental disease, kidney disease, multiple sclerosis, and Parkinson's disease.
MRFIT Study

The Multiple Risk Factor Intervention Trial (MRFIT) was a cardiovascular disease intervention trial. MRFIT began by screening 361,662 males between the ages of 35 and 57 from 1973 to 1975. More than 12,000 men were then enrolled in the intervention trial. Lifestyle data were collected from each participant as well as blood serum samples. Data have been used in studies measuring the relationship between such factors as serum cholesterol, smoking, hypertension, and stress with the development of cardiovascular disease.

Women’s Health Study

The Women’s Health Study, conducted at Brigham and Women’s Hospital, will evaluate the balance of benefits and risks of low-dose aspirin and vitamin E in reducing the risks for cardiovascular disease and cancer in women. The study population will consist of 40,000 U.S. female health professionals age 45 and older.

RESEARCH THAT SIMULTANEOUSLY CREATES TISSUE COLLECTIONS OR CONTRIBUTES TO A TISSUE BANK

Most research projects that use human tissue obtain specimens from pathology laboratories or existing tissue banks. However, some research studies require unique samples and must collect specialized tissue. Therefore, some research will create tissue collections and may end up contributing these samples to an established tissue bank for storage. Several examples of research that simultaneously creates tissue collections or contributes to a tissue bank are described below.

National Institute of Child Health and Human Development

NICHD performs and supports several research projects in pregnancy, delivery, and child development–related issues that involve collection and storage of tissue samples. To fulfill its needs for storage, monitoring and distribution of existing and yet-to-be-collected specimens, the NICHD contracts with commercial enterprises. For example, the Maternal Fetal Network Project, conducted by the Pregnancy and Perinatology Branch of NICHD, has contracted with Biotech Research Laboratory to establish a repository that will contain frozen plasma and sera samples from patients studied in several clinical protocols. This repository is a valuable source of biological markers for the study of preterm births and preeclampsia. In addition, two NICHD-funded research studies, the Diabetes in Early Pregnancy Study (DIEP) and a Longitudinal Study
of Fetal Growth and Perinatal Outcome, have contracted with Biomedical Research, Inc., to provide storage, monitoring, and distribution of serum samples. Both studies involved collecting multiple blood samples throughout the course of the study. Biomedical Research, Inc., also provided storage, monitoring, and distribution of serum, plasma, and urine from a double-blind, randomized, clinical trial of supplemental calcium for the prevention of preeclampsia during pregnancy. Five clinical centers, enrolling 4,500 women over a two-year period, contributed samples from study participants at baseline, early and late in the third trimester of pregnancy, and at the time of diagnosis of preeclampsia.

**Prostate Cancer Intervention Versus Observation Trial**

The primary objective of the Prostate Cancer Intervention Versus Observation Trial is to determine which of these two strategies is superior for the management of clinically localized prostate cancer: radical prostatectomy with early intervention or expectant management with reservation of therapy for palliative treatment. The VA Medical Center in Minneapolis, Minnesota, is the central location of the study, and the project is supported by the Department of Veterans Affairs. One thousand patients from 80 medical centers with clinically localized prostate cancer who are under 75 years of age and potential candidates for radical prostatectomy will be included in the study. A central laboratory will examine tissue specimen samples for confirmation of histopathologic diagnosis of prostate cancer. Also, a centralized serum bank will be established for PSA assays and future studies.

**Smoking Cessation Program for Patients Enrolled in SPORE Projects**

The VA Medical Center in Denver, Colorado, is conducting a study to understand the epidemiologic finding that former smokers remain at elevated risk for many years after cessation of smoking. The study is supported by the Department of Veterans Affairs. The aims of the study include assessing the degree and time course of reversion of preneoplastic markers to normal after smoking cessation in smokers who are at high risk for lung cancer and to characterize individuals who do not show reversion of these markers to normal after smoking cessation. A bank of sputum cytology samples will concurrently be established for a cohort of high-risk subjects. Samples from high-risk subjects before and after smoking cessation will be used for rapid pilot testing of new lung cancer markers.
Genetics of Familial Polycystic Ovary Syndrome

Researchers at the Milton S. Hershey Medical Center in Pennsylvania are studying polycystic ovary syndrome (PCOS) to find a genetic marker that would be useful in identifying women at risk for developing PCOS prior to the onset of complications. The study will include a few large, three-generation kindreds of PCOS to reduce genetic heterogeneity. A DNA bank of complete PCOS pedigrees is being assembled for genetic studies. A normative database will be established for age, weight, and ethnicity matched controls. Previously identified kindreds of familial PCOS will be phenotyped for clinical, biometric, and biochemical abnormalities. All available pedigree members—male and female—will be phenotyped. By identifying women at risk for PCOS, medical resources could be focused on preventing complications.

Molecular Basis of Split Hand/Split Foot Malformation

The University of North Carolina at Chapel Hill is characterizing the molecular defect responsible for split hand/split foot (SHSF) malformation, a human developmental disorder that results in abnormal hands and feet. A repository of cell lines from individuals with SHSF and related malformations is being established. This resource will facilitate cloning of the SHSF gene as well as future investigations of genotype-phenotype relationships in SHSF. SHSF pedigrees will also be analyzed. Isolation of the SHSF gene will provide an opportunity to investigate the molecular basis of pattern formation in the human limb.

Molecular Epidemiology of Breast Cancer

Case Western Reserve University in Cleveland, Ohio, is pursuing a study to understand the molecular epidemiology of breast cancer entitled “Establishment of an at-risk cohort and methods to improve the collection and use of risk.” The study is funded by the Department of the Army and will specifically investigate molecular markers and their interaction with other epidemiologic risk factors toward identification of relative risk factors for breast cancer development in Caucasian and African-American women with benign breast disease. More than 5,000 women are expected to be followed to yield an estimated 250 breast cancer cases. Benign breast disease and cancerous tissue samples will be archived in a specimen bank. A questionnaire will be developed to identify risk factors and will be used to construct an exposure index for lifetime exposure to sex hormones.
Human Conceptual Tissue: Characterization for Transplantation

The Puget Sound Blood Center of Seattle, Washington, is committed to determining the availability and suitability of embryonic tissue for transplantation research and therapy. In this project, investigators will focus on development and assessment of protocols for the collection, processing, and cryopreservation of embryonic tissue and will also characterize hematopoietic stem cells derived from embryonic fetal liver. This project is supported by the National Institute of Child Health and Human Development. Three institutions participate in this project (the Central Laboratory for Human Embryology, the Northwest Tissue Center, and the Fred Hutchinson Cancer Research Center), and together they have formed the Northwest Fetal Tissue Program. For more than 30 years, the Central Laboratory for Human Embryology has collected and processed more than 15,000 embryos and fetuses. The other groups have expertise in storage and cryopreservation of tissue and stem cell replacement therapy research.

Epidemiology of EBV-Defined Hodgkin’s Disease

The Northern California Cancer Center is conducting a study to explore the epidemiology of subtypes of Hodgkin’s disease defined by Epstein-Barr virus. The study will collect specimens archived between 1990 and 1995 from Hodgkin’s disease cases reported to the California Cancer Registry; apply standard techniques to classify each case as Epstein-Barr virus–positive or –negative; calculate risks of Epstein-Barr virus–positive and –negative Hodgkin’s disease for multiple variables; calculate incidence rates of Epstein-Barr virus–positive and –negative Hodgkin’s disease; and bank tumor specimens for future testing. It is expected that tumor specimens will be requested for more than 2,500 subjects.

Therapy and Biological Correlations of Soft Tissue Sarcoma

Fifty percent of patients who undergo surgery in conjunction with radiotherapy do not have successful survival rates, usually due to pulmonary metastases. These metastases can only be marginally controlled by toxic chemotherapy agents if they are not resectable. Other problems surrounding the understanding and successful treatment of soft tissue sarcomas include different and non-interconvertible staging systems, a lack of information about molecular determinants of sarcoma proliferation and metastasis, and long-term clinical trials due to the rarity of the disease resulting in slow drug production. This project at the University of Texas M.D. Anderson Cancer Center, supported by the NCI, will focus on these obstacles in the area of soft tissue sarcomas. A bioresource facility has been established that contains a tissue bank, short-term culture explants and cell lines, and paraffin-embedded tissue blocks.
Lifetime Alcohol Exposure and Breast Cancer Risk

The Department of the Army funds a population-based, case-control study to investigate the relationship between alcohol exposure and the risk of breast cancer at the State University of New York at Buffalo. African-American and Caucasian women, aged 35 to 79, both pre- and postmenopausal will be selected. Matched controls will be randomly selected. A specimen bank will be created to store biological samples for future studies.

Prospective Randomized Study of Adjuvant Chemotherapy Versus Vinorelbine and Cisplatin in Completely Resected NSCLC with Companion Tumor Marker Evaluation

This phase III study will be conducted at the VA Medical Center in East Orange, New Jersey, and is supported by the Department of Veterans Affairs. The study compares the overall survival between completely resected patients with T2NO, T1-2NI non–small cell lung cancer (NSCLC) who have received either adjuvant chemotherapy with vinorelbine and cisplatin or observation alone. A comprehensive tumor bank will be established and linked to a clinical database. These tissue specimens will be used for further study of molecular markers in resected NSCLC.

Case-Control Study of Hodgkin’s Disease in Children

This is an ongoing study at the University of Pittsburgh supported by the NCI to investigate the epidemiologic, virologic, and genetic components of the rare cases of Hodgkin’s disease in children. Previously, epidemiologic data had been gathered from 300 cases and 484 controls by telephone interviews. The project will be expanded to 415 cases and 675 controls. Tissue specimens will be collected from all 415 cases for virologic assays and to create a biologic specimen bank for future studies.

Markers for Differential Diagnosis and Virulence of Prostate Cancer

A project on molecular markers for differential diagnosis and virulence of prostate cancer is being conducted at the VA Medical Center in Seattle, Washington, and supported by the Department of Veterans Affairs. This study will focus on the development of reagents and immunoassays for various serum forms of PSA, to determine whether CD44 and specific isoforms enable prostatic cells to metastasize to specific sites and to construct cDNA libraries from a prostate cancer xenograft model. A human tumor/sera bank will also be established for multiple other projects.
The Role of IL-1 Cytokines in Colorectal Cancer

The VA Medical Center in Pittsburgh, Pennsylvania, is conducting a project to delineate gene products that are inappropriately expressed in colorectal tumors that may affect clinical outcome. A second goal of the project is to identify gene products essential to tumor cell proliferation and may serve as therapeutic targets. A tumor bank has been established of frozen tumors and polyps from more than 200 cases. A database contains clinical and pathological findings for each stored specimen.

Markers for Malignant Progression in Prostate Cancer

A study investigating molecular prognostic markers to assist in clinical management and classification of patients into clinical trials is being conducted at Georgetown University. The goal of the study is to identify molecular markers and activated oncogenes that indicate poor prognosis in prostate cancer. The study will actively accrue freshly frozen surgical material to a prostate tissue bank. The tumor bank will maintain demographic information and pathology records and blocks.

Pulmonary Hypertension—Mechanisms and Family Registry

This project will be conducted at Vanderbilt University Hospital in Nashville, Tennessee, and is supported by NHLBI. The goals of the project will be to investigate the basic mechanisms of primary pulmonary hypertension and to establish a registry and database of familial primary pulmonary hypertension pedigrees to determine the mode of inheritance. A tissue bank will be set up for DNA samples and transformed lymphocytes from families and patients with primary pulmonary hypertension. These samples will be made available to investigators both locally and nationwide.

Blood Test to Predict Prognosis in Patients with Gynecologic Cancer: Plasma Assay of GLB and GLB:TIMP-1 Complexes

The Department of Veterans Affairs supports this study at the VA Medical Center in Northport, New York. It is believed that the production and activation of enzymes known as gelatinases (GLA and GLB) are essential components for tumor metastasis. An ELISA test has been developed to measure the concentrations of GLB and its complexes in plasma from patients with cancer. It has been demonstrated that these enzymes are increased in plasma from patients with gynecologic and colorectal cancer. The goals of this study are to establish a plasma bank from patients with gynecologic cancers (ovarian, cervical, uter-
ine, vaginal), to measure the plasma concentration of GLB and its complexes and to determine whether the plasma concentrations of GLB and its complexes can be used as a prognostic and response factor to different treatment regimens.

**AIDS-Malignancy Clinical Trials Consortium**

The University of Southern California AIDS-Malignancy Clinical Trials Consortium (AM-CTC) helps design, develop, and conduct collaborative, innovative phase I and II clinical trials, employing novel agents and approaches in patients with various AIDS-related malignancies. In addition, the AM-CTC provides tumor tissue and other relevant biologic materials, derived from patients accrued into clinical trials, to the NCI-funded Tissue and Biological Fluids Bank of HIV Associated Malignancies. Since 1987, the AIDS Clinical Trials Group (ACTG) has accrued more than 470 patients onto various AIDS-malignancy protocols. The University of Southern California AIDS Malignancy Program has been actively engaged in phase I and II trials related to HIV-related cancers, with participation in 45 such studies, resulting in 17 publications, and 30 published abstracts.

**Pancreatic Cancer Case-Control Study in San Francisco**

This population-based, case-control study in men and women will examine the hypotheses linking adenocarcinoma of the exocrine pancreas and detailed occupational history and chemical exposures. This study is supported by the NCI. One thousand cases and 1,150 controls will be interviewed during a 3.5-year period. The study is based at the University of California, San Francisco, and will include participants from six San Francisco Bay area counties. Blood samples for genetic investigations will be drawn, and cells samples will be frozen in the Irwin Memorial Blood Bank. Whole-blood specimens will also be stored for future genetic and biomarker studies.

**Exogenous Toxicants and Genetic Susceptibility in Amyotrophic Lateral Sclerosis**

Stanford University is investigating the role of environmental toxicants and genetic susceptibility factors in the etiology of Amyotrophic Lateral Sclerosis (ALS) by conducting a case-control study of 175 incident ALS and 550 age- and gender-comparable control subjects. All 175 ALS cases and a subset of 350 control subjects will undergo measurement of bone lead stores using x-ray fluorescence and will have a venous blood sample drawn for copper-zinc superoxide dismutase (SOD1) enzyme genotyping and DNA banking. The collection
of detailed information regarding the duration and timing of environmental exposures will enable the evaluation of dose response trends and estimation of latent periods between putative exposure and the development of ALS. It is hoped that the proposed study will advance knowledge of neurotoxic and endogenous susceptibility factors important in the etiology of ALS.

**National Institute of Allergy and Infectious Disease—Division of AIDS**

DAIDS was created in 1986 to address the national research needs created by the cause and spread of HIV/AIDS. Several clinical research trials groups are sponsored by DAIDS and have collectively amassed a large number of specimens that are available for research.

**The HIV Network for Prevention Trials.** The HIV Network for Prevention Trials (HIVNET), established in 1994, is a network of clinical sites to conduct HIV vaccine efficacy trials and prevention trials in higher-risk populations. HIVNET consists of five contracts supported by DAIDS: the domestic HIV/AIDS vaccine efficacy trials, the international HIV/AIDS vaccine efficacy trials, a statistical and data coordinating center, a specialized laboratory testing center, and a specimen repository. As of September 1995, more than 3,600 volunteers had participated in HIVNET. Specimens collected from HIVNET trials are routinely sent to a central laboratory for testing. HIVNET specimens include serum, plasma, peripheral mononuclear cells, genital tract specimens, and saliva. The availability of specimens depends on the type of specimen requested.

**The Pediatric AIDS Clinical Trials Group.** The Pediatric AIDS Clinical Trials Group (PACTG), awarded in 1987, is a multicenter clinical trials network. The goals of this study group are to support the development and implementation of phase I, II, and III studies designed to test and optimize therapies to prevent and treat HIV infection and its sequelae in infants, children, and adolescents; to conduct studies throughout the United States at more than 50 pediatric AIDS Clinical Trials Units; and to collaborate closely with the adult ACTG studies. Specimens collected from PACTG trials included serum, plasma, peripheral mononuclear cells, culture supernatants, lymph node biopsies, tissues, urine, and other body fluids.

**The Adult AIDS Clinical Trials Group.** The Adult AIDS Clinical Trials Group (Adult ACTG), established in 1987, is a consortium of 30 clinical trial research groups. The goals of the adult ACTG are to evaluate innovative therapeutic strategies and interventions to control HIV infection and complications in adults; to facilitate rapid translation of basic research into clinical research and practice; and to provide a flexible resource for state-of-the-art, multidisciplinary clinical trials. To date, more than 35,000 adult volunteers at all stages of the disease have enrolled. Specimens collected during the clinical
trials include serum, plasma, peripheral mononuclear cells, culture supernatants, lymph node biopsies, tissues, urine, and other bodily fluids.

**The AIDS Vaccine Evaluation Group.** The AIDS Vaccine Evaluation Group (AVEG), consists of six AIDS Vaccine Evaluation Units that evaluate candidate AIDS vaccines in phase I and II clinical trials for safety and immunogenicity. As of October 1995, more than 1,800 volunteers had enrolled in AVEG trials. Specimens collected during clinical trials include serum, plasma, peripheral mononuclear cells, genital tract secretions, saliva, and tears. The availability of specimens depends on the type of specimen requested.

**The Division of AIDS Treatment Research Initiative.** The Division of AIDS Treatment Research Initiative (DATRI), established in 1991, conducts phase I and II studies of therapies for HIV and associated diseases. The DATRI Network performs small, focused studies and substudies of protocols conducted by other extramural programs. Clinical specimens will vary according to protocol and include serum, plasma, cells and cultured cells, and supernatant from PBMC and plasma HIV cultures.