Program Plan for the Barbara Davis Center at Fitzsimons Phase 3

September 17, 2003

University of Colorado Health Sciences Center
# Table of Contents

**I. Preface and Summary** ................................................................. 1

**II. Program Information** ........................................................................... 2
   A. Program Plan Purpose ................................................................. 2
   B. History, Role, and Mission ......................................................... 3
   C. Program Needs and Trends ......................................................... 5
   D. Relation to Academic or Institutional Strategic Plans ................. 16
   E. Relation to Other Programs or Agencies ....................................... 17
   F. Existing Programmatic/Operational Deficiencies ......................... 18
   G. Program Alternatives ............................................................... 18

**III. Facility Needs** .................................................................................. 19
   A. Total Program Space Requirements ............................................ 19
   B. Unique or Special Features ......................................................... 19
   C. Health, Life Safety and Code Requirements ............................... 20
   D. Site Requirements ................................................................. 22
   E. Equipment Requirements ......................................................... 25
   F. Acquisition of Real Property ..................................................... 26

**IV. Project Description** ........................................................................ 26
   A. General Project Description ...................................................... 26
   B. Phase 3 Project Scope ............................................................... 31
   C. Project Cost Estimate ............................................................... 35
   D. Life-Cycle Estimate ................................................................. 36
   E. Financial Analysis ................................................................. 36
   F. Project Schedule ................................................................. 37

**V. Relation to Master Plan/Other Projects** .............................................. 37

**VI. Facilities Alternatives** ....................................................................... 38

**VII. Appendices**
   A. Summary of Research Grant Activity for Phase 3 Programs
   B. Listing of Researchers to Utilize Phase 3 Space
   C. Barbara Davis Center Research Publications - 6/02 - 7/03
   D. CCHE Approvals for Barbara Davis Center, Phase 1 and Phase 2
   E. Third Party Review
I. Preface and Summary

A. Executive Summary

The Barbara Davis Center project involves the construction of a new 108,515 gross square foot (gsf) facility at Fitzsimons. This $32.8 million facility project is being completed in three project phases with the project completion anticipated for June 2005.

The $16.7 million, Phase 1 development involves the construction of 53,715 square feet of which 33,385 gsf will be finished on the first, fourth, and partial basement levels to house the research division research programs of the Barbara Davis Center. The remaining 20,330 gsf of space is being constructed as unfinished space during Phase 1. The design phase for the Barbara Davis Center at Fitzsimons - Phase 1 project was initiated in June 2002. The project design team is led by Anderson Mason Dale Architects of Denver, Colorado.

The Phase 2 project involves the fit-out/finishing of the 20,330 gsf of space on the first floor for the clinical program and clinical research division of the Center. The Phase 2 project cost for this project component is estimated to total $2.195 million. The Phase 2 project scope was revised in November 2002 to include the construction of two additional floors (54,800 gsf) of shelled research and related building support space. When completed the new four-story facility will total approximately 108,500 gross square feet. The Board of Regents approved the revised program plan for the Phase 2 project on November 14, 2002. Approval of the Phase 2 program by the Colorado Commission on Higher Education was granted on February 7, 2003. The Phase 2 project construction schedule is being coordinated with the Phase 1 development schedule with the completion of the entire 108,500 square foot building anticipated for June 2005.

The Phase 3 project, the purpose of this program plan, includes the finish of the remaining 46,800 gsf located on floors 2 and 3 of the new facility. This finished space will house the Autoimmunity and Immunotherapeutic Center program of the Barbara Davis Center. Floor 2 consists of approximately 22,600 gsf (14,690 asf) of unfinished/shell space and will house clinical research programs. The research program space on this floor will include dry laboratory offices, equipment and procedure rooms, investigator and staff support offices for research faculty in Preventive Medicine, Immunotherapeutics, Epidemiology Diabetes, Genetics, and Computational Biology components of the Autoimmunity Center.

Floor 3 consists of approximately 24,200 gsf (16,120 asf) of unfinished/shell space. The third floor laboratory space will be designed similar to the wet bench laboratory space located on the fourth floor. The research laboratory plan includes open laboratory modules, laboratory alcoves, support and equipment rooms, and researcher offices. A specialized GMP core laboratory facility is also planned for this floor. The wet research laboratories and laboratory support space will house faculty researchers in Clinical Immunology, Rheumatoid Arthritis, Pulmonary Immunology, Celiac Disease Research, and Transplantation Immunobiology research program components of the Autoimmunity Center.
The project cost for the completion of Phase 3 totals $6,442,374. The program plan for Phase 3 will be submitted for approval to the University of Colorado Board of Regents in September 2003. Project design will commence in July 2004, upon approval by the CCHE. It is anticipated that the complete structure can be available for occupancy approximately June 2005. The Phase 3 fit-out of the shell space within the Barbara Davis facility will coincide with the construction schedule of Phases 1 and 2.

B. Program Planning Process

The program plan was completed under the direction of the Barbara Davis Center Oversight Committee. This Committee is comprised of the Center’s Executive Director, Clinical and Research Division Directors, Center faculty, Barbara Davis Foundation representatives, and staff from the UCHSC Facilities Projects, Institutional Planning, and School of Medicine Dean’s Offices.

The program plan analysis was completed in two stages. The first programming stage involved an internal review of the Barbara Davis Center research and financial projections required for the future NIH/NCRR construction grant development and submission. The second programming stage evaluated the program and tentative space needs of related School of Medicine research programs resulting in the identification of programs to be included in the Phase 3 project scope. The resulting components include the School of Medicine’s Department of Preventive Medicine, and Divisions of Clinical Immunology and Rheumatology. Additionally, the major planning assumption for the Phase 1 and 2 projects were also reviewed by the Oversight Committee.

Upon completion of the campus review process, the Phase 3 program plan will be presented to the University of Colorado Board of Regents and the Colorado Commission on Higher Education for appropriate reviews and approvals.

II. Program Information

A. Program Plan Purpose

The primary purpose of this facility program plan is to seek appropriate approvals from the University of Colorado Board of Regents and the Colorado Commission on Higher Education (CCHE) to:

Permit the University of Colorado Health Sciences Center to proceed with the fit-out/finish of 46,800 gross square feet located on floors two and three of the new Barbara Davis Center at Fitzsimons. This space will be utilized to house basic science and clinical research program components of the Autoimmunity Center of the Barbara Davis Center and related research programs of the School of Medicine. The total project budget is $6.442 million. Project revenue sources will be exempt cash funds comprised of internal cash and federal construction grant funds. No state funds are being requested for this project.

The Phase 3 project involves the finish of floors two and three of the new Barbara Davis Center facility (46,800 gsf). The construction of this shell/unfinished space was a scope component of Phase 2 program plan revision approved by the Board of Regents in November 2002 and the
Colorado Commission on Higher Education in February 2003. The finished space will house existing basic science and clinical research programs with research projects directly related to the Barbara Davis Center’s research mission. These program elements, devoted to research in type 1 diabetes, transplantation immunobiology, clinical immunology, preventive medicine, and rheumatology, will be organized as the Autoimmunity and Immunotherapeutic Center of the Barbara Davis Center. A summary diagram illustrating program adjacencies in the new building is provided below.

The project cost for the completion of the Phase 3 project totals $6.442 million. The space will be finished as cash funding becomes available. Funding sources include tentative NIH (NCRR) federal grant construction funds and departmental cash funds. The Phase 3 project design will commence in July 2004, upon approval by the CCHE. It is anticipated that the entire building will be available for occupancy in June 2005.

B. History, Role and Mission of the Barbara Davis Center

The Barbara Davis Center for Childhood Diabetes, as an integral clinical and research component of the University of Colorado Health Sciences Center, has initiated its relocation to the new Fitzsimons campus, with philanthropic support from the Davis Foundation (Children’s Diabetes Foundation), and additional campus funding.
The Barbara Davis Center for Childhood Diabetes is the largest diabetes and endocrine care program in the Colorado community. The Center is managed as an administrative unit of the University of Colorado’s School of Medicine and is currently located within a 35,000 square foot building on the University of Colorado Health Sciences Center campus at Ninth Avenue and Colorado Boulevard in Denver, Colorado. This Center facility opened in 1980 and was expanded in 1983, 1986, and 1994. The Center’s independent budget, major fund-raising events and endowments provide unique facilities and resources for clinicians, clinical researchers and basic biomedical scientists working to help patients with Type I diabetes. The Barbara Davis Center provides state-of-the-art clinical diabetes care to a majority of children and many adults within the Rocky Mountain Region as well as receiving national and international referrals. In May 1980, 450 patients were seen at the Center, now more than 4,000 are seen and followed annually.

Current plans for Fitzsimons will create a four-story building of approximately 108,515 gsf, with the fourth floor (wet laboratory diabetes research) and the first floor (clinical diabetes care and clinical research) to replace the current Barbara Davis Center for Childhood Diabetes on the 9th Ave and Colorado Blvd. campus. The remaining space, the second and third floors in current plans, is shelled space that is designated as research space for basic science and clinical research programs of the Barbara Davis Center. The creation of shelled space at the time of initial construction of the building is cost effective, in contrast to building additions at a later date. Completion of the shelled space is partially contingent upon federal construction grant funding, which is currently being sought. This funding will allow the programmatic integration of wet and dry laboratory research space for the programs of Transplantation Immunobiology, Clinical Immunology, Rheumatology and Childhood Diabetes Autoimmunity Research into the Autoimmunity Center and Immunotherapeutic Center within the Barbara Davis Center for Childhood Diabetes. This integrated Autoimmunity and Immunotherapeutic Center will be one of the first in the nation with collaborative programs into disease pathogenesis, prediction and prevention. The organizational structure for the Autoimmunity Center within the Barbara Davis Center is summarized in the following figure.

**Autoimmunity and Immunotherapeutics Center of the Barbara Davis Center**

![Diagram of the Autoimmunity and Immunotherapeutics Center of the Barbara Davis Center]
The director of the Center, Brian Kotzin will report to the dean of the School of Medicine, Richard Krugman. Dr. Brian Kotzin (Chief of Clinical Immunology Department of Medicine, UCHSC) will be director with co-directors George S. Eisenbarth (Executive Director of the Barbara Davis Center for Childhood Diabetes, Department of Pediatrics, UCHSC) and Michael Holers (Chief of Rheumatology, Department of Medicine, UCHSC). The Executive committee of the Center in addition to the co-directors will include Drs. Gill (head Transplantation Immunobiology), Hutton (Research Division Director, Barbara Davis Center), and Rewers (Clinical Division Director, Barbara Davis Center). An advisory board will be formed of department chairman of the major departments whose faculty will be members of the Center (Pediatrics, Medicine, Preventive Medicine and Biometrics, Immunology).

C. Program Needs and Trends

Background of Individual Major Components

Barbara Davis Center for Childhood Diabetes

In 1976, the Davis family made a commitment to the foundation of a clinic for the treatment of childhood diabetes in Colorado that would rival any existing in the US or the world. Mrs. Davis, along with 3 other Denver women whom had family members afflicted with type 1 diabetes, established the Children’s Diabetes Foundation. This began fund-raising through solicitation of individual donations and charity events, most notably the Carousel of Hope Ball that has been held biannually. Proceeds from the Ball are distributed to the Children’s Diabetes Foundation (CDF), American Diabetes Association and the Juvenile Diabetes Foundation International. Through this mechanism and personal donation by the Davis family, the Barbara Davis Center for Childhood Diabetes (BDC) was built. It opened as an outpatient diabetes clinic in 1980 and extended in 1983 to incorporate a Research Division then headed by Dr. Kevin Lafferty, a prominent immunobiologist with a special interest in type 1 diabetes and transplantation. The clinic has grown from 450 pediatric patients in 1980 to around 3,500 in 2002, which includes the vast majority of children with diabetes in the state of Colorado, and an additional 20% of patients from throughout the United States and the world. A young adult clinic was opened in 1990 to provide continuing care and now follows more than 1500 patients. A second phase of building was completed in 1995 again with funds from the Davis family and the CDF: Recent development includes the creation of an Ophthalmology Clinic in 1996, a Transplant Immunobiology Research program in 1997, a Translational Research Unit in 1998 and an Islet Developmental Biology program in 1999 and human islet transplant program in 2001. It is planned that the Center will move to a new “Davis” building on the Fitzsimons campus in June of 2005, with the Clinic accommodated on the first floor, and Research Division (except for islet transplantation) on the fourth floor.

The Barbara Davis Center, with its emphasis on type 1 diabetes research, and in particular the immunology of type 1 diabetes has had a major impact on the development of this field. Dr. Lafferty the first research director and colleagues were the first to clone pathogenic T cells from islets (e.g. BDC2.5 clone) and prove their ability to transfer disease. Dr. Eisenbarth and coworkers pioneered the prediction of type 1 diabetes and its recognition as an organ specific autoimmune disorder. Dr. Chase and colleagues have been central to the development and implementation of trials for the prevention of diabetes. In particular the Barbara Davis Center and its affiliates contrib-
uted the most patients to the screening for anti-islet autoimmunity of any Center in the nation and entry into trials for the prevention of diabetes of the initial DPT-1 trials, and is a major component of the Trialnet, the North American Cooperative Trials group for the prevention of diabetes. Barbara Davis laboratories serve as the Trialnet’s biochemical autoantibody (GAD65 and ICA512) central laboratory as well as HLA laboratory. Drs. Garg and Chase have contributed to the clinical development of the field of continuous glucose monitoring, with the BDC one of four NIH sites in the country jointly studying this important technology. Dr. Marian Rewers, Clinical Division Director created the NIH DAISY study (Diabetes Autoimmunity in the Young) and this study has now expanded to 3 European sites and 3 U.S. sites with Dr. Rewers co-principal investigator. The DAISY study has screened with parental permission more than 25,000 newborns in Colorado for the HLA alleles associated with diabetes risk, and follows more than 2,000 individuals. The Barbara Davis Center web page (www.barbaradaviscenter.org) gives more detail concerning the Center. Last year, the ISI, evaluated citations in the field of diabetes for the past decade, and the University of Colorado was ranked 8th in the world.

The Center’s budget has grown more than 6-fold in the past decade with a similar dramatic increase in grant funding (more than 80% from NIH). The Center has trained more than 30 postdoctoral fellows/predoctoral students over the past decade and has just competed successfully for NIH and JDF grants (principal investigator Georgeanna Klingensmith) to train academic pediatric endocrinology faculty.

**BDC grant funding in millions of dollars (direct cost)**

**Transplantation Immunobiology**

UCHSC has a proud history in the field of transplantation. The first liver transplant in the world was performed at University hospital. Dr. Strazl, similarly pioneered the introduction of azathioprine therapy that made renal transplantation in non-twins practical. Dr. Lafferty developed techniques for islet transplantation taking advantage of removal of “passenger leukocytes” (in modern terms elimination of costimulation). With Dr. Gill he developed many of the paradigms for transplantation of islets in an autoimmune disease model, the spontaneously diabetic NOD mouse. Dr. Gill from the
Barbara Davis Center with Dr. Brian Freed of Clinical Immunology and Dr. Alex Wiseman of UCHSC renal division successfully competed for a Human Islet Cell Resource Center, one of ten in the nation. They are in the process of creating a human islet cell processing facility. Dr. Gill has been the mentor for two physician K0-8 applicants in the past four years. These K-08 physician scientist recipients trained in pediatric cardiac transplantation and renal transplantation.

Research in the Gill laboratory is focused on three main areas related to both the immunobiology of pancreatic islet transplantation as a treatment for Type I diabetes mellitus and the pathogenesis of this illness. The first area is allograft rejection, specifically the nature of the immune response that leads to rejection of a transplant from a donor of the same species. These studies address the mechanisms by which CD4+ and CD8+ T cells interact with other parts of the immune system, including innate immune cells and cytokines. The aim of these studies is to intervene in this interaction to prevent development of immunity to the transplanted tissues. The second area is xenograft rejection, or the rejection of grafts from donors of a different species. Studies here address the similarities and differences in immunopathogenesis of rejection compared to allograft rejection and are also focused on intervention strategies. The third area is autoimmune pathogenesis, or the mechanisms underlying autoimmune pathology resulting in islet damage. Here the roles of cytokines, complement receptors and activation fragments, innate immunity and T and B cell reactivity are being studied to determine the relative contributions of these systems to the development of Type I diabetes. Dr. Gill collaborates extensively with Dr. Holers on projects funded by the Juvenile Diabetes Foundation related to the roles of complement and complement receptors in diabetes pathogenesis.

**Clinical Immunology**

The Clinical Immunology Section was founded by Dr Henry Klaman a pioneer in studies of the thymus. Dr. Kotzin is now Head of the Division of Allergy and Clinical Immunology within the Department of Medicine at the University of Colorado Health Sciences Center. This division in addition to its research laboratories includes a histocompatibility typing laboratory and bone marrow transplantation program and has been instrumental in the development (Dr. Freed) of the human islet transplantation program. Research funding within the division has grown over the past five years as illustrated below.

The major goal of the Kotzin laboratory is to understand the immunologic and genetic mechanisms that result in autoimmune disease. New Zealand hybrid mice such as (NZB x NZW) F1 mice are considered to be an excellent model of human SLE and lupus nephritis. Studies in the Kotzin laboratory are focused on the genetic contributions to spontaneous disease development in this model. At least 12 loci have been mapped and loci on distal chromosome 1, distal chromosome 4, and mid-chromosome 7 have shown consistent linkage in different backcrosses. Congenic mice are being generated to narrow the chromosomal intervals encompassing the disease-susceptibility genes and additional studies are focusing on the mechanisms by which these genes contribute to disease. Separate studies in the Kotzin laboratory have focused on pathogenic T cells in rheumatoid arthritis (RA) and other human autoimmune diseases. Analyses of T cell receptor repertoire have revealed clonal expansions of particular CD4+ T cells in the synovium of RA patients. These clonal expansions are present in multiple joints of the same individual and persist in the same joint over long periods of time. Sequence analysis has provided additional evidence that sets of related clones have been selectively expanded in the synovium by a common antigen. Current efforts are focused on screening for the synovial antigens recognized by these T cells.
A remarkable series of studies headed by Drs. Fontenot and Kotzin with collaboration with John Kappler at the National Jewish Center, is the evaluation of patients with berylliosis. This is an immune mediated disease where T cells are sensitized to self-peptide plus beryllium can result in severe lung fibrosis, and the disorder progresses even after exposure to beryllium is ended. As recently published in the JCI this disease is telling us much about the localization of T cells causing inflammation with almost 30% of ung lavage T cells reactive with beryllium versus almost undetectable cells in the blood.

Clinical Immunology Research Funding
(Direct Costs)

Division of Rheumatology

The Division of Rheumatology at the University of Colorado Health Sciences Center was under the direction of Dr. William Arend from 1983 until 2000, with the appointment of Dr. Michael Holers as division head at that time. Dr. Arend is probably best known for his discovery of IL-1Ra, the IL-1 antagonist that is now one of our newest approved immunotherapeutics for Rheumatoid Arthritis. Dr. Arend’s current work is directed towards understanding the role in biology of the two intracellular isoforms of IL-1Ra, especially in murine models of inflammatory and autoimmune disease. Dr. Arend has been recognized for his research accomplishments through receiving the ILAR-Novartis prize in Rheumatology Research from the International League of Associations of Rheumatology and the Howley Prize from the Arthritis Foundation. Since 1986, an NIH training grant has been continuously funded with two primary objectives, the training of rheumatology fellows for a career in basic research within academic medicine and the training of Ph.D. postdoctoral scientists.

In 1993 Dr. Holers was recruited to the University of Colorado to be the first Smyth Professor of Rheumatology and Associate Professor of Medicine and Immunology. He was promoted to
Professor of Medicine and Immunology in 1998 and 1999, respectively. Since 1987, Dr. Holers has personally supervised the research training of 17 individuals, including M.D., Ph.D. and M.D./Ph.D. pre- and postdoctoral trainees. He is immediate past Chair of the Committee on Research for the American College of Rheumatology, was a cofounder of the ACR Basic Research Conference in 1998 that now precedes each annual meeting and is now a member of the ACR Board of Directors. He cochaired with Dr. Cambier the Basic Research Conference in 1999 entitled “B-Lymphocytes: Basic Biology and Roles in Autoimmune Disease”. The Committee on Research also oversees the activities of the newly formed Subcommittee on Clinical Research of the ACR, which is charged with improving this area of investigation through the development of novel programs. Dr. Holers is also Director of the Disease Oriented Basic Science track of the Ph.D. in Clinical Sciences Program at the University of Colorado Health Sciences Center and is a member of its Admissions and Executive Committees. Currently three MD fellows within the Division of Rheumatology are actively enrolled in this program and are well along an academic research path. Funding of research for the Division of Rheumatology has grown dramatically over the past five years as illustrated in the following diagram.

**Division Rheumatology Research Funding (direct costs)**

<table>
<thead>
<tr>
<th>Years</th>
<th>Funding (Millions of dollars)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997-98</td>
<td>0.5</td>
</tr>
<tr>
<td>1998-99</td>
<td>1.0</td>
</tr>
<tr>
<td>1999-00</td>
<td>1.5</td>
</tr>
<tr>
<td>2000-01</td>
<td>2.0</td>
</tr>
<tr>
<td>2001-02</td>
<td>2.5</td>
</tr>
<tr>
<td>2002-03</td>
<td>3.0</td>
</tr>
</tbody>
</table>

The focus of Dr. Holers’ laboratory is on the roles of complement receptors and membrane regulatory proteins in the immune response, with a special emphasis on B lymphocyte development and activation. Specific areas of emphasis include the roles of complement receptor type 2 (CR2, CD21) in B lymphocyte development, activation and tolerance. Using both human and mouse CR2 as a model, the Holers laboratory is analyzing the ways by which CR2 regulates B lymphocyte responses to antigens bound by complement. The specific mechanisms by which CR2 and other complement receptors act to modify B lymphocyte responses are incompletely understood, though his laboratory has shown that CR2 deficient mice have a markedly impaired humoral immune responses and that human CR2 transgenic mice can rescue this phenotype. They have also
demonstrated that CR2 ligation results in the rescue of B cells from apoptosis, increases B7-1/B7-2 expression, and alters cell-cell adhesion using a novel signal transduction pathway. His group is also studying the three dimensional structure of the CR2 ligand binding sites using NMR and X-ray crystallographic techniques in collaboration with other university faculty and have recently published the first co-crystal structure for a complement receptor with its ligand. An additional area of research interest is the transcriptional regulation of CR2 as a model of B lymphocyte development. The expression of CR2 on B-lymphocytes occurs as one of the first steps after escape from central tolerance. The Holers laboratory has identified an intronic silencer that controls cell and stage specific expression of CR2 and are further dissecting the mechanisms by which this silencer acts using cell line and transgenic approaches. The Holers laboratory is an analysis of the role of complement during the development of SLE in murine models. In these studies the laboratory is also using complement receptor knockouts and complement inhibitors they have created with recombinant techniques to determine how the alteration of these systems affects self tolerance and target organ damage in autoimmune and inflammatory disorders. Finally, as a key member of the new NIH-funded Center for the Prevention of Autoimmunity at UCHSC, the Holers group is working with members of the BDC and Preventive Medicine program to identify individuals at risk for the development of rheumatoid arthritis using techniques identical to those pioneered in Denver for type 1 diabetes.

**Preventive Medicine and Biometrics Diabetes Studies**

Dr. Richard Hamman, a pioneer in studies of the epidemiology of diabetes and in particular childhood diabetes and a leader in the current SEARCH study is the head of the department of Preventive Medicine and Biometrics, and recruited Dr. Marian Rewers to Denver and his department. Over the past 20 years, there has been an increasing relationship with investigators at the Barbara Davis Center and Preventive Medicine and Biometrics faculty, starting with Georgeanna Klingensmith and Peter Chase in the mid-1980’s with the establishment of the Colorado Type 1 diabetes registry. This was probably the first registry in the United States concerning type 1 diabetes and has helped in our development of our current registry program in the SEARCH study. Multiple projects over the years have been joint, including the SEARCH for Diabetes in Youth project, the Coronary Artery Calcification in Type 1 Diabetes (CACTI) study, the Diabetes Autoimmunity Study in Youth (DAISY) with Marian Rewers and George Eisenbarth, and studies of diabetic complications with William Jackson of the Barbara Davis Center as ophthalmologist. These studies, and those mentioned above, would be further benefited from the close physical location that shared space at Fitzsimons will hopefully allow.

Diabetes/Autoimmunity investigators of Preventive Medicine and Biometrics are enthusiastic about combining research locations, staff and investigators, in the to be completed dry research space on the second floor of the Davis building. These individuals with funded projects include: Jill Norris, PhD, genetics, gene-environment interaction in Type 1, and Type 2 diabetes, including early nutritional factors in the onset of autoimmunity in diabetes and arthritis; Julie Marshall, PhD, nutrition and physical activity as risk factors for type 2 diabetes and obesity, primary community prevention of diabetes, gene-environment interaction in obesity and diabetes; John Hokanson, PhD, genetics of dyslipidemia in diabetes and complications, gene-environment interaction in lipid disorders; Dana Dabelea, MD, PhD, epidemiology of childhood diabetes and complications, early life factors in etiology of diabetes; and Richard Hamman, MD, DrPH, (epidemiology of Type 1, 2 diabetes and...
complications, primary prevention of diabetes and atherosclerosis, community-based prevention programs and clinical trials).

The Investigation of Vitamins in Youth (IVY) (Norris, PI) is funded by NIDDK until 9/2006. This study investigates the relationship between nutritional components of the early diet, with a focus on antioxidants and vitamins, and the presence of beta-cell autoimmunity in children at risk for IDDM. The Study of the Etiology of Rheumatoid Arthritis (SERA) (Holers, Norris Co-PIs) is a project contained with the Autoimmunity Prevention Center (Eisenbarth, PI). The goal of this study is to study the natural history of autoantibodies that occur in relation to rheumatoid arthritis (RA) in individuals at risk for RA.

**Disease Specific Clinical/Research Resources**

Several different autoimmune disorders are important areas of research, both basic and clinical. A brief overview of some specific areas that will emphasized by the Center’s researchers occupying the new Phase 3 space is provided below.

A unique strength of the Barbara Davis Center is more than 8 years of experience in studying the development of autoimmunity from birth, in the DAISY study, which has been extended to studies of celiac disease and recently rheumatoid arthritis as part of our collaborative NIH Autoimmunity Prevention Center. This study has involved screening of more than 25,000 newborn from the general population as well as relatives with a series of autoimmune disorders. Though certain disorders with well-developed programs are highlighted below, we believe the concepts and techniques will be applicable to other autoimmune diseases and will be extended over time.

**Type 1 Diabetes**

For studies of patients with type 1 diabetes a major effort is centered and/or coordinated at the Barbara Davis Center for Childhood Diabetes (BDC), which is one of the largest pediatric diabetes centers in the United States. Physicians at the BDC currently see over 150 new-onset patients per year, and over 4000 patients with type 1 diabetes are followed at the Center. One unique clinical resource related to the BDC involves ongoing studies of newborns from both the general population and relatives of patients with type 1 diabetes who are HLA typed using cord blood and then evaluated prospectively for the development of autoantibodies associated with type 1A diabetes and disease. Dr. Marian Rewers of the BDC and Department of Preventive Medicine and Biometrics directs this study, referred to as the Diabetes Autoimmunity Study of the Young (DAISY). Dr. Rewers has just been appointed the director of the Clinical Division of the Barbara Davis Center. Dr. Peter Chase at the BDC has led the nation in recruiting approximately 1/3 of 50,000 screened relatives and entering 400 relatives into the multi-center diabetes prevention trial–1(DPT-1) study. Investigators at the BDC have completed a large trial of BCG vaccination in new-onset patients with type 1 diabetes and Dr. Peter Gottlieb has been awarded a NIH grant for the evaluation of mycophenolate mofetil for the prevention of further b-cell destruction at the onset of type 1 diabetes. Dr. Peter Gottlieb who has developed clones of DQ8 T cells reacting with the insulin peptide B:9-23, in collaboration with Dr. Kotzin and Dr. Bill, is developing B:9-23 DQ8 tetramers.

Related to the extensive ongoing clinical investigation focusing on the immunology of type 1 diabetes at the Barbara Davis Center, there are unique resources potentially available for collaborative multi-
center studies. For example, Dr. Eisenbarth and collaborators have developed semi-automated assays for specific anti-islet autoantibodies (to insulin, GAD65, ICA512, IA-2, phogrin, etc.). These assays can be applied to large numbers of samples. Currently, Dr. Eisenbarth’s laboratory functions as the core laboratory for determination of GAD65 and ICA512 autoantibodies for the national DPT-1 ancillary study, in which more than 100,000 samples have been processed. Laboratories in Denver also perform large scale HLA typing. For example, Dr. Eisenbarth’s laboratory has performed large scale HLA-DQ typing for the presence of DQA1*0102/DQB1*0602 for the DPT-1 national trial.

The BDC also includes multiple faculty studying the immunopathogenesis of type 1 diabetes. These faculty include Drs. Dale Wegmann, Ronald Gill, Peter Gottlieb, and John Hutton (Research Director of the BDC). All of these faculty have expressed a keen interest in being associated with the proposed center. In particular the Denver group has defined a large series of T cell clones able to transfer diabetes, including clones reacting with insulin, GAD, and the I-A2b (phogrin) molecule. Studies by Drs. Wegmann and Eisenbarth have focused on the B:9-23 peptide of insulin with the recent finding that immunization with this peptide is sufficient to generate anti-insulin autoantibodies in both NOD and normal Balb/c mice. These autoantibodies react with the intact insulin molecule and not the peptide, and with the combination of the peptide and poly-IC normal Balb/C mice can be driven to insulitis. The peptide when administered to NOD mice prevents diabetes, and an altered peptide of B:9-23 has completed a series of phase I trials and is about to enter phase II clinical evaluation. We suspect that the native B:9-23 peptide is an excellent candidate for a protective vaccine, even perhaps in the absence of adjuvant (recent information indicates induction of insulin autoantibodies without adjuvant).

Systemic Lupus Erythematosus and Lupus Nephritis

There currently exists an extensive amount of interest and research in systemic lupus erythematosus, especially lupus nephritis. The most active group involved in clinical research in lupus involves the Divisions of Rheumatology and Clinical Immunology. For example, Drs. Sterling West, William Arend, and Brian Kotzin have recently been involved in a new multi-center trial of high dose chemotherapy/radiation with autologous stem cell transplantation. This study has been coordinated by the University of Washington and Fred Hutchinson Cancer Center in Seattle and human subjects approval is pending at UCHSC. The Division of Rheumatology at UCHSC also has participated in these clinical trials. Dr. Kotzin currently has a GCRC-approved protocol investigating the non-MHC genetic contributions to disease development in patients with lupus nephritis. This study primarily involves the analysis of simplex families and extends susceptibility genes mapped in mouse models to syntenic human chromosomal regions using transmission dysequilibrium testing. Separate continuing studies directed by Sterling West focus on the long-term outcome of patients with central nervous system lupus and include analyses of the value of various diagnostic laboratory testing and neuropsychological testing.

Another strength of the Lupus group relates to the strong investigation involving animal models. It includes studies of the genetic basis of pathogenic autoantibody production and nephritis in New Zealand hybrid mice and other murine models (Dr. Kotzin’s laboratory), studies of T cell specificities and cytokines in murine models (Drs. Kotzin, Kappler, Wysocki), and the role of B cell alterations and complement and complement inhibition in the pathogenesis of lupus nephritis in murine models (Dr. Holers). Finally, over 400 patients are followed in the Rheumatology Clinics at UCHSC including patients brought from the NJMRC lupus clinic by Drs Kotzin and West, the
Rheumatology Clinics at Denver Health Medical Center the Nephrology clinics at UCHSC and Denver Health, and Dermatology Clinics at UCHSC and Denver Health.

**Rheumatoid Arthritis**

The Rheumatoid arthritis group within the Center is also characterized by a strong track record in clinical and basic research. Drs. West and Kotzin in the Divisions of Rheumatology and Clinical Immunology coordinated one of the first controlled trials of methotrexate in the treatment of patients with rheumatoid arthritis. More recently, Dr. West has been participating in multi-center trials examining the efficacy of IL-1Ra, IL10, and TNF inhibitors in the treatment of rheumatoid arthritis. Dr. Kotzin is currently collaborating with investigators at the University of Nebraska studying the use of high dose chemotherapy with autologous stem cell transplantation for patients with severe disease. The rheumatoid arthritis group is also strongly supported by the work of Dr. Michael Schiff at Denver Arthritis Clinic. In the last 5 years, he has enrolled over 500 patients into a variety of multi-center industry-sponsored protocols. These studies have investigated treatment of patients with multiple different nonsteroidal antiinflammatory agents, anti-TNF mAbs, soluble TNF receptor fusion proteins (rhuTNFR.Fc), IL-1Ra, mycophenolate mofetil, FK506, cyclosporine A, leflunimide as well as a number of other agents.

Within the rheumatoid arthritis group at UCHSC and NJC, Drs. Kotzin, Kappler, and Marrack have had a long-standing interest and have collaborated on studies of T cell receptor repertoire in patients. This group was the first to demonstrate oligoclonal T cell expansions in synovium. Recent studies have involved the use of DR4-collagen type II peptide and DR4-gp39 tetramers to examine the specificity of synovial cells in this disease. Another major effort within the Center involves studies in the laboratories of Dr. Arend and Dinarello of inflammatory cytokines in patients and murine models. Dr. Arend’s laboratory was the first to identify the IL-1 receptor antagonist (IL-1Ra) as a major anti-inflammatory molecule in the synovium of patients with rheumatoid arthritis.

Finally, the newest addition to studies of patients with rheumatoid arthritis has been studies pursued as part of the Prevention of Autoimmunity Center in which individuals at risk for the development of this disease are studied for the presence of predictive autoantibodies such as anti-cyclic citrulline peptide (CCP) antibodies. These studies grew out of the DAISY, IVY and other populations studies of type 1 diabetes and are being pursued by Drs. Holers, Norris, Kotzin and Arend under this funding mechanism. These rheumatoid arthritis studies will be pursued in direct proximity to DAISY in the research areas on the second floor of the building.

**Pulmonary Disease**

A separate group of lung diseases fall under the category of granulomatous lung diseases, primarily sarcoidosis and chronic beryllium disease. Dr. Lee Newman at NJC is a world leader in the study of these diseases and is currently Principal Investigator of an NIH funded case-control study to enroll patients for studies of etiology of sarcoidosis (entitled Clinical Centers for Etiology of Sarcoidosis). Overall, the ACCESS study will enroll 720 patients and a similar number of controls with about 1 out of 10 being enrolled in Denver. Drs. Newman and Kotzin have collaborated extensively on studies of the T cell repertoire and T cell specificities of CD4+ T cells accumulating in the lungs of patients with active disease. A related but separate disease occurs after exposure to beryllium usually in the workplace. This induced disease is pathologically identical to sarcoidosis.
and provides a model to study pathogenesis of the idiopathic disease. Since 1985, over 200 patients with chronic beryllium disease, 50 patients sensitized to beryllium, and over 100 controls have been studied, including collection of bronchoalveolar lavage cells. Major collaborative projects between Dr. Newman and T cell immunologists within the Autoimmunity Center, including Dr. Kotzin’s laboratory, focus on the T cell specificities of beryllium-reactive cells within the lung. These studies of granulomatous lung diseases, even if they are not true autoimmune diseases, will provide important insight into the etiology and mechanisms of disease in autoimmunity.

Celiac Disease (Gluten Enteropathy)

In studies at the Barbara Davis Center, 10% of patients with type 1 diabetes were found to express transglutaminase autoantibodies, which are characteristic of celiac disease. The majority of these patients demonstrated no symptoms of bowel disease; however, approximately one half showed evidence of celiac disease in bowel biopsies. Currently, based on these data, all patients at the Barbara Davis Center are screened for celiac disease transglutaminase autoantibodies, and patients being followed prospectively for the development of islet autoimmunity are also being prospectively evaluated for transglutaminase autoantibodies and evidence of celiac disease. A study headed by Dr. Marian Rewers (Preventive Medicine and Biometrics) with gastrointestinal evaluation by Dr. Ed Hoffenberg (Division of Pediatric Gastroenterology) provides prospective data for the detection and natural history of celiac disease. Thus far, more than 25,000 newborns from the general population have been HLA typed at birth from cord blood and more than 600 evaluated for expression of transglutaminase autoantibodies. In initial studies of high risk HLA class II alleles associated with celiac disease, the results suggest that one out of 10 infants with the genotype DQ2/DQ2 have these autoantibodies and initial biopsies indicate a high risk of celiac disease. As part of the above studies, Dr. Eisenbarth’s laboratory has developed a high-throughput semi-automated fluid phase radiossay for human tissue transglutaminase autoantibodies. This assay, using in vitro expressed transglutaminase has demonstrated superior sensitivity and specificity compared to other available assays, and will be available for collaborative clinical trials.

Addison’s and other Autoimmune Endocrine and Polyendocrine Syndromes

The Denver group also includes researchers with a major interest in autoimmune endocrine and polyendocrine syndromes with a focus on the genetic contributions to different clinical subtypes of autoimmune polyendocrine syndrome II. At the Barbara Davis Center for Childhood Diabetes, Dr. Peter Gottlieb and collaborators have been accumulating patient information and material regarding Addison’s disease and other autoimmune endocrine disease patients. In collaboration with the Colorado Society for Endocrinology and Metabolism, they are surveying Colorado endocrinologists regarding their patients with Addison’s disease and related syndromes. In addition, their contact with the National Adrenal Diseases Foundation has led to contact with over 30 families with Addison’s disease throughout the United States. Drs. Spritz, Fain, Gottlieb, and Eisenbarth are analyzing a genome screen of rare families with multiplex Addison’s disease, often with accompanying type 1 diabetes.

Dr. Pamela Fain is another member of the Human Medical Genetics Program with extensive experience and strong interest in autoimmune diseases. She has developed programs in the genetics of type 1 diabetes and associated disorders. She directed a recent project, which resulted in the identification (iddm 17), of a non-MHC locus (in combination with high-risk class II HLA alleles).
strongly linked with genetic susceptibility for type 1 diabetes in a family of Bedouin Arabs. Follow-up studies have narrowed the chromosome 10 interval to less than one centi-Morgan and sequencing of genes within the region is now underway. This linkage analysis is serving as a model in terms of identifying loci and genes contributing to complex autoimmune disorders under the hypothesis that the genetics of autoimmunity will often be heterogeneous between families, but major genes will underlie susceptibility in specific families.

**Other Studies of the Genetics of Autoimmunity**

The Center includes additional research groups investigating the genetic basis of autoimmune disease. For example, Dr. Kotzin’s laboratory has been centrally involved in studies of genetic contributions to disease development in murine models of lupus. In the New Zealand hybrid model, his laboratory group has mapped multiple loci contributing to the production of pathogenic IgG autoantibodies and the development of severe glomerulonephritis. Most of this work has been accomplished in backcross studies. Based on these initial mapping studies, animals congenic for New Zealand black (NZB) or New Zealand white (NZW) chromosomal intervals that encompass the susceptibility allele have been generated. Current studies are attempting to narrow the interval in order to allow positional cloning of the susceptibility gene at each locus. Dr. Kotzin’s group also has a GCRC-based study to extend these mappings in murine models to the human disease. This study involves the analysis of simplex families and extends susceptibility genes mapped in mouse models to syntenic human chromosomal regions using transmission dysequilibrium testing.

**Histocompatibility Laboratory**

The Center will be supported by a high quality Histocompatibility Laboratory, directed by Dr. Brian Freed (Division of Clinical Immunology). The laboratory is based within the Division of Clinical Immunology, and is fully experienced in all aspects of HLA typing using both serological and molecular (sequencing) techniques. This laboratory and Dr. Freed provide important support for several ongoing and proposed studies investigating genetic contributions to various autoimmune diseases and autoimmune disease phenotypes as well as studies investigating the immunopathogenesis of disease.

**Complement Biology**

Dr. Michael Holers’ laboratory has played a major role in studies of complement and autoimmunity. One of his primary areas of focus is on complement receptors. For example, he is actively working using NMR and other structural biology tools to define structure-function aspects of human complement receptor type 2 (CR2/CD21), which is also the receptor for the Epstein-Barr virus. He is defining the transcriptional control elements that regulate CD21 expression. With Dr. Kotzin, he is working to determine how CD21 levels contribute to the regulation of central and peripheral tolerance in the setting of lupus. Using CD21 knockout mice, he is dissecting the specific contributions of CD21 to humoral and cellular immunity. In addition, he is using several novel complement inhibitors created in his laboratory as well as mice deficient in specific complement components to determine the role of complement in tissue injury in inflammatory, autoimmune and ischemic tissues.
D. Relation to Academic or Institutional Strategic Plans

This program plan is consistent with the current institutional master plan and the research, clinical care, education, and community service missions of the University of Colorado Health Sciences Center. The research mission of the University of Colorado Health Sciences Center is to develop new knowledge, which will be applied to the prevention and treatment of human disease and to the improvement of human health. To better serve the people of Colorado and the public good, research discoveries are the scientific basis for improved patient care. This Phase 3 project will support the Barbara Davis Center and the UCHSC research and clinical programs by providing new, state-of-the-art space for research. The new Barbara Davis Center at Fitzsimons will integrate clinical and basic science research to encourage a more effective flow of new discoveries to their application for the benefit of the diabetic patient and the community at large.

Specific UCHSC institutional planning, policies and facility program plans that relate to the Phase 3 project include:

1. Barbara Davis Center at Fitzsimons (Phase 2) Program Plan Revision (November 2002)

The Phase 2 program plan revision was approved by the Board of Regents in November 2002 and by the Colorado Commission on Higher Education in February 2003. The revision to the Phase 2 program plan included the following project and budget modifications: 1) increasing the project scope by approximately +54,800 gross square feet to include the addition of two floors of shelled research space and related building support; and 2) decreasing the project budget for the fit-out/finish of the 20,330 gsf to house the Center’s clinical division programs. The approved total project budget for the Phase 2 project is $9.637 million and is proposed as an entirely cash-funded project.

2. Barbara Davis Center at Fitzsimons (Phase 2) Program Plan (August 2002)

The Phase 2 program plan for the fit-out/finish of 20,330 gsf to house the Center’s clinical division programs was approved by the Board of Regents in August 2002. The approved project budget for the Phase 2 project was $3.395 million and was proposed as an entirely cash-funded project. The Regent Action Item for the Phase 2 program plan included an option to revise the plan to allow for the possible addition of two floors of unfinished (shell) space to the Phase 2 project scope.

3. Barbara Davis Center at Fitzsimons (Phase 1) Program Plan (August 2000)

The Board of Regents approved the program plan for the Phase 1 design and construction of the Barbara Davis Center at Fitzsimons in August 2000. The CCHE approved this program plan in January 2001. The Phase 1 project scope involves the construction of a new 50,902 gross square foot (gsf) facility of which 33,141 gsf (21,542 net assignable square feet (nasf) is to be finished to house the research division of the Barbara Davis Center. The remaining 17,761 gsf/ 11,544 nasf of space to house the clinical programs is be constructed as shelled space during Phase 1 and finished at a future date. During the program plan verification analysis completed in June 2002, in order to relocate all Center programs, the total Phase 1 space requirement was increased to 53,715 square feet.

The University of Colorado Board of Regents approved the annual supplements to the 1998 Institutional Master Plan in September 1999, August 2000 and December 2001, and November 2002. The Colorado Commission on Higher Education approved the Year 2002 Supplements in February 2003. The Barbara Davis Center project is consistent with the UCHSC’s mission as outlined in these Master Plan Supplements. The Health Sciences Center strives to “improve human health” through the advancement of knowledge through research in the health sciences; the education of health professions; and the delivery of both health care and community services. An international reputation for excellence in research, teaching, and clinical care has been achieved by the UCHSC in fulfilling this mission. The UCHSC currently ranks in the top 20 among academic research institutions in the country in terms of extramural funding. During the past 11 years, funding for UCHSC’s sponsored programs has more than tripled - from $89.1 million in FY 1991 to $294.6 million in FY 2002.

E. Relation to Other Programs or Agencies

The Barbara Davis Center for Childhood Diabetes is managed as a distinct administrative unit of the School of Medicine. Its independent budget, fund raising and endowments provide a unique facility and resource for clinicians, clinician researchers and basic biomedical scientists working to help patients with type I diabetes.

The Center is partially funded by two major endowments from the Children’s Diabetes Foundation and the Barbara Davis Center Research Trust. Additionally, all Center faculty are appointed in the School of Medicine in collaboration with appropriate department chairs. The Barbara Davis Center has affiliations with a number of university department and graduate training programs including the Department of Pediatrics, Department of Immunology, Department of Medicine, Department of Cell and Structural Biology, Department of Biochemistry and Molecular Genetics. The great majority of these programs will be housed in the Research Complex 1 directly adjacent to the new Barbara Davis Center building on the Fitzsimons campus and will move to that campus within the same academic year. A listing of the principal investigators who will utilize the new Phase 3 space is provided as an appendix to this document.

The UCHSC campus is home to a number of Centers of Excellence that, along with various program projects, provide a number of core facilities which are accessible to the researchers of the Barbara Davis Center. These include: Biostatistics, Cytogenetics, Fermentation, Transgenics, Protein Microsequencing, Microarray Screening, Radiological Sciences, Monoclonal Antibody production, Tissue Procurement. Shared or available large-scale instrumentation includes NMR, X-ray crystallography and analytical centrifugation. The great majority of these cores will be located on the Fitzsimons campus at the same time.

Major infrastructure support for the Autoimmunity Center and other research program of the Barbara Davis Center is provided by the Diabetes and Endocrine Research Center, which is also housed at the Barbara Davis Center. The DERC provides Pilot and Feasibility project funding to investigators. The other major contribution of the DERC is the funding of core facilities which will complement the activities of the program and greatly enhance the cost-effectiveness of the Center.
The current faculties of the Barbara Davis Center have extensive collaborations with a national/international community of researchers seeking to understand and cure autoimmune disorders and it is envisioned that this will only be enhanced with new facility at Fitzsimons. In particular it is envisioned that the Center will house an fluid phase autoantibody core that will provide high specificity/sensitivity measurements of autoantibodies reacting with a series of autoantigens, and particularly for type 1 diabetes research. In particular Dr. Eisenbarth’s laboratory is the core islet autoantibody facility for the National Institutes of Health Immune Tolerance Network and the Trialnet international Diabetes prevention program. It is planned that this laboratory will be the U.S. autoantibody core facility for the international study of the Environmental Determinants of Type 1 Diabetes (TEDDY) headed by Dr. Marian Rewers. Dr. Gill heads one of ten designated U.S. Human Islet Cell Resource Centers. Dr. Eisenbarth’s laboratory is the HLA class II typing laboratory for Trialnet. Dr. Hutton heads a national program project for islet cell biology.

F. Existing Programmatic/Operational Deficiencies

Both the future of the Barbara Davis Center, the growth of the Center’s and related campus research programs depend upon the availability of new and expanded research space at Fitzsimons. The space made available in the new Barbara Davis Center is necessary to house the research programs of the Barbara Davis Center and the School of Medicine transitioning to the Fitzsimons site. The UCHSC’s Master Plan provides a guide for the expedited and efficient relocation of the research programs from the campus site at Colorado Boulevard and Ninth Avenue to Fitzsimons. In a manner consistent with the direction of the Colorado Commission on Higher Education and the University of Colorado Board of Regents, the Fitzsimons master plan strategy includes the following goals and requirements: 1) to reduce the total cost of the total development by accelerating the transition to the Fitzsimons campus, however possible; 2) to realize the economic impact of the Fitzsimons development sooner; and, 3) to develop an efficient plan to vacate the 9th Avenue campus. As a result, any delay in the construction and finish of the Barbara Davis Center and the other new research facilities at Fitzsimons may result in the continued operation of a split campus and the need to operationally support research programs residing on both campus sites.

Completion of the shelled space is contingent upon cash funding, which is being sought from the NIH/NCRR with matching funds provided by philanthropy, the School of Medicine, and the University of Colorado Health Sciences campus. The total cost of the building is estimated at $32.8 million dollars, but with the two shelled floors to be completed at a cost of approximately $6.4 million. The Phase 3 project, resulting in the completion of the shelled floors, will allow the programmatic integration of wet and dry laboratory research space for the programs of Transplantation Immunobiology, Clinical Immunology, Rheumatology and Childhood Diabetes Autoimmunity Research into a single Autoimmunity Center. Such an integrated Autoimmunity and Immunotherapeutic Center on the Fitzsimons campus will be one of the first in the nation with collaborative programs into disease pathogenesis, prediction and prevention.

G. Program Alternatives

The only possible program alternative to not proceeding with the Phase 3 project is to delay the anticipated relocation of Barbara Davis and related School of Medicine research program components to Fitzsimons. This option may result in the continued separation of programs - a concept
inconsistent with a major program plan assumption of having related programs efficiently relocated to Fitzsimons facility by the end of Phase 3 construction.

III. Facility Needs

A. Total Program Space Requirements

There are no existing CCHE guidelines directly applicable to the space requirements of the proposed facility. The space requirements have been developed based upon the program requirements of the basic science and clinical research activities to be carried out in those spaces.

The 108,500 gsf building on the Fitzsimons UCHSC campus is envisioned to accommodate the Barbara Davis Center for Childhood Diabetes that is moving from the current campus at 9th and Colorado. The first and second floors will be ‘dry’ and the third and fourth floors will house ‘wet’ bench laboratory research. The first and fourth floors are being completed (Phases 1 and 2) for existing diabetes clinical and research programs of the Barbara Davis Center and include the pediatric, young adult, and ophthalmology clinics and clinical research space (first floor), and basic research laboratories devoted to developmental biology of islets, characterization of islet antigens, endocrine research, and a subset of diabetes related autoimmunity research (fourth floor).

The Autoimmunity and Immunotherapeutic Center will house integrated programs of faculty from the Divisions of Clinical Immunology and Rheumatology of the Department of Medicine, Transplant Immunobiology Program (including Human Islet Transplantation Research Program), and the Diabetes Clinical Research Translational Research Unit. The Phase 3 project involves the finish of a total of 46,800 gsf (30,810 asf) of space on floors two and three in the new Barbara Davis facility to house these programs.

The space on floor two (22,600 gsf / 14,690 asf) will include dry laboratory offices, procedure rooms, investigator and staff support offices for Preventive Medicine, Immunotherapeutics, Epidemiology Diabetes, Genetics, Computational Biology programs.

The third floor (24,200 gsf / 16,120 asf) will be designed similar to the wet bench laboratory space located on the fourth floor. The research laboratory plan includes laboratory modules (14 per floor) aligned on either side of a double loaded corridor. The open laboratory areas are connected to lab alcoves and lab support rooms all planned within the module dimensions. The cGMP human islet core facility will also be located on this floor. The wet research laboratories and laboratory support space will house Clinical Immunology, Rheumatoid Arthritis, Pulmonary Immunology, Celiac Disease Research, Transplantation Immunobiology research programs.

Please refer to the Project Description Section of this document for a detailed listing of space requirements to be completed during Phase 3

B. Unique or Special Features of Phase 3

The Barbara Davis Center is a clinical outpatient and research facility. The new research space
should have flexible design plans which respond to the unique aspects of the growing Barbara Davis Center research programs. The new research space needs to be flexible and adaptive to respond to grant-based research and evolving research paradigms. The space plan and design must also be conducive to collaboration and sharing of research by the clinicians and research investigators.

**The cGMP Facility**

A specialized program space component included in the Phase 3 project space is the cGMP human islet isolation facility. The Barbara Davis Center is one of ten national programs participating in the NCRR Islet Cell Resources (ICR) system. The key purpose of the ICR centers is to provide high quality human pancreatic islets to support clinical transplantation programs. Importantly, human islet isolation and purification is a FDA-regulated process and requires a clean room and support areas that meet federal cGMP standards. This involves a dedicated tissue processing room that includes HEPA-filtered air, specific human islet isolation equipment, thorough cleaning and documentation of room conditions, and barrier separation from animal research. The air quality is of utmost importance and involves a committed HVAC supply. In addition, this processing area must be supported by additional laboratory space for the storing and preparation of isolation and quality control reagents and record keeping. This laboratory space is essential for FDA-required analysis of isolated islet tissue morphology and function. This requires laboratory space for sterile tissue culturing, analysis of DNA content, and assessment of islet function by standard glucose-response assays. Finally, this facility requires a cleanup and autoclaving area for the washing and sterilization of reusable supplies and gowing. Combined, clean room tissue processing areas plus support laboratory space require approximately 800 assignable square feet.

**C. Health, Life Safety and Code Requirements**

The UCHSC has the overall jurisdiction for the project and will provide final interpretation on code issues. The campus requires that construction projects conform to the following codes and regulations. Unless otherwise indicated, the latest edition of listed codes and regulations will be used. There are no existing health, life safety or code issues as this is new construction.

The codes, regulations, and guidance documents that govern this project include:

- 1997 Uniform Building Code (UBC);
- 1997 Uniform Mechanical Code;
- 1997 Uniform Plumbing Code;
- 1997 Uniform Fire Code;
- 1997 Uniform Building Code Standards;
- 1997 National Electrical Code (NFPA No. 70);
- 1994 Life Safety Code (NFPA No. 101);
- National Fire Codes (13 Volumes by NFPA);
- American National Standards Institute Standard Safety Code ASME with Interpretations A17.1, A17.3, A17.5, QEI-1 (most recent);
- C.R.S. (Colorado Revised Statutes) Volume 3B – Title 9, Article 2 – Safety Glazing Materials;
- 1991 Americans with Disabilities Act;
The life safety design of Barbara Davis Center follows the UBC Code interpretation and direction of the UCHSC code official. This is as documented and agreed to in both the Statement of Criteria (SOC) and the Basis of Design (BOD) for the Barbara Davis Center project.

A building code study was performed as part of the Phase 1 and 2 project design. Based on review of the 1997 UBC, the project is a Type II F.R., “B” Occupancy structure, fully sprinklered. Since the building contains laboratory occupancies, specific control areas and laboratory occupancy 1-hour separations are required. The future Class 10,000 / 100,000 clean room (the cGMP facility) is planned for this phase of construction. The design plans for floors 2 and 3 will include stairways, egress corridors, 1-hour separations and toilet room facilities based on the code review.

**Laboratory Safety Issues**

The configuration of the open laboratories requires specialized safety and egress considerations, all of which were considered during Phase 2 project design and will be reexamined during the Phase 3 project design process. The safety issues pertinent to the open labs are listed below:

**Radioactive Materials**
- Entrance to the lab area from the public corridor will be controlled by card access
- Materials used on bench top must be secured in locked cabinets or under constant surveillance by the individual using it
- Materials that have the potential to release hazardous vapors or aerosols must be handled in alcoves or support areas
- Iodinations must take place only in specifically constructed iodination suites
- Access to a spill will be restricted during cleanup to prevent widespread contamination

**Chemical Waste**
- Adequate locking cabinets or containers will be required at the point of waste generation
- Chemical waste will not be moved from the point of generation to another storage area
• Adequate, safe secure storage in alcoves or support areas will be provided for volatiles
• Spills will be compartmentalized by smoke control doors to assure safe egress

Infectious Agents
• Operation of an entire open lab space at Biosafety Level 2, will require tight procedures to control potential exposures between laboratory modules
• The use of select agents or controlled substances will require procedural controls and means to lock up these materials in the lab
• Operations generating hazardous aerosols must take place in the alcoves or support areas.

Fire Safety
• Storage of flammable liquids in the open lab will be limited, with biosafety cabinets provided in support areas to facilitate safe storage of these materials
• Smoke detectors, sprinklers, and smoke control doors will facilitate compartmentalization of fire areas

Waste Management
• Radioactive and chemical waste will be collected at the labs and transported by electric vehicles to the central waste processing facility

D. Site Requirements

*Not applicable to this Phase 3 project scope.*

The discussion of site requirements of the new Barbara Davis Center at Fitzsimons was included in the Phase 1 and 2 program plan documentation. A site map showing the location of this facility is included in the Appendix.

The building is situated at the heart of the Fitzsimons campus in the foreground of the historic Building 500 structure. The new building capitalizes on its relationship to the Ursula Green. The position of the facility on the Green provides a very public and identifiable east facade, a visible reinforcement of the importance of the program within to the campus as a whole. With the “playhouse” structure (playroom for children) and outdoor public court area facing Ursula, the new building seeks to reinforce the nature of the children’s care within and provide a welcome and inviting space.

A number of site planning parameters informed the building’s location and massing. The campus master plan has designated zones for development of facilities by predominating use. The facility is sited in the research zone immediately adjacent to the Research Complex 1 facility. The Anschutz Center for Advanced Medicine, Cancer Center, and Eye Institute are located in the adjacent clinical zone to the south. The infrastructure development necessary to support the new facility has been completed.

The UCHSC physical master plan defines the goals for the design of the site circulation, building placement, scale, massing and materials. It also reinforces the organization of open space and
building edges, serving to reinforce the campus community and character. The concept of “buildings in a park” is of particular importance to this project given its strategic location on the “campus green” at Ursula Drive at the heart of the campus. The future additions of the 17th Place Esplanade to the north of the site and 17th Avenue bordering the south of the site will provide major campus pedestrian and vehicular routes adjacent to the new facility. Along with establishing the building’s footprint and orientation, the landscape, parking and site circulation concepts were developed in the concept design phase.

The major vehicular circulation entry point is from 17th Avenue, coinciding with the east entry point for the new RC-1 facility. A separate, gated security entryway will serve the Barbara Davis facility patient group parking needs with +/- 26 parking spaces for their use. Overflow parking is planned opposite the RC-1 parking area to the west, as the combined lot has space available for these additional spots. Fire lane access is provided with north / south access routes for both facilities planned through the lot. The loading dock is positioned directly opposite the RC-1 dock, providing access for 30’-0” vehicles. A number of dedicated service vehicle spots are located adjacent to the loading dock. This area is to be screened with landscaping and/or site screen walls. The north and south ends of the site are planned for pedestrian pathways and landscaping. The prominent landscape feature of the site is in a “Garden Plaza” area on the east side of the building. This area serves as a forecourt to the most visible side of the building, connecting the interior clinic public lobby / waiting area to the Ursula Green.

E. Equipment Requirements

The estimated project cost of $6.443 million includes fixed and moveable equipment and furnishings. The specialized research equipment for the GMP and core laboratories is not included in the project budget. Equipment requirements and related design issues are noted below.

Research Laboratory Casework and Accessory Equipment

Laboratory casework in the third floor open laboratory areas will consist of a flexible modular steel system that provides the capability to relocate, add or remove all casework units below the bench top surface. In addition, the height of all benches and shelving in the open laboratory area will be adjustable. Casework in the core support laboratories and adjoining fume hood alcoves will be fixed modular steel. All tall casework will be designed to be relocatable without modification. Molded epoxy resin work surfaces will be provided in all laboratory and laboratory support spaces. Steel corrosive and solvent storage cabinets will be located in the fume hood alcove spaces for safe storage of hazardous material. Adjustable reagent and wall shelving in the core support laboratories and fume hood alcove spaces will be constructed of hardwood plywood with high-pressure plastic laminate material applied to all surfaces. PVC safety edge will be provided at all reagent-shelving locations. Heavy-duty utility type adjustable shelving will be located in storage and support spaces. Stainless steel drying racks are provided at all sink locations. Heavy-duty cylinder racks and straps are located at selected laboratory locations requiring cylinder gases. A laboratory glassware washer and dryer will be provided on the third floor. One floor mounted single door gravity type sterilizer with loading cart will be provided.

Laboratory Fume Hoods and Cabinets

All constant volume/bypass fume hoods will be provided in the fume hood alcoves with a frameless vertical rising sash constructed of safety glass. Fume hood liners will be acid resistant polyresin.
Work surfaces will consist of 1" thick molded epoxy resin with a raised edge at a single cup sink (size to be confirmed). Fume hood services will be controlled from the exterior vertical sidebars. Local hood alarms with remote alarm connection will be installed with each fume hood.

**Deionized Water System**

Laboratory reagent grade Type III water (with minimum 1.0 megohm/cm resistivity at all bench top outlets) will be provided from a central recirculating system. Where a higher quality of water is required, end-polishing units will be provided. Deionized water piping will be natural unpigmented polypropylene with socket fusion joints.

**Special Laboratory Gases**

There are no requirements for any centrally piped specialty gas services on either the second or third floors. All gas requirements will be handled by local cylinders within each laboratory as necessary with manifolds and piping provided by the mechanical contractor. A laboratory compressed air system and compressor for the third floor wet bench laboratory space is not required.

**Laboratory Vacuum System**

Laboratory vacuum will be served from a central vacuum pump system. The vacuum pump will be a duplex system with one pump able to handle the required demand with the other pump on standby. The vacuum piping distribution system includes valved and capped points of connection for the future tenant finish spaces on floor three.

**Emergency Fixtures**

Emergency showers will have a floor drain. Emergency eyewash units not located at sink will have a connection to the drainage system.

**F. Acquisition of Real Property**

*Not applicable to this Phase 3 project.*

All property pertaining to the Barbara Davis Center facility development is already University of Colorado (State of Colorado) property. There is no need for the acquisition of additional lands, buildings, or properties for this project.

**IV. Project Description**

**A. General Project Description**

The Barbara Davis Center project involves the construction of a four-story, research and clinical building consisting of 108,515 gross square feet. The $32.8 million facility project is being completed in three project phases with the project completion anticipated for June 2005.

The $16.7 million, Phase 1 development involves the construction of a new 53,715 gross square foot (gsf) facility, of which 33,385 gsf is being finished on floors 1 and 4 to house the research division research programs of the Barbara Davis Center. The design phase for the Barbara Davis...
Center at Fitzsimons - Phase 1 project was initiated in June 2002. The project design team is led by Anderson Mason Dale Architects of Denver, Colorado.

The Phase 2 project involves the fit-out/finishing of the 20,330 gsf of space on floor 1 for the clinical program and clinical research division of the Center. The Phase 2 project cost for this project component is estimated to total $2.195 million. The Phase 2 project scope was revised in November 2002 to include the construction of two additional floors (54,800 gsf) of shelled research and related building support space. When completed the new four-story facility will total approximately 108,500 gross square feet. The project cost for the construction of the additional two floors is estimated to total $7,443,072. The Board of Regents approved the revised program plan for the Phase 2 project on November 14, 2002. Approval of the Phase 2 program by the Colorado Commission on Higher Education was granted on February 7, 2003. The Phase 2 project construction schedule is being coordinated with the Phase 1 development schedule with the completion of the entire 108,500 square foot building anticipated for June 2005.

The Phase 3 project includes the finish of a total of 46,800 gsf located on floors 2 and 3 of the new facility. Floor 2 consists of approximately 22,600 gsf (14,690 asf) of unfinished/shell space and will be finished to support clinical research programs. The research program space on this floor includes dry laboratory offices, equipment and procedure rooms, investigator and staff support offices for Preventive Medicine, Immunotherapeutics, Epidemiology Diabetes, Genetics, Computational Biology.

Floor 3 consists of approximately 24,200 gsf (16,120 asf) of unfinished/shell space. The third floor laboratory space will be designed similar to the wet bench laboratory located on the fourth floor. The research laboratory plan includes 14 open laboratory modules, laboratory alcoves, support and equipment rooms, and researcher offices. A specialized GMP core laboratory facility is also planned for this floor.

The project cost for the completion of Phase 3 totals $6,442,374 million. The program plan for Phase 3 will be submitted for approval to the University of Colorado Board of Regents in September 2003. Project design will commence in July 2004, upon approval by the CCHE. It is anticipated that the complete structure can be available for occupancy approximately June 2005.

**Building Plan Layout**

A summary of the floor space plan for the new Barbara Davis Center facility at Fitzsimons is provided below.

The first level pedestrian circulation begins with a major building entry point and 2-story lobby leading from the parking area to the west. A secondary public entryway is positioned on the east, leading from an automobile drop-off from Ursula Drive. An additional entry point is located at the southeast corner, providing access from another automobile drop-off, from 17th Avenue, allowing a separate entrance to the Eye Clinic. A service entry is located at the southwest corner at the loading dock. These entryways reinforce the connections to the internal program areas. The clinical program will be located on the first floor level, dry clinical laboratory research programs will be located on the first and second floor levels, and the wet research laboratories will be on the third and fourth floor level. The partial basement will include lab support functions and a small mechanical area and is
accessed from stairways and an adjacent service elevator. A service elevator will also connect to the upper floors and the enclosed rooftop penthouse that houses the majority of the building’s mechanical equipment. A second passenger elevator is adjacent to the main entry at the northwest, and serves the four floors.

Vertical stairway circulation is accommodated by two stairways, located at the northwest and southeast corners of the building. The northwest stair extends from the first level to the roof and the southeast stair serves the basement through fourth floors. A second egress stair from the first level to the basement is located adjacent to the loading dock.

**Basement**

3,715 gsf (2,415 asf)
Partial basement – includes cold room, freezer archives, storage room, animal holding room and mechanical area.

**First Floor Level**

25,800 gsf (16,770 asf)
Clinics: Pediatrics, Young Adult, and Eye Clinic
Clinical Research: Translational Clinical DM Research and Islet Tx Research

The first floor space is being designed and completed as part of the Phase 2 Barbara Davis project. The clinical program space includes examination rooms, consultation rooms, teaching rooms, procedure and equipment rooms, storage areas, clinical laboratories, records storage, patient reception, and faculty and staff offices.

**Second Floor Level (PHASE 3)**

22,600 gsf (14,690 asf)
Clinical Research (Dry): Preventive Medicine, Immunotherapeutics, Epidemiology Diabetes, Genetics, Computational Biology

This floor consists of approximately 14,690 asf of unfinished/shell space. The finish of the entire second floor space will be completed as part of the Phase 3 Barbara Davis Center project. This space will house the clinical research programs listed above. The clinical research program space on this floor includes dry laboratory offices, equipment and procedure rooms that are aligned along two corridors. Investigator and staff support offices will be clustered and aligned at the west end of the floor plan.

**Third Floor Level (PHASE 3)**

24,200 gsf (16,120 asf)
Research Laboratories (Wet) and Laboratory Support: Clinical Immunology, Rheumatoid Arthritis, Pulmonary Immunology, Celiac Disease Research, Transplantation Immunobiology, and cGMP Islet Core

The third floor consists of approximately 24,200 gsf of unfinished/shell space. The third floor laboratory space will be designed similar to the completed laboratory space on the fourth floor. The research laboratory plan for the laboratory floor consists of a series of 14 laboratory modules aligned on either side of a double loaded corridor. The corridor is designed for lab egress only, and not intended for any lab storage or equipment. The open lab areas are connected to lab alcoves and lab support rooms all planned within the module dimensions. The GMP core facility will also be located on this floor. Researcher offices are aligned at the north and south ends of the floor plan.
Fourth Floor Level
24,200 gsf (16,120 asf)
Research Laboratories (Wet) and Laboratory Support: Barbara Davis Research – Islet Developmental Biology, Islet Biochemistry, Islet Auto Ab, Mouse Pathogenesis

The entire fourth floor space is being designed and completed as part of the Phase 1 Barbara Davis project. Similar to the third floor plan, the research laboratory plan for the fourth floor consists of a 14 laboratory modules located on either side of a double loaded corridor. The open laboratory modules are connected to lab alcoves and lab support rooms, including a centralized glasswash and autoclave room. Administrative and faculty offices are located at the north and south ends of the floor plan.

As of this date, the UCHSC has completed the schematic and design development design phases for Phases 1 and 2 of the Barbara Davis Center project including the construction and finish of the basement, first and fourth floor levels, and the core and shell construction of the second and third levels.

Design Objectives for Barbara Davis Center Facility

The primary objective for the new Barbara Davis Center is to facilitate and enable diabetes health care and science. To that end, the new facility provides clinical and basic science research laboratories that meet the programmed requirements with state-of-the-art research facilities.

Major objectives for the design of the building include:

- Functionality
  Facilitate basic science research and clinical research adjacencies.
  Clear and direct relationship among the laboratories, the procedure rooms and the offices.

- Ability to maintain the building
  Design includes materials, concepts and arrangements that facilitate and simplify maintenance.

- Flexibility of the laboratories
  Generic lab design to accommodate various research functions
  Open labs to increase interaction among investigators
  Moveable adjustable tables

- Functional and pleasing work environment
  Windows in the labs for access to natural light and views
  Proximity of office to research laboratories
B. Phase 3 Project Scope

The total project scope includes the completion of 46,800 gsf (30,810 asf) of clinical research and wet laboratory research space. The space to be completed on floor 3 totals approximately 24,200 gsf (16,120 asf). The amount of space to be finished on floor 2 totals approximately 22,600 gsf (14,690 asf).

Third Floor Project Scope

The research program space components to be finished include:

- Laboratory modules ‘wet’ (8,400 asf) which includes
  - 14 laboratory modules (600 asf each)
- Associated laboratory support and office space (7,720 asf) which includes:
  - 28 laboratory alcoves (2,800 asf)
    - 28 alcoves (100 asf each)
  - 5 procedure/equipment rooms (2,000 asf)
    - 2 Type A procedure rooms (200 asf each)
    - 2 Type B procedure room (400 asf each)
    - 1 Type C procedure room (800 asf) – cGMP Islet Core Lab
  - 1 glasswash/autoclave room (400 asf)
  - 16 researcher offices (2,040 asf)
    - 12 Type A offices (120 asf each)
    - 4 Type B office (150 asf each)
  - 1 conference room (250 asf)
  - 1 informatics lab (230 asf)

Total space = 16,120 asf

A tentative floor plan of the third floor space is provided on the following page.

These research laboratory facilities will house the following programs: Clinical Immunology, Rheumatoid Arthritis, Pulmonary Immunology, Celiac Disease, Transplantation Immunobiology

Second Floor Project Scope

Approximately 14,690 asf of clinical research space on the second floor will be finished during Phase 3 to house the following clinical research programs: Preventive Medicine, Immunotherapeutics, Epidemiology Diabetes, Genetics, and Computational Biology.

The tentative clinical research program space components to be finished include:

- Consult/examination rooms (1,600 asf)
  - 16 @ 100 asf each
- Procedure rooms/laboratories (1,800 asf)
- Researcher offices (3,360 asf) (10 @ 180 asf each)
- Staff workstations (2,400 asf) (24 @ 140 asf each)
- Consultation rooms/laboratories (1,600 asf) (4 @ 400 asf each)
- Patient check-in areas/waiting (450 asf) (3 @ 150 asf)
- Storage/support (400 asf)
- Circulation space (3,080 asf)

Total space = 14,690 asf

A tentative space plan of the second floor space is provided on the following page.

An open-laboratory design was selected for the Barbara Davis Center facility to optimize interactions among the laboratories. This design is found in many state-of-the-art laboratories including the new Research Complex 1 at Fitzsimons, Buildings 49 and 50 at the NIH, BRB 1 & 2 at the University of Pennsylvania, and the Ross Research Building at Johns Hopkins University. In this concept there are no walls or other barriers between adjacent laboratories, thereby promoting collaborative experiments and efficient use of space through sharing of fixed equipment/facilities (fume hoods, radioisotope hoods, biohazard waste and storage areas, etc). The open lab space is designed to be generic and universally functional for a variety of space users. The design is adaptable, providing for a highly interactive environment, while preserving the requirements of individual research programs.

The laboratory floor space design for the Barbara Davis Center consists of laboratory modules with movable workstations for up to four technicians per module, movable/adjustable workbenches, a fixed sink/equipment zone, a transverse circulation aisle, and equipment/procedure room alcoves. The 10’ x 10’ alcoves, which are open to the laboratory space on one side only, are designed to accommodate those functions that require a degree of closure and are best carried out somewhat separate from the open lab space. They may be used to house primary freestanding equipment to suit the needs of the specific research, and provide additional flexibility to alter the ratio of laboratory support space to laboratory space as programmatic needs change over time.

The only truly fixed elements in the open lab space are vertical umbilical (service columns) and the sink cabinets. Basic services are located at the umbilical, with a standard distribution provided throughout. Electrical power is also distributed in a wire way located beneath the adjustable shelves and immediately above the tables.

The third floor laboratory space will be designed with alcoves for equipment storage, microscopy, tissue culture, or fume hoods. The fume hood alcoves will contain one 5-foot chemical fume hood provided by the project, well as hazardous storage cabinets for flammables, acids, dry waste chemicals, and radioactive materials. Tissue culture alcoves are equipped with recirculating biosafety cabinets.
Procedure rooms are totally enclosed lab spaces. They are nominally 10 by 20 feet, but vary in size depending upon program and core laboratory requirements. Procedure rooms are intended to be used for those functions requiring special isolation and/or containment, such as tissue culture. Generally, each procedure room is provided with one sink cabinet, one movable table, and adjustable shelving and brackets on one wall. Electrical raceways are located on each of the long walls.

The office portion of the laboratory floor is separated from the lab and lab support areas. Access to the office areas is possible via passenger elevator or fire stairs at either end of the floor. Movement from the publicly accessible office corridors to the labs and lab support spaces is controlled. The office area on each typical floor contains private office, open administrative areas, and a conference room.

C. Project Cost Estimate

The capital construction budget for the Phase 3 space completion is $6,442,374. The sources of these costs are professional estimating resources as well as recent experiences with actual construction costs of the University of Colorado Health Sciences Center with projects under construction on the Fitzsimons campus. The project is a cash project without contribution of state capital funds and will be funded by federal grant, and cash funds. The estimated project cost is detailed in the following table.

Capital Construction Budget
Barbara Davis Center - Phase 3

<table>
<thead>
<tr>
<th>Category</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Land Acquisition:</td>
<td>$0</td>
</tr>
<tr>
<td>Land Purchase Cost</td>
<td>$0</td>
</tr>
<tr>
<td>B. Professional Services:</td>
<td>$506,000</td>
</tr>
<tr>
<td>Site Surveys, Investigative Reports</td>
<td>$0</td>
</tr>
<tr>
<td>Architectural/Engineering/Basic Services</td>
<td>$388,000</td>
</tr>
<tr>
<td>Code Review/Inspection</td>
<td>$23,000</td>
</tr>
<tr>
<td>Construction Management</td>
<td>$95,000</td>
</tr>
<tr>
<td>Total Professional Services</td>
<td>$506,000</td>
</tr>
<tr>
<td>C. Construction:</td>
<td>$5,184,741</td>
</tr>
<tr>
<td>Infrastructure</td>
<td>$0</td>
</tr>
<tr>
<td>(a) Services/Utilities</td>
<td>$0</td>
</tr>
<tr>
<td>(b) Site Improvements</td>
<td>$0</td>
</tr>
<tr>
<td>New Construction (Finish 46,800 gsf)</td>
<td>$5,184,741</td>
</tr>
<tr>
<td>Total Construction Costs</td>
<td>$5,184,741</td>
</tr>
<tr>
<td>D. Equipment and Furnishings:</td>
<td>$354,948</td>
</tr>
<tr>
<td>Equipment and Furnishings</td>
<td>$329,948</td>
</tr>
<tr>
<td>Communications</td>
<td>$25,000</td>
</tr>
<tr>
<td>Total Equipment &amp; Furnishings Costs</td>
<td>$354,948</td>
</tr>
<tr>
<td>E. Miscellaneous:</td>
<td>$0</td>
</tr>
<tr>
<td>Art in Public Places</td>
<td>$0</td>
</tr>
</tbody>
</table>
Relocation $0
Total Miscellaneous Costs $0

F. Project Contingency
Project Contingency 5% $396,685
Total Contingency $396,685

Total Project Budget $6,442,374

Source of Funds
Cash Funded Exempt (CFE) $6,442,374

Cost Effects of Project Delay

Construction and equipment purchasing costs can increase at rates from 0% to 10% per annum. In recent years, costs increases have often been in the range of 3% to 5%. Any delay in commencing this project would probably result in increased costs of this magnitude.

D. Life-Cycle Estimate

Life cycle costs were not a determining factor as to how the Phase 3 project was developed. Space needs and programmatic services are significant drivers behind the actual scope. An analysis for the new Barbara Davis Center was included in the Phase 1 program plan and is omitted in this planning document.

The following are estimated expenses for the 46,800 gsf of space to be completed during the Phase 3 project.

<table>
<thead>
<tr>
<th>Expense</th>
<th>Cost (annually)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Building Maintenance</td>
<td>$83,772</td>
</tr>
<tr>
<td>Grounds</td>
<td>$10,296</td>
</tr>
<tr>
<td>Custodial</td>
<td>$31,824</td>
</tr>
<tr>
<td>Utilities</td>
<td>$194,688</td>
</tr>
<tr>
<td>Police/Security</td>
<td>$34,632</td>
</tr>
<tr>
<td>Env. Hlth &amp; Safety</td>
<td>$5,148</td>
</tr>
<tr>
<td>Insurance</td>
<td>$8,892</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>$369,252</strong></td>
</tr>
</tbody>
</table>

E. Financial Analysis

The project cost for the completion of Phase 3 totals $6,442,374 million. Funding sources include NIH/NCRR federal construction funds of $3.22 million (pending grant award) and institutional cash funds totaling $3.22 million. No state funds are being requested for this project.

The UCHSC will submit a federal construction grant application to the NIH/NCRR in November 2003. Notification of the possible award is anticipated for May 2004.
F. Project Schedule

The information below reflects the project implementation schedule for the design and construction of the Barbara Davis Center. The Phase 3 project schedule will coincide with the construction of the Phase 1 and 2 projects with completion of all project phases anticipated for June 2005.

<table>
<thead>
<tr>
<th>Project Activity</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase 1</strong></td>
<td></td>
</tr>
<tr>
<td>Phase 1 Program Plan</td>
<td></td>
</tr>
<tr>
<td>Regent Approval</td>
<td>August 2000</td>
</tr>
<tr>
<td>CCHE Approval</td>
<td>January 2001</td>
</tr>
<tr>
<td>Legislative Authorization</td>
<td>June 2001</td>
</tr>
<tr>
<td>Architect Selection</td>
<td>January 2002</td>
</tr>
<tr>
<td>Plan Verification</td>
<td>March 2002 - May 2002</td>
</tr>
<tr>
<td>Design</td>
<td>June 2002 - October 2003</td>
</tr>
<tr>
<td>Construction Completion</td>
<td>June 2005</td>
</tr>
<tr>
<td><strong>Phase 2</strong></td>
<td></td>
</tr>
<tr>
<td>Phase 2 Program Plan</td>
<td></td>
</tr>
<tr>
<td>Regent Approval</td>
<td>August 2002</td>
</tr>
<tr>
<td>Phase 2 Program Plan Revision</td>
<td></td>
</tr>
<tr>
<td>Regent Approval</td>
<td>November 2002</td>
</tr>
<tr>
<td>CCHE Approval</td>
<td>February 2003</td>
</tr>
<tr>
<td>Legislative Authorization</td>
<td>May 2003</td>
</tr>
<tr>
<td>Design</td>
<td>July 2003 - October 2003</td>
</tr>
<tr>
<td>Construction Completion</td>
<td>June 2005</td>
</tr>
<tr>
<td><strong>Phase 3</strong></td>
<td></td>
</tr>
<tr>
<td>Phase 3 Program Plan</td>
<td></td>
</tr>
<tr>
<td>Regent Approval</td>
<td>September 2003</td>
</tr>
<tr>
<td>Legislative Authorization</td>
<td>May 2004</td>
</tr>
<tr>
<td>Design</td>
<td>July 2004 - October 2004</td>
</tr>
<tr>
<td>Construction Completion</td>
<td>June 2005</td>
</tr>
</tbody>
</table>

V. Relation to Master Plan/Other Projects

The University of Colorado Health Sciences Center’s paramount and time-honored mission of education, research, patient care, and clinical care will continue into the next century. The UCHSC is a unique regional public resource because it generates new knowledge and translates these discoveries to superior health education and human health. In all of its endeavors, the UCHSC will continue to achieve excellence and outstanding accomplishments, which will place the institution in the top tier of academic health centers.

The University of Colorado Health Sciences Center’s Master Plan creates a development guide for the relocation and expansion of the education, research, and clinical care programs from the Denver
campus at Colorado Boulevard and Ninth Avenue to the Fitzsimons campus in Aurora. The new Fitzsimons campus development will allow the UCHSC to reach its goal of becoming a top-tier health sciences institution by accommodating program growth needs through the next century. The Fitzsimons development involves approximately nine million square feet of new program space and associated infrastructure for the Health Sciences Center, University of Colorado Hospital, and affiliate institutions.

The availability of new research space is essential to ensure the current and future success of the research enterprise at the University of Colorado Health Sciences Center. A total of approximately 1.4 million gross square feet of new research facilities is necessary by the year 2008 to adequately transition all research programs from the Denver site to the new Fitzsimons campus. This research space requirement will be accommodated at Fitzsimons by the development of the new research complexes/facilities. This includes the new Barbara Davis Center for Childhood Diabetes.

The Barbara Davis Center is a tremendous asset to the Health Sciences Center and the University of Colorado by functioning as a unique research facility for basic science and clinical researchers working on the prevention, treatment and management of Type 1 diabetes. The construction and completion of the new Barbara Davis Center facility at Fitzsimons is consistent with the research and clinical care missions of the UCHSC as outlined in the Institutional Master Plan.

VI. Facilities Alternatives

When completed in June 2005, the new four-story Barbara Davis Center facility will total approximately 108,500 gross square feet. The project scope was revised to include the construction of the two additional floors of shelled research and related building support space. The Phase 2 program plan revision was approved by the Board of Regents in November 2002 and by the Colorado Commission on Higher Education in February 2003. The design phase for the construction of the shell space is currently in progress.

Other than delaying the building’s completion to result in the possible delay of Barbara Davis Center and other related UCHSC research program relocation to the Fitzsimons campus there are no acceptable alternatives other than to proceed with the Phase 3 project completion.

The delay of this Phase 3 project will result in the need to utilize the existing 9th and Colorado Blvd. to house basic science and clinical research programs of the campus and Center, and the possible lease off-campus space for the clinical research programs. Since the result of these alternatives result in the division of research programs on two sites, and possible additional lease expenses, neither of the alternatives are considered viable.

VII. Appendices

A. Summary of Research Grant Activity for Phase 3 Programs
B. Listing of Researchers to Utilize Phase 3 Space
C. Barbara Davis Center Research Publications - 6/02 - 7/03
D. CCHE Approvals for Barbara Davis Center, Phase 1 and Phase 2
E. Third Party Review
University of Colorado Health Sciences Center

Program Plan for the
Barbara Davis Center at Fitzsimons - Phase 3

September 17, 2003

Appendix

A. Summary of Research Grant Activity for Phase 3 Programs
University of Colorado Health Sciences Center

Program Plan for the
Barbara Davis Center at Fitzsimons - Phase 3

September 17, 2003

Appendix

B. Listing of Researchers to Utilize Phase 3 Space
University of Colorado Health Sciences Center

Program Plan for the
Barbara Davis Center at Fitzsimons - Phase 3

September 17, 2003

Appendix

C. Barbara Davis Center Research Publications - 6/02 - 7/03
University of Colorado Health Sciences Center

Program Plan for the
Barbara Davis Center at Fitzsimons - Phase 3

September 17, 2003

Appendix

D. CCHE Approvals for Barbara Davis Center, Phase 1 and Phase 2
University of Colorado Health Sciences Center

Program Plan for the
Barbara Davis Center at Fitzsimons - Phase 3

September 17, 2003

Appendix

E. Third Party Review
Pending