2. Program Overview

The National Heart Institute (NHI) was established in 1948 through the National Heart Act with a mission to support research and training in the prevention, diagnosis, and treatment of cardiovascular diseases (CVD). Twenty-four years later, through section 413 of the National Heart, Blood Vessel, Lung, and Blood Act (P.L. 92–423), Congress mandated the Institute to expand and coordinate its activities in an accelerated attack against heart, blood vessel, lung, and blood diseases. The renamed National Heart, Lung, and Blood Institute (NHLBI) expanded its scientific areas of interest and intensified its efforts related to research on diseases within its purview. Over the years, these areas of interest have grown to encompass genetic research, sleep disorders, and the Women's Health Initiative (WHI).

The mission of the NHLBI is to provide leadership for a national program in diseases of the heart, blood vessels, lung, and blood; sleep disorders; and blood resources management. The Institute:

- Plans, conducts, fosters, and supports an integrated and coordinated program of basic research, clinical investigations and trials, observational studies, and demonstration and education projects related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases, and sleep disorders conducted in its own laboratories and by other scientific institutions and individuals supported by research grants and contracts.
- Plans and directs research in development and evaluation of interventions and devices related to the prevention of diseases and the treatment and rehabilitation of patients suffering from such diseases and disorders.
- Conducts research on the clinical use of blood and all aspects of the management of blood resources.
- Supports career training and development of new and established researchers in fundamental sciences and clinical disciplines to enable them to conduct basic and clinical research related to heart, blood vessel, lung, and blood diseases; sleep disorders; and blood resources through individual and institutional research training awards and career development awards.
- Coordinates relevant activities with other research institutes and all Federal health programs in the above areas, including the causes of stroke.
- Conducts educational activities, including development and dissemination of materials for health professionals and the public in the above areas, with emphasis on prevention.
- Maintains continuing relationships with institutions and professional associations, and with international, national, state, and local officials, as well as voluntary agencies and organizations working in the above areas.
- Oversees management of the WHI.

Each year, the NHLBI assesses progress in the scientific areas for which it is responsible and updates its goals and objectives. As new opportunities are identified, the Institute expands and revises its areas of interest. Throughout the process, the approach used by the Institute is an orderly sequence of research activities that includes:

- Acquisition of knowledge
- Evaluation of knowledge
- Application of knowledge
- Dissemination of knowledge.

The programs of the NHLBI, as shown on page 10, are implemented through five extramural units: the Division of Heart and Vascular Diseases (DHVD), the Division of Lung Diseases (DLD), the Division of Blood Diseases and Resources (DBDR), the Divi¬sion of Epidemiology and Clinical Applications (DECA), and the National Center on Sleep Disorders Research (NCSDR); and one intramural unit, the Division of Intramural Research (DIR). Although the NHLBI has primary responsibility for the WHI, it is run by a consortium that includes the National Cancer Institute (NCI), the National Institute on Aging (NIA), and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). The Divisions and the Center pursue their own scientific missions but cooperate in areas of common interest. The extramural Divisions and the NCSDR use a variety of funding mechanisms, such as research grants, cooperative agreements, program project grants, Small Business Innovation Research grants, Small Business Technology Transfer grants, Specialized Centers of Research (SCOR) and Specialized Centers of Clinically Oriented Research (SCCOR) grants, comprehensive center grants, contracts, and research training and career development programs. Descriptions of the Division and Center programs, as well as the WHI, follow.

National Heart, Blood Vessel, Lung, and Blood Diseases and Blood Resources Program

Heart and Vascular Diseases

Heart Research
Heart Development
Cardiac Function and Heart Failure
Ischemic Heart Disease
Arrhythmias and Sudden Cardiac Death

Vascular Biology Research
Atherosclerosis
Hypertension Biology and Pathophysiology of Blood Vessels
Gene Therapy for Prevention and Treatment of Vascular Diseases

Clinical and Molecular Medicine
Cardiovascular Medicine
Bioengineering/Systems
Genomic and Proteomic Applications Imaging/Nanotechnology
Bioinformatics

Lung Diseases

Airway Biology and Disease
Asthma
Chronic Obstructive Pulmonary Disease (COPD) and Environmental Lung Diseases
Cystic Fibrosis (CF) Neurobiology and Sleep

Lung Biology and Disease

Lung Cell and Vascular Biology
Developmental Biology and Pediatric Lung Disease
Critical Care and Acute Lung Injury

Acquired Immunodeficiency Syndrome (AIDS) and Tuberculosis (TB)
Immunology and Fibrosis

Blood Diseases and Resources

Blood Diseases
Sickle Cell Disease (SCD)
Thalassemia
Erythropoiesis
Red Cells
Thrombosis and Hemostasis
Hemophilia and Other Bleeding Disorders
Hematologic Immune Disorders

Blood Resources
Transfusion Medicine Use, Safety, and Availability of
Blood and Blood Components
Stem Cell Biology
Myelodysplasia, Marrow Failure, and Myeloproliferative Disorders
Hematopoietic Stem Cell Transplantation
Novel Cellular Therapies for Repair and Regeneration
Immune Deficiencies, Reconstitution, Response, and Tolerance

Epidemiology and Clinical Applications

Clinical Applications and Prevention
Clinical Prevention and Translation
Clinical Trials
Behavioral Medicine and Prevention

Epidemiology and Biometry
Field Studies and Clinical Epidemiology
Analytical Resources
Genetic Epidemiology

National Center on Sleep Disorders Research
Sleep
Sleep Disorders and Related Conditions

Women's Health Initiative

Intramural Research

Clinical Research Program
Cardiovascular
Hematology
Molecular Disease
Pulmonary/Critical Care Medicine
Animal Medicine and Surgery

Laboratory Research Program
Biochemical Genetics
Biochemistry
Biophysical Chemistry
Cardiac Energetics
Cell Biology
Cell Signaling
Developmental Biology
Kidney and Electrolyte Metabolism
Molecular Cardiology
Molecular Immunology

Division of Heart and Vascular Diseases

The DHVD plans and directs a coordinated research program on the causes of heart and vascular diseases and on their prevention, diagnosis, and treatment. Fundamental biomedical research, including cutting-edge areas such as genomics, proteomics, nanotechnology, cell-based therapeutics, and gene therapy, is emphasized. Multidisciplinary programs are supported to advance basic knowledge of disease and to generate the most effective methods of clinical management and prevention. Clinical trials are an important part of the research program; they provide an opportunity to test and apply promising preventive or therapeutic measures.

The Division is organized into three major research programs:

- Heart Research Program
- Vascular Research Program
- Clinical and Molecular Medicine Program

and the Research Training and Special Programs Scientific Research Group (SRG).

Heart Research Program

The Heart Research Program supports basic and clinical research in cardiac diseases, from embryonic life through adulthood. Targeted areas include heart development, cardiac disorders, inflammation and infectious disorders of the heart, heart transplantation, and myocardial preservation. Individual studies focus on normal and abnormal cardiac development, diabetic cardiomyopathy, gene–nutrient interactions in the pathogenesis of congenital heart defects, pathogenesis of heart failure, electrical remodeling, and various aspects of HIV infection as it relates to the heart. SCORs support collaborative studies in ischemic heart disease, sudden cardiac death, heart failure, pediatric CVD and ischemic heart disease in blacks. The Program comprises the two SRGs described below.

Heart Development, Function, and Failure SRG

The Heart Development, Function, and Failure SRG oversees a research program in heart development, cardiac function, and heart failure. It includes basic studies examining normal functional and structural development of the heart and major blood vessels, as well as the genetic, molecular, environmental, and mechanical etiology of congenital cardiovascular malformations. Clinical research networks are used to evaluate new treatment methods and

management strategies for congenital malformations and acquired pediatric heart disease. Research on cardiac function and failure focuses on fundamental mechanisms associated with the structure, function, mechanics, and bioenergetics of normal and diseased myocardium; the role of contractile proteins in the cardiovascular system; and causes of cardiac hypertrophy and the subsequent transition from hypertrophy to heart failure. Individual projects include molecular, cellular, and physiological studies of diabetic cardiomyopathy; pathogenesis of heart failure, with emphasis on apoptosis (programmed cell death), myocyte division and growth, and cell transplantation; and studies to identify modifiers of gene defects leading to hypertrophic cardiomyopathy and heart failure.

Arrhythmias, Ischemia, and Sudden Cardiac Death SRG

The Arrhythmias, Ischemia, and Sudden Cardiac Death SRG oversees a research program on cardiac arrhythmias that focuses on elucidating the mechanisms involved in control of cardiac electrical activity; determining the contribution of cardiac membrane biophysics, membrane structure and organization, ion pumps and channels, and transport and gap junction proteins to electrogenesis; and understanding the long-term control of cardiovascular function as it relates to the onset or maintenance of arrhythmias. Investigators are seeking knowledge that will lead to the development of new approaches to diagnosis, treatment, and prevention of arrhythmias.

The SRG also oversees a research program on the etiology and pathophysiology of ischemic heart disease and its consequences and control and treatment of cardiac electrical activity, rhythm, and rate, especially as they relate to sudden cardiac death. Researchers are seeking ways to improve the diagnosis and treatment of myocardial ischemia. Special attention is directed toward understanding the pathophysiology of ischemic heart disease in blacks, a population that is disproportionately affected by the disorder.

Vascular Biology Research Program

The Vascular Biology Research Program supports research in atherosclerosis, hypertension, basic vascular biology, and gene therapy for prevention and treatment of vascular diseases. Other targeted areas focus on the etiology, pathogenesis, and treatment of excess CVD in diabetes mellitus and cardiovascular complications of HIV/AIDS. SCORs support collaborative studies on molecular medicine and atherosclerosis, molecular genetics of hypertension, and basic and clinical gene therapy. The Program comprises the two SRGs described below.

Atherosclerosis SRG

The Atherosclerosis SRG oversees a comprehensive research program on the etiology, pathogenesis, diagnosis, prevention, and treatment of atherosclerosis. Areas of emphasis include pathobiology and genetics of the vasculature; vascular growth and angiogenesis; interactions of the vascular wall with systemic and humoral factors promoting atherogenesis; and lesion progression, complication, and regression. Individual studies focus on characterization of vulnerable atherosclerotic plaque, pathogenesis of abdominal aortic aneurysms, role of homocysteinemia in atherosclerosis, mechanisms of atherosclerosis in various vascular beds, and research on atherosclerotic lesions. Additional projects target pathobiological determinants of atherosclerosis, cardiovascular complications of diabetes mellitus, vessel-wall calcification, the role of infectious agents in atherosclerosis, immunobiology of the vessel wall, obesity-associated CVD, exercise physiology, peripheral artery disease (PAD), and effect of protease inhibitors on

atherosclerosis development in HIV infection. Of special interest is understanding atherosclerosis risk among minorities.

Hypertension SRG

The Hypertension SRG directs a research program to identify and characterize genes and their corresponding phenotypes involved with hypertension; elucidate regulation mechanisms associated with blood pressure control; clarify functional control of the cerebrovasculature; and identify causative factors of essential hypertension and rare forms of high blood pressure. It also seeks to determine the mechanisms by which high blood pressure increases the risk of, or occurs concomitantly with, other diseases such as kidney failure, stroke, metabolic syndrome X, obesity, diabetes mellitus, atherosclerosis, preeclampsia, and left ventricular hypertrophy. Further, it fosters studies to develop preventive strategies and interventions for hypertension, understand the biological underpinnings of salt sensitivity and the basis of target-organ damage in hypertension, and identify neurological mechanisms responsible for long-term control of blood pressure and functional neurological changes that result in essential hypertension. Attention is directed to eliminating health disparities among minorities and between men and women.

Clinical and Molecular Medicine Program

The Clinical and Molecular Medicine Program supports clinical, basic, engineering, and quantitative research on CVD and health. Areas of interest include genetics, genomics, and proteomics; engineering theory and practice applied to cardiovascular biology and medicine; informatics and simulation; computational systems; and cohort, case-control, and randomized clinical trials. Individual projects focus on heart failure, revascularization, the implantable artificial heart, and understanding minority and women's health. The program comprises the two SRGs described below.

Cardiovascular Medicine SRG

The Cardiovascular Medicine SRG directs a research program on CVD in adult and pediatric patients. It examines the role of lipid interventions, nutrition, and exercise in preventing heart disease. Areas of emphasis include development of treatments or new applications of existing medical and surgical strategies for acute and chronic ischemic heart disease; dietary and medical management of dyslipidemia; quantitative measurement of atherosclerosis; diagnosis and management of arrhythmias; resuscitation; cardiomyopathies of different etiologies (e.g., ischemic, valvular, metabolic, HIV-related, other infectious); congenital malformations; peripheral vascular disease; restenosis after revascularization procedures; cardiovascular applications of radiotherapy; and cardiovascular dysfunction in long-term pediatric cancer survivors.

Bioengineering and Genomic Applications SRG

The Bioengineering and Genomic Applications SRG directs an interdisciplinary research program that applies engineering theory and practice to increase knowledge at the genetic, molecular, cellular, tissue, and organ level and examines materials, processes, and devices for the cardiovascular system. Individual projects focus on innovative ventricular assist systems, implantable total artificial hearts, genetically enhanced cardiovascular implants, nanotechnology, magnetic resonance angiography, physical stress and strain, micromechanics, self-assembly,

mathematical models, simulation and systems, imaging, biomaterials, tissue engineering, and therapeutic devices

Division of Lung Diseases

The DLD plans and directs a coordinated research program on the causes and progression of lung diseases and on their prevention, diagnosis, and treatment. Areas of interest include the biology and function of the respiratory system, fundamental mechanisms associated with specific pulmonary disorders, and development of new treatment strategies for patients. SCORs support collaborative studies on asthma, CF, the pathobiology of lung development, and the pathobiology of fibrotic lung disease; a SCCOR supports collaborative studies on acute lung injury. Demonstration and education projects to transfer basic research and clinical findings to health care professionals and patients, as well as training and career development programs for individuals interested in furthering their professional abilities in lung diseases research, also are important activities.

The Division is organized into two major research programs:

- Airway Biology and Disease Program
- Lung Biology and Disease Program.

Airway Biology and Disease Program

The Airway Biology and Disease Program supports basic and clinical research, education, and training related to asthma, COPD, CF, control of breathing, bronchiolitis, respiratory neurobiology, sleep, and other adult airway diseases. It comprises the four research SRGs described below and a Training and Special Programs SRG, which manages training and career development in lung diseases research for individuals at all stages of their professional development.

Asthma SRG

The Asthma SRG oversees a broad research program in asthma. Basic research focuses on elucidating the etiology and pathophysiology of the disease. Studies include elucidating the cellular and molecular mechanisms associated with development, exacerbation, and persistence of asthma and the impact of the environment on these mechanisms; identifying susceptibility genes that influence development, progression, outcome, and response to treatment in different racial groups; determining the differences between the pathophysiology of severe asthma and mild-to-moderate asthma; and investigating the role of the immune system, its function in early life, and its influence on asthma development.

Clinical research focuses on improving asthma management and reducing health disparities in asthma that exist between whites and other ethnic groups, as well as economically disadvantaged populations. Two asthma networks have been established to assess new treatment strategies and ensure rapid dissemination of research findings to health care professionals. The Division has established cooperative partnerships between minority-serving institutions and research-intensive institutions to examine factors that contribute to health disparities and to develop strategies for their elimination. The purpose of the partnerships is to conduct collaborative research on asthma

disparities and provide reciprocal training experiences to enhance research opportunities and capabilities and enrich the cultural sensitivity at both institutions.

Chronic Obstructive Pulmonary Disease/Environment SRG

The COPD/Environment SRG oversees research on the underlying causes of COPD and improving disease treatment and management. Studies include examining the role of inflammation in the pathogenesis of COPD; searching for genes that may make some individuals more susceptible to the development of the disorder; identifying and characterizing biomarkers of COPD presence, severity, and exacerbation; evaluating treatment strategies (i.e., lung volume reduction surgery, long-term smoking cessation intervention, and retinoic acid therapy); and applying gene therapy to correct the defective gene or to introduce the functional gene for alpha-1 antitrypsin in deficient individuals with familial emphysema.

A Clinical Research Network has been established to conduct clinical trials of promising therapies for COPD that may reduce the frequency and severity of disease exacerbation. Additionally, a program was initiated to provide researchers with lung tissue specimens that were removed for medical reasons and are not needed for diagnostic purposes.

Cystic Fibrosis SRG

The CF SRG oversees basic and clinical research related to the origins and control of infections and inflammatory and immune responses in the lungs of CF patients, loss of CF transmembrane conductance regulation on development of CF, effects of other genes on its manifestation, and genetic and metabolic defects underlying pulmonary complications associated with CF. Developing new genetic, pharmacologic, and nonpharmacologic (e.g., gene transfer) treatments also is an area of emphasis.

Sleep and Neurobiology SRG

The Sleep and Neurobiology SRG oversees sleep research on the neurobiology, health consequences, and treatment of sleep disorders, sleep disordered breathing, and ventilatory control.

Lung Biology and Disease Program

The Lung Biology and Disease Program supports research, education, and training programs in lung cell and vascular biology; developmental biology and pediatric lung diseases; acute lung injury and critical care medicine; interstitial lung diseases, including pulmonary fibrosis; and AIDS and TB. It comprises the five research SRGs described below and a Training and Special Programs SRG that manages training and career development in lung diseases research for individuals at all stages of their professional development.

Acquired Immunodeficiency Syndrome/Tuberculosis SRG

The AIDS/TB SRG oversees a research program that investigates the basic pathogenetic mechanisms involved in HIV-related lung disorders and develops animal and mathematical models to gain information that may lead to new treatment strategies. Many of the studies employ genetic, molecular, and cellular approaches. Additional areas of interest include cardiopulmonary complications of HIV infection in infants, children, and adults; pathobiology of TB and *Pneumocystis carinii* and basic cell biology of pulmonary manifestation of AIDS; lung-

specific drug delivery systems for enhanced TB treatment; behavioral interventions for control of TB; and educational programs to improve training in TB.

Acute Lung Injury/Critical Care SRG

The Acute Lung Injury/Critical Care SRG oversees research on the etiology and molecular and cellular pathogenesis of acute respiratory distress syndrome (ARDS). It supports an ARDS clinical network to evaluate therapeutic strategies such as pulmonary artery catheterization, fluid management, and use of antiinflammatory agents, including corticosteroids, in patients with the disorder and those at risk. Studies to improve the diagnosis, treatment, and outcome of critically ill patients with lung injury also are supported.

Developmental Biology and Pediatrics SRG

The Developmental Biology and Pediatrics SRG oversees research on normal lung development and on factors that may contribute to its abnormal development such as prenatal and postnatal infections and reactive inflammation. Additional areas of emphasis include understanding the regulation of lung alveoli development in order to design new treatments for lung diseases, creating a molecular profile of bronchopulmonary dysplasia to advance understanding of the condition and lead to effective clinical intervention, evaluating the safety and efficacy of nitric oxide in preventing and treating chronic lung disease in newborn infants, and evaluating the efficacy of nasal continuous positive airway pressure compared with conventional ventilation, with and without surfactant, in the management of premature newborns. Issues at the core of lung developmental biology also are relevant to therapeutic interventions using cell-based therapies.

Immunology/Fibrosis SRG

The Immunology/Fibrosis SRG oversees research on interstitial lung diseases, such as sarcoidosis, idiopathic pulmonary fibrosis (IPF), and lymphangioleiomyomatosis (LAM), which are characterized by chronic inflammation and progressive fibrosis of the lung alveolar walls and surrounding tissue. Specific projects focus on elucidating the cellular and molecular mechanisms of lung inflammation and fibrosis; identifying potential targets and agents for IPF therapy; identifying genetic factors that influence sarcoidosis in blacks and genes that increase susceptibility to pulmonary fibrosis; translating basic research findings into clinical applications for LAM; and improving allograft function after lung transplantation.

Lung Cell and Vascular Biology SRG

The Lung Cell and Vascular Biology SRG oversees research on the molecular and cellular biology of epithelial and endothelial cells of the alveoli and the lung surfactant system. Additional areas of interest encompass studies on regulation of the pulmonary vasculature, including cell growth and signaling; cellular and molecular mechanisms of primary pulmonary hypertension; identification of genes related to lung function; and development of new methods to deliver drugs via lung epithelial cells.

Division of Blood Diseases and Resources

The DBDR plans and directs a coordinated research program on the causes and prevention of blood diseases and disorders. Areas of interest encompass a broad spectrum of research from

stem cell biology to medical management of blood diseases, with a focus on nonmalignant and premalignant processes. The Division also has a major responsibility to improve the adequacy and safety of the Nation's blood supply. It has recently taken a leading role in developing cell-based therapies, combining the expertise of transfusion medicine and stem cell technology with the exploration of repair and regeneration of human tissues and biological systems.

The Division is organized into two major programs:

- Blood Diseases Program
- Blood Resources Program.

Blood Diseases Program

The Blood Diseases Program supports research and training in nonmalignant disorders, including anemias, SCD, and thalassemia; premalignant processes such as myelodysplasia and myeloproliferative disorders; hemophilia and other abnormalities of hemostasis and thrombosis; and immune dysfunction. It comprises the two SRGs described below and a Research Training Group that manages training and career development in blood diseases research for individuals at all stages of their professional development.

Hemoglobinopathies and Genetics SRG

The Hemoglobinopathies and Genetics SRG oversees a comprehensive program focusing on reducing morbidity and mortality caused by disorders of the hematopoietic system and preventing their occurrence. Diseases include SCD, thalassemia, Fanconi anemia, and Diamond Blackfan anemia.

Research in SCD and thalassemia ranges from elucidating their etiology and pathophysiology to improving disease treatment and management. Areas of emphasis include genetics, regulation of hemoglobin synthesis, iron chelation, development of drugs to increase fetal hemoglobin production, and gene therapy. Developing animal models for preclinical studies is another area of interest. Clinical studies in SCD are investigating stroke prevention and the long-term effects of hydroxyurea therapy. A Phase III clinical trial is determining whether hydroxyurea is effective in preventing chronic end organ damage in children with SCD.

The SRG oversees a program of Comprehensive Sickle Cell Centers, which collectively form a SCD clinical research network—and which individually conduct basic and clinical research—and provide state-of-the-art patient care, educational activities for patients and health professionals, community outreach, and genetic counseling services.

A thalassemia clinical network is evaluating new treatment strategies and ensuring that research findings on optimal management of the disease are rapidly disseminated to practitioners and health care professionals.

Thrombosis and Hemostasis SRG

The Thrombosis and Hemostasis SRG oversees a comprehensive program of basic research, clinical studies, and technology development in hemostasis, thrombosis, and endothelial cell biology, with a focus on understanding the pathogenesis of both arterial and venous thrombosis

in order to improve the diagnosis, prevention, and treatment of thrombosis in heart attack, stroke, and peripheral vascular diseases. A major goal is to find additional platelet inhibitors, anticoagulants, and fibrinolytic agents that will improve specificity and reduce side effects when used in treatment of thrombotic and thromboembolic disorders. SCORs support collaborative studies on hemostatic and thrombotic disorders.

Finding an effective treatment for hemophilia is another priority. Bleeding disorders associated with defects in coagulation proteins or abnormal platelet function, such as the immune thrombocytopenias, also are being studied. Other emerging areas being supported are gene transfer, clinical proteomics, inflammation and thrombosis, coagulation activation, autoimmune disease, and thrombotic complications of obesity, diabetes, and cancer.

Blood Resources Program

Transfusion Medicine Cell Therapies SRG

The Blood Resources Program, through its Transfusion Medicine Cell Therapies SRG, plans and directs research and training in transfusion medicine, stem cell biology and disease, and clinical cellular medicine. Areas of interest in transfusion medicine include transmission of disease through transfusion, development of methods to detect and inactivate viruses in donated blood, improvement of blood donor screening procedures, and emerging diseases that may be transmitted by blood transfusions. Also supported are basic and clinical investigations related to transfusion immunobiology, focusing on graft versus host disease, graft versus leukemia effect, and dendritic cell therapies.

The SRG oversees research on hematopoiesis, stem cell biology and diseases, and cellular therapies. Determining the factors that cause stem cells to start and stop dividing, move throughout the body, and lodge in a specific place, and understanding the fundamentals of stem cell biology that will lead to cell-based therapies are areas of major focus.

The Program also supports two clinical research networks to promote efficient comparison of innovative treatment strategies—one for patients undergoing blood or marrow transplantation and the other for patients with hemostatic disorders, such as idiopathic thrombocytopenia and thrombotic thrombocytopenic purpura. SCORs support collaborative studies on hematopoietic stem cell biology and transfusion biology and medicine.

Division of Epidemiology and Clinical Applications

The DECA supports clinical research on the causes, prevention, and treatment of cardiovascular, lung, and blood diseases. It oversees a broad array of epidemiological studies, including field studies, genetic epidemiology, and clinical epidemiology; clinical trials on prevention and treatment of disease, particularly chronic CVD; demonstration and education research; and basic and applied behavioral studies. Research often focuses on defined populations (e.g., minorities, occupational groups, school children, and health professionals) and community settings. For planning and evaluation purposes, the Division provides statistics on cardiovascular, lung, and blood diseases from national data and cohort studies.

The Division is organized into two major research programs:

- Clinical Applications and Prevention Program
- Epidemiology and Biometry Program

and an Office of Biostatistics Research. Research training and career development opportunities are included within each program.

Clinical Applications and Prevention Program

The Clinical Applications and Prevention Program supports research on the effects of specific clinical and behavioral interventions for preventing and treating heart and vascular disease. Research includes efficacy studies to determine whether specific interventions improve disease outcomes under rigorously controlled and ideal circumstances, effectiveness studies to determine whether specific interventions result in positive outcomes in more applied settings, and translational studies that test interventions to improve the delivery of proven approaches in clinical or public health settings. The Program comprises the three SRGs described below.

Behavioral Medicine and Prevention SRG

The Behavioral Medicine and Prevention SRG oversees research that examines psychological, social, cultural, lifestyle, and other behavioral factors that influence disease etiology, pathophysiology, prevention, and treatment. Included are studies that investigate basic behavioral principles related to health; relationships between psychosocial and lifestyle factors and CVD risk; effects of psychosocial factors in prevention, treatment, and rehabilitation; efficacy and effectiveness of behavioral, psychosocial, or lifestyle interventions to reduce disease risk and to lower risk factors; effects of health-promotion interventions in community settings; and methods to disseminate effective lifestyle programs to communities. Key topics include stress, depression, social support, adherence, quality of life, diet, physical activity, and obesity.

Clinical Trials SRG

The Clinical Trials SRG oversees multicenter, randomized trials to evaluate new therapies for CVD and to study disease mechanisms for future interventions. Areas of emphasis include heart failure, coronary artery disease, sudden cardiac death, and supraventricular arrhythmias, particularly atrial fibrillation.

Clinical Prevention and Translation SRG

The Clinical Prevention and Translation SRG oversees research to determine the efficacy of interventions for CVD prevention, particularly those that would be delivered in outpatient clinical settings. Included are studies that examine pharmacologic treatments of known or suspected CVD risk factors for primary prevention and lifestyle interventions for primary and secondary prevention. Additional studies investigate effective methods for disseminating and implementing preventive or treatment interventions consistent with evidence-based guidelines as an integral part of routine medical care.

Epidemiology and Biometry Program

The Epidemiology and Biometry Program supports research and research training in epidemiological studies of heart and vascular, lung, and blood diseases in defined populations.

Research includes examining trends and population patterns in prevalence, incidence, morbidity and mortality from the diseases; risk factors for disease development and progression; genetic and environmental influences and their interactions in the development of subclinical and clinical heart, lung, and blood diseases; and design and analysis of long-term observational studies. The Program is organized into three SRGs and two Research Units.

Analytical Resources SRG

The Analytical Resources SRG conducts research on biometric and epidemiologic methods and their application to studies involving the incidence of and mortality from cardiovascular, lung, and blood diseases. Using family, longitudinal, and demographic information and vital statistics, it studies the natural history, etiology, and epidemiology of cardiovascular, lung, and blood diseases. Other activities include providing the Program and the Institute with statistical and epidemiological consultation, including national trends in cardiovascular, lung, and blood diseases; advising the Program, the Institute, and outside investigators on design and analysis of large prospective epidemiological studies; and compiling, cataloging, maintaining, and distributing data sets and files from epidemiological studies.

Field Studies and Clinical Epidemiology SRG

The Field Studies and Clinical Epidemiology SRG conducts multicenter cohort studies on the development and progression of CVD and their risk factors in various segments of the U.S. population. It convenes working groups to determine critical new research areas, proposes epidemiological research with appropriate study designs, initiates epidemiological studies, manages large and complex field studies, evaluates study proficiency and productivity, and collaborates on scientific research. The SRG advises the Program and other Divisions on clinical epidemiology, measurements of subclinical CVD, and management of complex and large, field-based epidemiology studies.

Genetic Epidemiology SRG

The Genetic Epidemiology SRG conducts research studies on twins, sibiling pairs, and families to determine genetic and environmental contributors to heart, lung, and blood diseases and to characterize gene–gene and gene–environment interactions. It advises the Program, the Institute, and outside investigators on the design and analysis of epidemiological studies associated with genetically characterized individuals, and promotes the collection, storage, and maintenance of blood samples in existing studies to allow genotypic characterization of study cohort members for analyses in relation to phenotypic data.

Framingham Epidemiology Research Unit

The Framingham Epidemiology Research Unit (FERU) oversees research in cardiovascular, lung, and blood diseases in the Framingham Cohort and Offspring Studies. FERU staff are involved in all aspects of protocol development; clinic operations; event review; research training; and development of research hypotheses, analyses, reports, and publications.

Jackson Epidemiology Research Unit

The Jackson Epidemiology Research Unit (JERU) oversees research in cardiovascular, lung, and blood diseases in the Jackson Heart Study. JERU staff members are involved in all aspects of protocol development; clinic operations; event review; research training; and development of research hypotheses, analyses, reports, and publications.

Office of Biostatistics Research

The Office of Biostatistics Research (OBR) provides statistical expertise to the Institute and performs diverse functions in planning, designing, implementing, and analyzing NHLBI-sponsored studies. It has primary responsibility for providing objective, statistically sound, and medically relevant solutions to problems arising in NHLBI-sponsored studies. The OBR is concerned with designing efficient studies and monitoring data from ongoing studies.

The methodological interests of the OBR concern survival analysis, longitudinal data analysis, and efficient study designs, including monitoring ongoing clinical studies for efficacy and safety. Recently the OBR has made contributions to statistical genetics and has extended its expertise to bioinformatics.

National Center on Sleep Disorders Research

The NCSDR plans, directs, and supports basic, clinical, and applied research, health education, training, and prevention research in sleep, chronobiology, and sleep disorders. It oversees developments in its program areas; assesses the national needs for research on causes, diagnosis, treatment, and prevention of sleep disorders and sleepiness; and coordinates sleep research activities across the Federal Government and with professional, voluntary, and private organizations. The Center promotes information sharing and coordinates implementation of interagency programs.

The NHLBI sleep research program seeks to understand the molecular, genetic, and physiological regulation of sleep and the relationship of sleep disorders to CVD. It also supports efforts to understand the relationships of sleep restriction and sleep-disordered breathing to the metabolic syndrome, including obesity, high blood pressure, dyslipidemia, insulin resistance, and vascular inflammation. Ongoing NHLBI-funded research projects include elucidating the etiology and pathogenesis of sleep disorders, particularly sleep apnea; determining the role of sleep apnea in CVD and cerebrovascular disease; examining sleep and sleep disorders in children; and identifying new animal models of sleep disorders.

In 2004, the NCSDR and other Federal and non-Federal cosponsors conducted the first national sleep conference entitled “Frontiers of Knowledge in Sleep and Sleep Disorders: Opportunities for Improving Health and Quality of Life” to focus on sleep and sleep disorders and to determine ways to disseminate relevant information at the community level to improve sleep-related public health. A conference summary, the remarks of Dr. Richard Carmona, U.S. Surgeon General, and other information can be accessed via the NCSDR Web site at www.nhlbi.nih.gov/sleep.

Multidisciplinary research training programs in sleep biology and sleep disorders are being supported to ensure that highly trained scientists are available to address important gaps in the current biomedical and biological understanding of sleep, including those outlined in the 2003 National Sleep Disorders Research Plan. The Sleep Academic Award Program is designed to develop comprehensive curricula on sleep and sleep disorders for enhanced learning by medical students, residents, and practicing physicians, and other health care professionals. The Web site supported by the American Academy for Sleep Medicine (MedSleep) provides direct public access to more than 50 curriculum resources for basic science and clinical educators in the health sciences.

The NCSDR continues to work closely with the NHLBI Office of Prevention, Education, and Control (OPEC) on education pertaining to sleep problems and sleep disorders for physicians, other health care providers, and the general public. A video program, “Sleep Apnea: Is Your Patient at Risk,” was developed for clinicians and hospital staff as part of a continuing medical education series.

Reaching children and adolescents with messages about sleep and sleep disorders is a priority. Educational activities for 2003 included disseminating a new high school supplemental curriculum on the biology of sleep, preparing a manuscript on the etiology, consequences, recognition, and treatment of sleepiness in adolescents by the NCSDR Working Group on Sleepiness in Adolescents/Young Adults, and making additional refinements in the Garfield Star Sleeper Web site.

Women’s Health Initiative

The WHI, which was established by the NIH in 1991, was transferred to the NHLBI on October 1, 1997. Its mission is to address the most common causes of death, disability, and impaired quality of life in postmenopausal women. These include heart disease, breast and colorectal cancer, and osteoporosis.

The WHI is a 15-year project consisting of three major components: a randomized, controlled, clinical trial of promising but unproven approaches to prevention; an observational study to identify predictors of disease; and a study of community approaches to developing healthful behaviors.

The clinical trial and the observational study enrolled more than 161,000 women aged 50 to 79, 18.5 percent of whom are minorities. More than 68,000 women were enrolled in one of three clinical trials for 8.5 years with the goal of assessing the preventive use of hormone therapy, diet modification, and calcium and vitamin D supplements.

Hormone Therapy: Investigate risks and benefits of combined estrogen (conjugated equine estrogen) and progestin (medroxyprogesterone acetate) on CHD, breast cancer, and osteoporosis risk in women with a uterus, and estrogen alone in women without a uterus.

Dietary Modification: Determine whether a diet low in fat but high in fruits, vegetables, and grains can prevent breast and colorectal cancers and heart disease.

Calcium and Vitamin D Supplements: Determine whether two nutrients can prevent fractures and reduce the risk of colorectal cancer.

Women who were ineligible or unwilling to participate in the clinical trial were encouraged to enroll in a concurrent long-term observational study that involves no specific intervention, but is tracking their medical history and health habits for 8.5 years. The study is looking for predictors and biological markers—including genetic markers—for disease.

A key aim of the observation study is to assess the health effect of other forms of hormone therapy that are not studied in the clinical trials. Investigators will compare the data from the clinical trials with the data from the observational study to determine the benefits and risks of various forms of estrogen.

Forty clinical centers have recruited postmenopausal women for the clinical trial and the observational study. Ten of the centers recruited primarily minority populations: blacks, Hispanics, Asian Americans, Pacific Islanders, and American Indians.

Unlike the the clinical trial and observation study components, the Community Prevention Study component of the WHI focuses on community-based strategies to persuade women, especially those of different races, ethnic groups, and socioeconomic strata, to adopt healthful behaviors. Its goal is to conduct prevention research that translates into model intervention programs, which, in turn, can be widely disseminated to communities throughout the United States. Areas of emphasis include reduction of CVD, especially among black women; peer support among minority women; environmental factors and physical activity; osteoporosis prevention, education, and outreach; diabetes care in minority women; methods to enhance physical activity; and a survey of women's attitudes regarding surgical menopause and hormone therapy.

On July 9, 2002, after an average of 5.6 years of follow-up, the NHLBI announced an early end to the estrogen plus progestin trial, which was scheduled to run until 2005, because the risks outweighed the benefits. Specifically, investigators discovered increased risks of invasive breast cancer, heart attacks, strokes, and blood clots in study participants on combined hormone therapy of conjugated equine estrogen and medroxyprogesterone compared with women taking placebo pills. They also found decreases in hip fractures and colon cancer in the treatment group compared with the control group. Although the actual increased risk of breast cancer or CVD for women on long-term estrogen plus progestin was small—less than one-tenth of 1 percent per year—applied to the entire population of women over several years, its potential public health impact could be significant.

In 2003, a memory substudy of the WHI found that older women taking combination hormone therapy had twice the rate of dementia, including Alzheimer's disease, compared with women who did not take the medication. The study also found that the combined therapy did not protect against development of mild cognitive impairment, a form of cognitive decline less severe than dementia.

The study of estrogen-alone hormone therapy among women who have had a hysterectomy was halted at the end of February 2004 because of safety issues. Investigators found that conjugated equine estrogen resulted in no reduction in coronary heart disease (CHD) risk, but increased the risk of stroke in postmenopausal women who had been followed an average of 6.8 years. The study, which was scheduled to run until March 2005, also found that estrogen-alone therapy significantly increased the risk of deep vein thrombosis, had no significant effect on the risk of breast or colorectal cancer, and reduced the risk of hip and other fractures.

The memory substudy of these women, aged 65 to 79 at the beginning of the trial, showed that older women using estrogen-alone hormone therapy could be at a slightly greater risk of developing dementia, including Alzheimer's disease, than women who do not use any menopausal hormone therapy. In addition, scientists found that estrogen alone did not prevent cognitive decline.

Division of Intramural Research

The NHLBI DIR conducts clinical research on normal and pathophysiologic functioning of the heart, lung, blood, and vascular systems, and basic research on normal and abnormal cellular behavior at the molecular level. In FY 2003, the Laboratory Research Program was modified to consolidate some of the research effort. Four Centers—the Genetics and Development Biology Center, the Cell Biology and Physiology Center, the Biochemistry and Biophysics Center, and the Immunology Center—were established, and all Sections were abolished. The new organizational structure of the Program can be found under Division of Intramural Research in Chapter 1, Directory of Personnel.

In FY 2004, the Cardiovascular Intervention Program was established within the Cardiovascular Branch of the Clinical Research Program.

Research foci of the DIR range from structural organic chemistry to cardiology. Major areas of interest include mechanisms of gene regulation, stem cell biology, gene transfer, and gene therapy; molecular basis of lipoprotein dysfunctions and atherogenic process; molecular basis of vascular diseases; molecular basis of diseases of alveolar structures of the lung and design of new therapeutic modalities; cellular and molecular events underlying ischemic heart disease and myocardial hypertrophy; biochemical events associated with aging and certain pathologic processes; molecular, structural, and developmental aspects of muscle and nonmuscle contractile systems; biochemistry and physiology of calcium channels; molecular and cellular processes for conversion of metabolic energy into useful work; molecular basis of transmembrane signaling and signal transduction pathways; pathophysiology of renal function at cellular and molecular levels; biochemistry of trace nutrients; enzyme kinetics, metabolic regulation, and protein chemistry; and cellular and molecular basis of toxicity induced by drugs and other foreign compounds.

Office of Prevention, Education, and Control

The Institute’s OPEC coordinates the translation and dissemination of research findings and scientific consensus to health professionals, patients, and the public, so that information can be adapted for and integrated into health care practice and individual health behavior. NHLBI health education programs and initiatives established through the OPEC address high blood pressure, high blood cholesterol, asthma, early warning signs of heart attack, obesity, sleep disorders, women’s heart health, PAD, and COPD. For reducing high blood pressure, high blood cholesterol, and obesity, two approaches are used: one focuses on individuals at high risk and the other on the general public. Special attention is given to minority populations that are disproportionately affected by disorders within the Institute’s mandate

The four largest education programs have coordinating committees consisting of national medical, public health, and voluntary organizations and other Federal agencies. The committees help to plan, implement, and evaluate the Institute’s professional, patient, and public education programs.

The National High Blood Pressure Education Program (NHBPEP) was initiated in 1972 to reduce death and disability related to high blood pressure. It employs a comprehensive strategy to mobilize, educate, and coordinate groups concerned with hypertension prevention and control.

In 2004, the *Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents* was released. It identifies hypertension and prehypertension as significant health issues in the young due to the marked increase in the prevalence of overweight children. The report recommends lifestyle changes, including weight management, physical activity, and dietary changes for children with high blood pressure and drug therapy if needed.

The National Cholesterol Education Program (NCEP) was initiated in 1985 to educate health professionals and the public about high blood cholesterol as a risk factor for CHD and about the benefits of lowering cholesterol levels to reduce illness and deaths from CHD. Its goal is to reduce the prevalence of elevated blood cholesterol in the United States, and thereby contribute to reducing CHD morbidity and mortality.

An update to the *Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults* (ATP III) was published in 2004. Based on the findings of five major clinical trials of statin therapy conducted since the 2001 release of the ATP III Report, it offers physicians the option to consider more intensive treatment for people identified at high and moderately high risk for a heart attack.

The National Asthma Education and Prevention Proram (NAEPP) was initiated in 1989 to raise awareness of asthma as a serious, chronic disease; to promote more effective management of asthma through professional, patient, and public education; and to provide up-to-date information on asthma care. The Program works with schools, health care professionals, and patients to improve asthma care, prevent disruptions of daily routine, limit hospitalizations, and reduce deaths caused by uncontrolled asthma.

The NAEPP employs a number of outreach strategies. Major emphasis is placed on developing, disseminating, and implementing national guidelines on the diagnosis and management of asthma. In 2004, the NAEPP convened an Expert Panel to update the NHLBI clinical practice guidelines for asthma. The NAEPP also is developing a basic guide on asthma for patients and the public.

The National Heart Attack Alert Program (NHAAP) was initiated in June 1991 to reduce morbidity and mortality from heart attack, including out-of-hospital cardiac arrest, through education of health care providers (e.g., physicians, nurses, and emergency medical services personnel), patients, and the public about the importance of rapid identification and treatment of individuals with heart attack symptoms. In 1997, the Program's scope was broadened to include early identification and treatment of individuals with unstable angina.

In 2004, the NHAAP continued to promote the "Act in Time to Heart Attack Signs," a campaign that creates national and local partnerships to urge physicians, in collaboration with allied health care providers, to educate their patients about heart attack risk, warning signs, and survival. Educational materials for the public and for health care providers are available from the NHLBI Web site.

The NHLBI Obesity Education Initiative (OEI) was launched in January 1991 to inform the public and health professionals about the health risks associated with overweight and obesity. Obesity is not only an independent risk factor for CVD, but also a contributor to high blood pressure and high blood cholesterol and is related to sleep apnea.

The OEI employs a comprehensive strategy to mobilize, educate, and coordinate groups interested in preventing and treating overweight and obesity. One of the major OEI prevention activities is “Hearts N’ Parks,” a national community-based program located in 50 at-risk communities in 11 magnet center States. The program, conducted in collaboration with the National Recreation and Park Association, is designed to reduce the growing trend of obesity and risk of CHD in the United States by encouraging Americans of all ages to seek a healthy weight, follow a heart-healthy eating plan, and engage in regular physical activity while participating in local park and recreation department programs.

In 2004, the OEI convened a strategy development workshop for the NHLBI Healthy Weight Community Outreach Initiative to begin in FY 2005. The national public education outreach initiative will focus on reducing overweight and obesity in children and adolescents.

The NHLBI Women’s Heart Health Education Initiative was begun in 2001 to coordinate research and educational programs related to CVD in women. In 2002, it started *The Heart Truth* campaign to raise awareness of heart disease among women, 40 to 60 years old. A creative element of the campaign is The Red Dress Project, which uses the red dress as a symbol for women and heart disease awareness. In 2003 and 2004, the Institute promoted the symbol in partnership with top fashion designers who contributed to a collection of *Heart Truth* red dresses.

In 2004, the NHLBI directed its attention to raising public awareness about PAD. Together with the newly formed PAD Coalition, it will initiate planning for a 3-year public awareness campaign in FY 2005. The NHLBI also is continuing its collaboration with the Vascular Disease Foundation and other interested organizations to identify short- and long-term goals associated with raising awareness of PAD, educating health care providers and others about PAD, and addressing other vascular diseases.

COPD is another new area of education emphasis for the NHLBI. In 2004, the Institute convened a strategy development workshop to identify awareness and educational activities related to COPD prevention, diagnosis, and treatment that can form the basis of an action plan over the next few years, beginning in FY 2005.

Educational activities associated with von Willebrand disease also were initiated in 2004. The NHLBI convened an expert panel to review current literature on the diagnosis and treatment of von Willebrand disease and to formulate clinical recommendations. The Institute will disseminate the panel’s report to relevant health care providers.

The OPEC also is responsible for coordinating the Institute’s nutrition program. The NHLBI Nutrition Coordinator serves as a major source of nutrition policy and nutrition science knowledge and advises the NHLBI Director on nutrition program policies and priorities. The Coordinator also is the Institute’s representative to other relevant components of the NIH, the Department of Health and Human Services (DHHS), and the Federal Government on nutrition research and policy. Major activities in 2004 include contributing to the revision of the *Dietary Guidelines for Americans* to be released jointly with the DHHS and the USDA in 2005, joining in the DHHS/USDA dialogue on revising the Food Guide Pyramid, and working with the FDA on changes to consumer education efforts around food labels.

The Institute convened a think tank to develop research recommendations on addressing obesity and its effects on chronic diseases. The *Think Tank on Enhancing Obesity Research at the National Heart, Lung, and Blood Institute* was published in 2004. Its recommendations will serve as a guide to the NIH Obesity Research Task Force and the Institute as they develop a strategic plan for enhancing obesity research.

As a key part of its response to the Healthy People 2010 Objectives for the Nation, the NHLBI initiated a new funding mechanism in 2001 to establish CVD educational outreach programs in high-risk communities. The program—Enhanced Dissemination and Utilization Centers (EDUCs)—is a partnership between the NHLBI and local communities to eliminate cardiovascular health disparities and improve the health of underserved populations. Since its inception, two sets of six EDUCs have been awarded that served more than 30 communities in 10 States. In 2004, the first set of EDUCs were completed; the findings and insights from the first and second sets will be used to develop a framework for the next EDUC solicitation.

One EDUC, the Baltimore City Cardiovascular Health Partnership, was started in 2003 to eliminate health disparities and improve the cardiovascular health of public housing residents. Several public housing residents have been trained as community health workers to spread heart health information throughout the public housing community. Encouraging preliminary results from the Partnership have led the Institute to consider developing chronic disease prevention and health promotion activities in public housing nationally. In 2004, the NHLBI convened a planning workshop, the Education Strategy Development Workshop—Public Health in Public Housing: Improving Health, Changing Lives, to share lessons learned from working in the Baltimore public housing community and hear from experts in relevant fields regarding opportunities and needs for addressing chronic diseases in public housing nationally.

The Institute's "Salud para su Corazón" (Health for Your Heart) Initiative, a community-based heart health program for Latinos, has expanded across the United States to include communities along the Texas/Mexico border and along the southern border areas of California and New Mexico. Trained local lay health workers (promotores), applying the values and culture of the communities and mobilizing partners, teach people how to reduce their risk of developing CVD. As advocates for change, they have increased the number of Latinos in their communities who are engaging in heart healthy behaviors.

The NHLBI and the Indian Health Service (IHS) have worked together since 2000 to bring heart health to American Indian and Alaska Native (AI/AN) communities. Initial steps were focused on identifying the unique needs and issues that affect tribal communities. The NHLBI developed a training manual, *Honoring the Gift of Heart Health*, for community instructors to enable them to provide a culturally appropriate 10-session course on heart health. In 2003, a national training workshop was held for key tribal leaders and health practitioners in AI/AN communities across the United States. As a result, trainers will be available to conduct future training sessions. In 2004, a regional skills-building training workshop was conducted to build local tribal capacity and to extend the reach to include other nearby tribes.

The NHLBI's Asian American and Pacific Islander (AAPI) Cardiovascular Health Outreach effort focuses on four underserved groups with high levels of CVD risk factors such as high blood pressure, obesity, and physical inactivity. Individuals of Philippine, Vietnamese, Cambodian, and Native Hawaiian heritage comprise the targeted audience. To date, cardiovascular health educational materials have been developed for those of Filipino and

Vietnamese heritage. A school-based intergenerational cardiovascular health education curriculum to be used to educate Native Hawaiian elementary school children is under way.

International Activities

The Institute is a world leader in research and policy development in heart, lung, and blood diseases, sleep disorders, and blood resources. Through its international programs, the NHLBI contributes to and benefits from the rapidly developing global knowledge base in medicine, science, and technology related to its mission. The Director and senior NHLBI staff serve as consultants to and partners with the Pan American Health Organization (PAHO) and the World Health Organization (WHO).

The Institute's international activities are conducted through multiple mechanisms, including government-to-government and institute-to-institute agreements; joint research projects; joint symposia and workshops; and joint documents, publications, grants, contracts, and fellowships. In addition, the Institute is providing training in its laboratories to international research fellows from approximately 30 countries. Canada, India, Italy, Japan, Korea, Poland, Russia, and Vietnam are among the countries that maintain a collaborative working relationship with the NHLBI. The partnerships extend the benefits of the Institute's prevention and treatment programs to other countries.

The NHLBI contributes to worldwide health plans by working through international organizations in areas within its mandate. In recognition of its leadership and contributions to global and international health, the NHLBI was redesignated as a WHO Collaborating Center for Research and Training in 2004.

At the regional level, the NHLBI is addressing the pandemic of CVD in North, Central, and South America and the Caribbean through support of the Pan American Hypertension Initiative (PAHI), a public/private partnership initiated by the NHLBI and the PAHO in collaboration with seven international scientific organizations—the World Heart Federation, the Inter-American Heart Foundation, the Inter-American Society of Cardiology, the Inter-American Society of Hypertension, the Pan American Network of CARMEN Programs, the Latin American Society of Nephrology and Hypertension, and the World Hypertension League (WHL). The initiative seeks to reduce morbidity and mortality from CVD by controlling hypertension, a major risk factor for the disease, in an estimated 160 million people who already have the condition and by preventing it in millions more at risk because of their unhealthy lifestyles. In 2003, the Institute and PAHO began a 5-year collaboration in CVD prevention and control based on PAHI and the Institute's "Salud para su Corazón" Initiative.

The NHLBI and the Institute of Circulatory and Respiratory Health, Canadian Institutes of Health Research (CIHR), continue their collaborative effort in cardiovascular, pulmonary, and blood diseases research that began in 2003. Three joint programs were implemented in the following areas:

- Clinical Research Consortium To Improve Resuscitation Outcomes
- Cellular and Molecular Imaging of the Cardiovascular, Pulmonary, and Hematopoietic Systems
- Inflammation and Thrombosis.

The NHLBI supports a substantial effort to encourage collaboration and new research endeavors for rare diseases. In the area of blood diseases, the Institute supports a collaborative effort with Ghana to compare the differences in epidemiology and etiology of infections in SCD in Africa with that in the United States. It supports clinical studies in the Cooley's anemia in the United Kingdom and has initiated research into the genetics and basic mechanisms of Diamond-Blackfan anemia and other rare inherited bone marrow failure syndromes with Australia, Canada, and Sweden.

In 2004, a working group of national and international experts in Transfusion Medicine met to develop the NHLBI Strategic Plan on Global Blood Safety. Their task was to identify research areas that would lead to the strengthening of national blood programs and transfusion services in developing countries. Additionally, the working group was requested to provide recommendations to the NHLBI on effective interventions to prevent transmission of HIV/AIDS and other blood-borne infections through blood products.

Understanding malarial anemia is a primary concern in many parts of the world, especially in sub-Sahara Africa, where severe anemia is one of the deadliest complications in children infected with malaria. The Institute is supporting research in Kenya to identify the pathogenesis of severe malarial anemia in children who live in an area that is endemic for malaria.

All of these activities strengthen the Institute's international partnerships and coalitions and extend the benefits of the Institute's national prevention and treatment programs to other countries.