Research Plan

I. Overall Strategy and Vision
   Introduction

   Specific Aims
   1 page

   Strategy and Vision
   12 pages
I. OVERALL STRATEGY AND VISION INTRODUCTION

A. OVERALL STRATEGIC GOALS (SPECIFIC AIMs)

Funded in 2008, the Colorado Clinical and Translational Sciences Institute (CCTSI) at the University of Colorado Denver (CU-D) has taken impressive steps to transform and improve the research and training enterprise in the Colorado region and to accelerate the translation of discoveries into improved patient care and public health. The CCTSI, as a partnership of CU-D, CU Boulder (CU-B), six hospitals and 30 community organizations, has established new infrastructure and improved existing resources and services for investigators; tripled the number of training and education programs supporting the full lifespan of an investigational career; administratively centralized and expanded the breadth of clinical research capacity and expertise; established system-wide informatics capabilities; promoted team science and encouraged interdisciplinary research through robust pilot grant programs and technology cores; established an extensive community engagement program and enhanced life cycle research; streamlined processes and reduced the regulatory burden for investigators; and created an academic home for clinical & translational scientists and trainees. Despite these successes, there remain many challenges to accelerating the translational research process locally and nationally. This application maps our path forward to meet these challenges. Through 2013 CTSA funding, we will expand our capacities through new programs and a new partner University (Colorado State University), and will institute new policies and procedures to a) improve efficiency and quality of the full spectrum of translational research and b) ensure the cost-effectiveness and safety of the research process. With our partners, CU-D will achieve a new level of measurable performance in training translational team scientists, engaging regional communities as partners in clinical research, collaborating and moving best practices into the national CTSA consortium and accelerating the translation of discoveries into improved health and patient care. We will do this by embracing the following five Overall Strategic Goals:

**Goal 1:** Further enrich and expand our integrated statewide academic home for clinical and translational sciences across the entire translational research spectrum.

**Goal 2:** Institute new Clinical Research Management strategies to strengthen quality, safety, efficiency, cost-effectiveness and innovative team science throughout our research enterprise.

**Goal 3:** Centralize and enhance the delivery of our resources, services and technologies to promote innovation and quality science.

**Goal 4:** Infuse key concepts of community engagement into the full spectrum of translational research.

**Goal 5:** Increase the translational research workforce capacity through a broad curriculum of education and training opportunities.

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**Commonly Used Abbreviations Throughout this Application**

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<thead>
<tr>
<th>AMC</th>
<th>Anschutz Medical Campus</th>
<th>CTR</th>
<th>Clinical and Translational Research</th>
<th>PT-D/I</th>
<th>Practical Trials &amp; Dissemination/Implementation program</th>
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<td>Biostatistics, Epidemiology and Research Design</td>
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<td>Technology Transfer Office</td>
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<td>Network of Translational Technologies</td>
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<td>Novel Methods Pilot Program</td>
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<td>Colorado State University</td>
<td>OGC</td>
<td>Office of Grants and Contracts</td>
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<td>Clinical Trials Office</td>
<td>PACT</td>
<td>Partnership of Academicians and Communities for Translation</td>
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Program Director/Principal Investigator (Last, First, Middle): Sokol, Ronald J.
B. SIGNIFICANCE AND BACKGROUND

B.1. THE CHALLENGE AND OPPORTUNITY OF TRANSLATIONAL RESEARCH AT CU DENVER

One of medicine’s greatest challenges today is the efficient, seamless and safe translation of biomedical research discoveries into clinical applications that improve human health. New methodologies, technologies and integrated information systems offer unprecedented promise for discovery and growth of translational successes; however significant barriers continue to confound our ability to rapidly move discoveries into clinical practice. These barriers are characterized by the scientific and societal complexities of conducting clinical and translational research (CTR) and the ingrained obstacles in our academic enterprise. Moreover, communities and practices may be hesitant to partner with academic researchers due to historic distrust, unaddressed cultural differences, poor access to clinical services, confusing terminology, and limited experience with mutually beneficial, bi-directional, academic-community collaborations.

To address these challenges and accelerate the pace of research and its translation into improved health, the University of Colorado Denver (CU-D) and its partner institutions established the Colorado Clinical and Translational Sciences Institute (CCTSI) in 2008. The CCTSI is today supported by an NIH CTSA grant and substantial institutional support. The mission of the CCTSI over the past 4½ years has been to transform clinical and translational research infrastructure and training at CU-D and our partner institutions. We have established 11 integrated programs that have instilled a new research culture of interdisciplinary collaboration, have improved and expanded our research infrastructure, have broadened “pipeline” training and career development opportunities, have created an academic home for clinical and translational scientists across our partner institutions and have forged new collaborations with industry and with the communities that we serve. Our Tracking & Evaluation Dashboard undergirds a new sense of accountability, allowing us to make rapid, targeted and rational adjustments in deployment of resources.

Despite these successes, challenges remain and there is more to learn. Our state budget woes have led to a 28% reduction in state funding support of CU-D over the past 4 years. The new NIH formula for calculating CTSA budgets for this grant cycle will reduce our CTSA grant size substantially over the next five years. Moreover, the costs of research continue to rise. Because of what we have learned in the first 4 1/2 years, we are ideally positioned to address these budget challenges through re-engineering of our research processes. In the proposed grant cycle, we will maintain our essential and valuable functions (which will be re-evaluated annually), become more efficient in our operations, remove functions that are not contributing to the new mission, institute cost recovery for services (with the exception of junior investigators and trainees), increase our institutional support substantially to help cover budget shortfalls, and further develop philanthropic and industry funding partnerships. As we will demonstrate in this application, CU-D with its six health profession schools, CU Boulder (CU-B), Colorado State University (CSU; a new CCTSI partner), our six affiliated academic hospitals/health care institutions, and over 20 community organizations are committed to work together to advance translational research and train the next generation of investigators.

B.2. VISION AND MISSION OF THE CCTSI

The Vision of the CCTSI is to accelerate and catalyze the translation of innovative science into improved health and patient care. To reach this vision, the Mission of the CCTSI is to further enrich and expand our integrated statewide academic home and research environment for clinical and translational science in order to enhance the quality, efficiency, safety and innovation of research and training across our institutions and communities. In short, our mission is to support, connect and train our CTR investigators. The CCTSI will continue to support the full range of T0.5 through T4 translational research (Fig. 1) in a disease-agnostic manner across the breadth of the life cycle. Through our new partnership with CSU, which is recognized for its world class school of veterinary medicine, we will expand the spectrum of translational research to include what we now term innovative T0.5 research, translating promising pre-clinical discoveries into naturally occurring animal models (companion to domestic animals) of human disease. We see this as an extremely valuable pathway for establishing proof-of-principle prior to exposing humans to the risks of new diagnostics or therapeutics. CCTSI supports biomedical and...
biobehavioral scientific disciplines and researchers in all organ-based and public health specialties, across medicine, nursing, dentistry, pharmaceutical sciences and public health and incorporates the expertise of many colleges and schools at the downtown CU-D campus, CU-B and CSU. This broad spectrum of research performed is demonstrated by the utilization of our clinical research units in 2011 by over 290 investigators in 45 different research groups or specialty areas. The CCTSI values inclusivity and collaboration, thus CCTSI Members will include those pursuing important translational questions in the basic and engineering sciences; laboratory and naturally occurring pre-clinical animal models; pharmaceutical and device development; first-in-human trials; pathophysiology and physiologic human phenotyping studies; large scale and multi-site clinical trials (especially those supported by NIH Institutes/Centers); pragmatic/practical clinical trials; community outreach and engagement and community based participatory research; outcomes, implementation and comparative effectiveness research; and public and global health research.

**Reorganization of CCTSI.** Although the original organizational structure of the CCTSI served us well during its first 4 ½ formative years, to better address the specific goals of the new CTSA FOA TR-12-006, the CCTSI will be re-organized to assure that operational efficiencies better align with the new CCTSI mission. The new CCTSI (Fig. 2) will be based in a Centralized Administrative Core, which will include a new Quality and Process Improvement Center (QPIP), and organized into five Pillar Programs, each with multiple cores and programs: 1) Translational Pilot Program, 2) Enhanced Research Environment 2) Clinical and Translational Resources and Services, 4) Education, Training and Career Development, and 5) Translational Informatics. These Pillar Programs will be centralized at one of the most modern integrated health science facilities in the nation, CU’s Anschutz Medical Campus (AMC). Programs will extend to the campuses of our partner institutions at CU Boulder, Downtown Denver CU-D and our new partner CSU, providing an academic home that encompasses the three largest biomedical research universities in the state of Colorado, all of which have considerable NIH funding and a legacy of collaboration and partnerships. The six academic Hospitals and health care organizations in the state will also be CCTSI partners, as will over 20 state-wide community organizations and practice based research networks (PBRNs). An essential and continuing component of the mission of the CCTSI is to take an active role in the National CTSA Consortium, providing leadership; sharing resources, expertise, experiences and best practices; and, importantly, collaborating with other CTSA institutions to leverage our collective abilities and optimize our funding to advance translational sciences and achieve the five National CTSA Consortium Strategic Goals.

**Clear Metrics of the success of the CCTSI** will be used to gauge performance across our partner institutions, programs, individuals, and communities participating in the CCTSI. Success will be measured in five domains aligned with the CCTSI Strategic Goals: 1) interdisciplinary team science embedded in the institutional culture; 2) reorganized processes that enhance efficiency, quality and safety in the full spectrum of translational research; 3) effective and efficient program management, alignment, operations and cost-recovery; 4) high quality innovation and impactful research that addresses the full translational spectrum; and 5) effective researchers thriving throughout their training, research initiatives, and career pathways. Progress toward achieving these Goals will be carefully monitored through a customized evaluation design administered by an external evaluation team, our Tracking & Evaluation Center (TEC).
B.3. **UNIQUE INSTITUTIONAL STRENGTHS.** The CCTSI will achieve our five Strategic Goals by capitalizing on a set of unique attributes that differentiate the CCTSI program. These attributes include:

1. An extensive CTR Education, Training and Career Development (ETCD) program spanning from high school students through senior faculty. ETCD’s 11 educational programs include the well-established (in 1999) successful Clinical Science PhD and Masters Programs, one of the first such programs in the nation.
2. One of the first Centralized IRB models in the nation (Colorado Multiple Institution Review Board; COMIRB), now being the sole IRB of record for five of our partner institutions with established agreements with 160 entities. COMIRB has also ensured a high level of data security by mandating the use of REDCap or similar databases for data storage in all clinical research protocols.
3. A strong tradition of high impact clinical research supported by a robust network of five Clinical Research Centers continuously funded for >50 years, the busiest among current CTSAAs.
4. Robust Academic-Community partnerships and Practiced-Based Research Networks throughout the state of Colorado in our Partnership of Academicians and Communities for Translation (PACT).
5. An expanding Biomedical Informatics Infrastructure, the direct result of CCTSI initiatives, including a new academic Division and the Center for Biomedical Informatics and Personalized Medicine at CU-D.
6. A unique Naturally Occurring Animal Model Core based at the CSU College of Veterinary Medicine, in which naturally occurring animal models of human disease, sharing similar biology, are utilized to test new diagnostics, imaging technologies and clinical trials of therapeutics before initiating human studies, thus reducing risk for human subjects in early phase development. We have labeled this pre-clinical translational research as phase T0.5. This Core will provide a rich environment for interdisciplinary team science.
7. Longstanding Child and Maternal Health Research Programs nationally recognized for innovation in therapeutics development and prevention of key disorders of childhood.
8. A mature affiliated network of six academic hospitals and health care organizations which have worked collaboratively for decades to establish outstanding health professional training and research programs that bridge across diverse populations. In addition, the newly established UC Health system, a network of four hospitals (including University of Colorado Hospital) which will share a single electronic medical record, creates new opportunities for data sharing, expansion of clinical trials, personalized medicine and outcomes research.
9. The Medicinal Chemistry and Translational Pharmacology program, which opened in 2010, with high throughput/content screening, computer modeling and therapeutics optimization and synthesis capabilities.

B.4. **DEVELOPMENT AND GROWTH OF THE CCTSI**

**Origins of the CCTSI.** CU-D submitted its first CTSA grant application in 2007 receiving NIH funding in 2008. The CCTSI incorporated the previous two NIH-funded GCRC grants and K-30 program plus the integration of other loosely organized infrastructure and educational/training programs, establishing new centralized management and communication strategies that invigorated our scientific enterprise. Major efforts were put forth to centralize and streamline research resources, training programs and administration, build a new innovative and easily accessible operational structure and website portal, make available pilot grant funding that incentivized team science across the translational research spectrum, engage communities, and effectively communicate electronically and personally with stakeholders and constituencies. The CCTSI program included all nine original CTSA Key Functions specified in the 2007 RFA, a Tracking and Evaluation Program and a special Child and Maternal Health Research Program. Building on this platform, we are prepared with 2013 funding to re-engineer the CCTSI organizational structure in ways that will accelerate and streamline the research process to meet new national CTSA goals and achieve new operational efficiencies and revenue sources. Facilitating the CCTSI mission is our new integrated biomedical academic campus, the Anschutz Medical Center (AMC) in which most of our institutions and programs reside.

**The AMC vision.** In 1995 the University of Colorado acquired 227 acres of the then newly closed Fitzsimons Army Hospital Base in the east Denver suburb of Aurora, with the plan to relocate and rebuild the overcrowded CU-D Health Sciences Center campus over the next 30-40 years. In response to unprecedented growth in research funding, and through a variety of public and private funding mechanisms, this rebuild was swiftly completed with relocation accomplished in 2008. The resulting AMC (Fig. 3) has geographically brought together for the first time the three major CU-D teaching hospitals and new educational, administrative and research facilities for all six health science professional schools. Soon to total over 1100 combined inpatient beds at AMC, the University of Colorado Hospital (UCH), Children’s Hospital Colorado (CHCO) and the Denver...
Veteran Affairs Medical Center (DVAMC; to be completed in 2014) are located adjacent to each other (Fig. 3) and within easy walking distance of the education and research facilities. The 6.5 million ft² of new facilities will ultimately attract more than $4 billion in facility-related investments. The AMC is the largest academic health center between Chicago, Texas and the West Coast and the only completely new education, research and patient care facility in the nation today. Available research space will eventually total 3.4 million ft², which is further enhanced by the adjacent 160 acre Colorado Bioscience Park Aurora, in which industry partners and faculty start-up companies are flourishing.

**Growth of Translational Research under the CCTSI.**

During its initial 4½ years, the CCTSI transformation has hastened the productivity, collaboration, and breadth of translational research and training at CU-D and our partner institutions, as demonstrated by the following metrics. Membership of the CCTSI has grown to over 2,700 members (Fig. 4), the number of projects supported by CCTSI resources has increased steadily to 938 in yr 4, the number of investigators using CCTSI resources is over 520 per year (nearly double the number from year 1) and the number of publications that received CCTSI support has grown to 371 in yr 4 (Fig. 4). The annual external NIH grant support of investigators that is facilitated by CCTSI resources has grown to $156 million in yr 4, representing a 10:1 leverage of federal resources. The four Pilot Grant programs have generated substantial subsequent external grant funding with a return on investment of over 11.3:1 for the yr 1 pilot awards (n=43 pilots; Fig. 5). The five Clinical Translational Research Center (CTRC) facilities (our clinical research units) are used for over 25,000 outpatient and 850 inpatient research visits annually, a number that is among the highest achieved by any of the CTSA programs. Our Clinical Sciences Graduate Program (PhD and MS) has grown from 36 students in yr 1 to 85 in yr 5, and we have trained over 1,050 research coordinators and investigators in our clinical trials training core curriculum. Our KL2 graduates have all received subsequent external independent funding. Our Biostatistics Epidemiology and Research Design (BERD) Core has consulted with over 500 investigators.
Over 2,700 researchers now use REDCap in >1400 research projects as their HIPAA compliant secure database or as their survey instrument, fully supported by the CCTSI. Our website portal receives over 5,500 visits and 25,000 page views per month and our newly installed Colorado Profiles searchable database already receives over 4,200 visits per month. Our Community Engagement Program has trained 58 young investigators through the Community Immersion program and 50 community members through the Academic Immersion program, and our seven state-wide PBRNs cover 300 physician practices and one million patients. The CCTSI has facilitated and supported the development, testing and implementation of numerous new diagnostics and therapeutics in the fields of heart disease, cystic fibrosis, cancer, chronic liver and lung disease, diabetes, epilepsy, allergic diseases and autoimmune and inflammatory disorders, to name a few. These selected achievements attest to the broad impact that the CCTSI has had in transforming the infrastructure and culture at CU-D and our partners during its first 4½ years.

**Future Needs and Resources.** In preparation for this grant application, the CCTSI Tracking and Evaluation Core conducted a comprehensive Needs Assessment Survey in spring of 2011 to determine if CCTSI resources and programs were meeting the needs of investigators and trainees. A similar survey conducted in 2005 paved the path for the focus of the first five years of the CCTSI. In the 2011 survey, 639 individuals responded, including members and non-members of the CCTSI at all campuses and hospitals. The survey results indicated the most highly valued CCTSI resources were the translational technology laboratories, research nursing support, educational programs, biomedical informatics and biostatistical support and the availability of subsidized CTRC ancillary and core lab services. Areas for improvement or expansion included streamlining the regulatory processes, improved access to research participant data (e.g. transferring data from the electronic medical record), assistance with recruitment and enrollment of research participants, and assistance in identifying research collaborators and mentors. The CCTSI leadership has plans in place to address each area identified. For example, implementation of the Colorado Profiles searchable database in summer of 2012 provided the means to locate collaborators and mentors, now receiving over 4,200 visits per month. This survey has guided priorities for the CCTSI re-engineering that will be outlined below.

**Budget Challenges and Opportunities.** A critical challenge for the CCTSI will be working with significantly reduced NIH support by the end of the proposed five year grant cycle. Based on the new formula (designated in the RFA) used to determine the CTSA NIH budget for year 5, the CCTSI calculation is 3% x $287,689,324 (total NIH funding for CU-D and our partner institutions in 2011) = $8,630,879 for the year 5 budget, compared to the current CCTSI annual NIH budget of approximately $15.1 million. Thus we are faced with the challenge of a 43% reduction in NIH funding by year 5. To address this potential budget shortfall, all partner Universities and hospitals have significantly stepped up their funding support commitments to a total of over $43.5 million (detailed in Table 2 in subsection E.). Furthermore, the CCTSI will institute charge-backs to investigators for many of our services, generating new program income. Considering these three sources of funding (Fig. 6), we will be able to maintain our year 5 funding close to our current funding (year 0). We believe the remaining difference can be partially made up by new cost-saving efficiencies through our Quality and Process Improvement Program (QPIP). Finally, we are also working with the CU Foundation to garner philanthropic support. We believe that these measures will ensure the sustainability of our programs and services and maintain the critical role of the CCTSI at our institutions.

**C. INNOVATION**

An expressed purpose of the CCTSI re-engineering outlined in this application is to stimulate innovative science and programs, processes and infrastructure that will accelerate T0.5 through T4 translation. With our experience and evaluations, new approaches have been proposed to break down silos separating basic, clinical, translational, and population science disciplines and, importantly, to remove obstacles that have hampered our ability to conduct research built on the best scientific interchange possible in a timely manner. Moreover, the CCTSI leadership is committed to expanding its leadership and partnerships within the National CTSA Consortium, capitalizing on best practices learned from our CCSTI and bringing forth novel ideas to test...
and share within the CTSA collective. The innovative vision and strategies of the CCTSI are emphasized in the Approach section below and demonstrated throughout each Section of this application.

D. APPROACH

D.1. PRELIMINARY DATA: PARTICIPATING INSTITUTIONS

The CCTSI, based on the Anschutz Medical Center (AMC) of CU-D, will be the academic home for clinical and translational investigators and sciences at the 4 largest Colorado public research university campuses (AMC, CU-D Downtown, CU-B, & CSU), 6 academic hospitals and health care organizations, and over 20 community organizations and PBRNs located throughout Colorado (Fig. 3 and 7). The academic institutions and hospitals are located between Downtown Denver and Aurora, with the exception of CU-B (25 minutes away) and CSU (60 minutes away). These Colorado institutions and communities have collaboratively achieved success over the past 35 years in promoting excellence in education and training in all health care professional fields and in cutting-edge research programs. The first 5 years of the CCTSI program transformed and solidified the academic and training relationships among these institutions. With this new CTSA grant application, the CCTSI will now further expand its partnerships to include the 3rd largest research university in Colorado, Colorado State University (CSU) and the new University of Colorado Health System. The following describes each partner institution and its important role in the CCTSI.

D.1.1. CU-D AND PARTNER RESEARCH UNIVERSITIES (summarized in Table 1 and Fig.7)

- UNIVERSITY OF COLORADO DENVER (CU-D) is a comprehensive University within the region’s largest metropolitan area, with a Downtown Denver Campus and the Anschutz Medical Center Campus nine miles east in Aurora, CO. With more than 27,000 students and 100 degree programs in 12 schools and colleges, CU-D awards more than 3,400 degrees each year and more graduate degrees than any other institution in Colorado. The Downtown Denver Campus is the most ethnically diverse college campus in Colorado, providing opportunities for improving minority and underserved population participation in training. AMC, the only Academic Health Center within the state of Colorado, is the central location of the CCTSI and is home to the 6 health profession schools. CU-D research and training grant awards exceeded $430 million in FY 2012 with $179 million received from NIH (Table I). The Chancellor of CU-D and the Deans of each CU Health Profession School have provided Letters of Support.

The AMC is home to the CU School of Medicine (SOM), one of the outstanding public medical schools and research institutions in the United States. SOM houses the NIH-funded CU Comprehensive Cancer Center, a working partner of the CCTSI with many shared resources. Over 60 SOM multi-disciplinary and interdisciplinary research centers, institutes and biotechnology core facilities form the nexus for outstanding basic, translational and clinical research and training, integrated with many of the programs and core services of the CCTSI. The CU College of Nursing (CON) is the premier nursing school in the Rocky Mountain West and is best known as the birthplace of the nurse practitioner, and for research in community outcomes, informatics, and human caring. CON trainees and faculty will have major involvement in the Clinical Science PhD graduate program, informatics and the Community Engagement and Research activities of the CCTSI. The CU Skaggs School of Pharmacy and Pharmaceutical Sciences (SOP) is consistently ranked

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<th>University or School</th>
<th>Location</th>
<th># Faculty</th>
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<td>AMC</td>
<td>3279</td>
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<td>77,315</td>
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**Figure 7. CCTSI Participating Institutions**
among the top pharmacy graduate programs and ranked 5th in NIH funding in 2012. The school has developed a cutting-edge Medicinal and Translational Pharmacology Program, including a molecular modeling facility with computerized macromolecular structure analysis and drug design, high throughput and high content compound screening and medicinal chemistry cores, all of which are supported within the T1 CTR Resources and Services Program of the CCTSI. The CU School of Dentistry (SOD) is the preeminent dental school within the Rocky Mountain West Region. The school pioneers research in oral cancer, Native American oral health, salivary gland disease, neurobiology, pain control and tissue engineering. The Colorado School of Public Health (CSPH) was created in August 2007 as a partnership between CU-D, CSU and University of Northern Colorado. The CSPH plays a major role in the training programs and T3 and T4 translational research programs within the CCTSI, and houses the CCTSI Biostatistics (BERD) Program. CU-D Graduate School offers 21 PhD graduate programs and five Masters programs. PhD degrees may be obtained in multiple basic and clinical science fields (including the Clinical Science PhD program). Within this program is a long-standing highly successful Medical Scientist Training Program (MSTP). The CCTSI pre-doctoral TL1 program funds 8 PhD students each year and encourages the application of basic techniques to study human health and disease processes through novel coursework and interdisciplinary interactions. The CU-D, Downtown Denver Campus is a comprehensive urban university which offers bachelor to doctoral degrees in the full spectrum of liberal arts and professional fields. The School of Education and Human Development houses our Tracking & Evaluation Core and faculty from the School of Engineering and Applied Sciences, and the College of Liberal Arts and Sciences have joined as CCTSI Members.

- UNIVERSITY OF COLORADO AT BOULDER (CU-B) is a premier academic and research University, including 8 schools and colleges and 44 doctoral degree programs. With 5 Nobel Laureates on the faculty, there is a rich history of innovative discovery leading to human applications in fields of biotechnology, medical research, biochemistry, biology, and engineering. Interdisciplinary collaboration between CU-B and CU-D investigators has led to major discoveries in bioengineering, tissue engineering, congestive heart failure, congenital heart disease, the microbiome, pharmaceutical biotechnology, and molecular biology. The new BioFrontiers Institute, directed by Nobel Laureate Thomas Cech, employs a unique interdisciplinary team of scientists with laboratory adjacencies and cutting edge biotechnology. A CCTSI CTRC is located at CU-B. One of the major CCTSI goals will be to expand collaborative interdisciplinary research and training programs between CU-B and CU-D. The VC of Research has provided a letter of support.

- COLORADO STATE UNIVERSITY (CSU) is the newest official partner university in the CCTSI. CSU is a public land grant institution founded in 1870 located in Fort Collins, a midsize city one hour north of Denver. CSU includes 8 colleges, including the renowned College of Veterinary Medicine and Biomedical Sciences. CSU is considered one of the leading research universities in fields such as animal sciences, atmospheric science, infectious diseases, clean energy technologies, and environmental science. Collaborative research and education programs have taken place for decades between CSU faculty and CU-D and CU-B faculty (e.g., over 80 ongoing CSU-CU-D collaborations identified in a survey conducted in Nov. 2012). CSU is a partner in the CU Comprehensive Cancer Center (NCI), the Nutrition and Obesity Research Center (NIDDK), and the CSPH, with major CU-D research collaborations in infectious disease, exercise physiology, HIV/AIDS research, community engagement and research. CSU partnership in the CCTSI will expand the use of natural animal models of human diseases in translational research projects, bridging across CCTSI institutions. The Vice President of Research has provided a letter of support.

**D.1.2. HOSPITAL AND HEALTH CARE ORGANIZATION PARTNERS**

**NOTE:** All researchers at the following hospitals have faculty appointments at CU-D.

University of Colorado Hospital (UCH), located on the AMC, is a private, not-for-profit hospital for adults and is one of the primary teaching hospitals for CU-D. UCH is consistently ranked among the top hospitals in the country by US News and World Report and the University Health System Consortium. The new facilities include a 600 bed hospital, the Anschutz Outpatient Pavilion (550,000 outpatient visits annually), and the Anschutz Cancer Center. UCH is dedicated to research and quality improvement in clinical care. CCTSI CTRCs are located at UCH. John Harney, UCH President, gives his full support to the CCTSI and CTRCs (see letter of support), and has and will continue to commit substantial resources and funds to support the CCTSI.

University of Colorado Health System (UC Health). Created in 2011, this newest and largest health system in Colorado combines UCH with Poudre Valley Hospital Health System (PVH) in Ft. Collins, Medical Center of the Rockies (MCR) in Loveland and Memorial Hospital in Colorado Springs (Fig. 3), totaling 1,500
hospital beds and 1.3 million outpatient visits. Unprecedented opportunities for expanding clinical trials, personalized medicine and community-based research will unfold over coming years as a single electronic medical record (Epic) is being installed in all of the hospitals. The CCTSI will play a major role in developing and integrating clinical research infrastructure, data sharing and training across UCHealth. Bruce Schroeffel, UC Health CEO, has provided a letter of support.

Children's Hospital Colorado (CHCO), one of the preeminent academic pediatric healthcare institutions in the nation, is a private, not-for-profit independent hospital with a strong affiliation with CU-D. CHCO, consistently ranked in the top 10 Children’s Hospitals by US News and World Report, relocated to its brand new 1.4 million ft² facility at AMC in 2007, putting it in close proximity for the first time to the health science schools, UCH, and the CU-D training and research facilities. A new addition to open in 2013 will increase the total inpatient beds to 400. The CHCO CTRC has received substantial support and over 22,000 ft² of rent-free space at CHCO. The CHCO Research Institute works closely with the CCTSI. James Shmerling, President and CEO of CHCO, has pledged his support to the CCTSI, committing to substantial financial, personnel and space support (see letter of support). CHCO funds support two KL2 scholar positions, Child Maternal Health (CMH) pilot grants, the CHCO Core Laboratory and the Bionutrition Core, as well as a waiver for rent.

National Jewish Health (NJH) is known world-wide for ground-breaking basic and translational research and treatment of respiratory, immune, and allergic disorders. NJH is a non-sectarian, not-for-profit academic hospital which has been ranked #1 in respiratory diseases for 15 consecutive years by US News and World Report. NJH is primarily an outpatient facility. NJH and CU-D collaborate extensively on training and research, with shared fellowships, co-investigators on grant applications, and shared core facilities. NJH faculty receive over $33 million in annual federal research funding ($25 million from NIH) in 2012, with approximately $22 million for clinical and translational research. A CCTSI CTRC unit and Core Lab facilities have been housed at NJH for the past 18 years. Building on these, NJH has launched three personalized medicine centers that are integrated with the CCTSI: an Integrated Bioinformation and Specimen Center, an Integrated Center for Genes, Environment and Health, and a Center for Advanced Diagnostics. Michael Salem, MD, President and CEO of NJH, has pledged his ongoing support to the CCTSI (see letter of support).

Denver Health (DH), a premier safety net hospital, provides healthcare for over 25% of all residents in the City of Denver. DH is a comprehensive, integrated health care organization, including a 477 bed hospital, the Denver Public Health Department, an 11-site network of school-based health centers in the Denver Public Schools, correctional care, and a 9-clinic network of family health centers throughout the city of Denver. DH admits over 25,000 patients per year, and administers over 450,000 outpatient visits. DH faculty of the SOM have been international leaders in trauma and surgical research, health outcomes research, community translational research and informatics technology, and HIV prevention and treatment. Arthur Gonzalez, the President and CEO of DH, has committed partnership and support for the CCTSI (see letter of support).

Denver Veteran's Affairs Medical Center (DVAMC) is a training site for CU-D residents in all adult specialties. The DVAMC will relocate in 2014 to a new 182 bed 1.1 million ft² facility on the AMC (Fig. 3), bringing the three major CU-D teaching hospitals to the same campus for the first time. Supported by over $58 million of grant funding, DVAMC conducts major clinical and translational research in cardiovascular epidemiology, gastrointestinal cancer, chronic hepatitis, mental health, neurodegenerative diseases, diabetes, substance abuse and geriatrics. DVAMC faculty hold leadership positions within the CCTSI. Ms. Lynette Roff, Director of DVAMC, has pledged her support and continued CCTSI partnership (see letter of support).

Kaiser Permanente of Colorado, Institute for Health Research, (KP), directed by John Steiner, MD, Professor of Medicine, is the research arm of KP in Colorado, and employs over 120 investigators and staff receiving over $22 million of extramural funding for 160 active projects that focus on advancing preventive health care and personalized lifestyle changes to improve population health, community-based clinical trials, and improving process and health care delivery. KP investigators will play major roles in the community engagement and research, translational informatics, study design and biostatistics, and research training, functions of the CCTSI. Donna Lynne, President of Kaiser Foundation Health Plan of Colorado, has committed support to the CCTSI (See letter of support).

D.1.3. COMMUNITY ORGANIZATIONS AND PARTNERSHIPS. Through the CCTSI Community Engagement & Research (CE&R) program, sustained relationships with over 30 community organizations have been established. The Partnership of Academicians & Communities for Translation (PACT) is the governing body of the CE&R program and is a statewide collaborative of academic researchers, community-based
organizations, PBRNs and healthcare provider networks working together to provide a platform for innovation in CE&R. The PACT is governed by an 18 member Council, meeting quarterly, with equal representation from communities and from the academic institutions. Among the PACT members is the Shared Network of Colorado Ambulatory Practices & Partners (SNOCAP), which includes 7 large PBRNs which cover the state of Colorado and have performed over 80 research studies. PACT organizations cover nearly 300 physician practices, 30 hospitals and one million individuals, representing rural, underserved and minority populations.

D.1.4. RELATIONSHIPS WITH INDUSTRY. Collaborations with partners in the private business community and biotechnology industries are key elements to translating discoveries into new diagnostics and treatments to improve patient care. These interactions are facilitated through our CU Technology Transfer Office (TTO) and our new Office of Corporate Alliances. The TTO provides patent and commercialization support to investigators at CU campuses and serves as a liaison for industry partners seeking to commercialize CU technologies. CCTSI works closely with TTO to identify potential intellectual property of pilot award recipients and other CCTSI supported innovative faculty research, as well as to communicate to CCTSI members the availability of TTO proof of principle grant opportunities for promising diagnostics and therapeutics. The success of TTO and CCTSI efforts is demonstrated by steady growth in patents issued, filed and licensed from AMC investigators since the start of the CCTSI (Fig. 8). To further enhance alliances and partnerships with biotechnology, pharmaceutical, device, and medical information technology companies, the new CU-D Office of Corporate Alliances was established in 2010 and is directed by Laura Simon, MD who came to CUD from industry. This office integrates and facilitates discussions between campus and private organizations (Fig. 9), ensuring that partnering discussions with CU-AMC inventors proceed in a streamlined, comprehensive process with a single point of contact. Dr. Simon will work with CCTSI and CU Denver leadership to establish venture capital funding pathways and other innovative funding and collaboration models to promote commercialization of CU Denver biomedical intellectual property during the 5 year CCTSI grant period.

D.2 RESEARCH STRATEGY

In this application, we will restructure our CCTSI organization, develop a new business model and re-engineer operations to better promote the highest quality research and safety, while achieving maximum efficiencies and cost-effectiveness. We will make every effort to integrate CCTSI programs with other institutional research infrastructure (such as our shared resources with the CU Comprehensive Cancer Center) in order to best utilize precious resources and eliminate wasteful duplication. Moreover, sharing our best practices with the National CTSA Consortium and being actively involved in its functions and initiatives is a high priority of each Strategic Goal. The following briefly describes our new innovative initiatives to achieve our Strategic Goals, with full details provided in the subsequent Sections of this application.

Goal 1: Further enrich and expand our integrated statewide academic home for clinical and translational sciences across the entire translational research spectrum

One of our key Strategic Goals is to further develop the CCTSI as the integrated academic home. In this application, CCTSI will expand its reach to CSU which will become an official CCTSI partner University. The CCTSI will remain inclusive in its Membership policy, reaching out to all investigators and trainees with interest and experience in the entire spectrum of clinical and translational research, through a simple online registration process on our Website Portal. Members will retain allegiance to their home departments, schools and institutions, but can avail themselves of the multiple rich career development and shared science opportunities, programs and mentoring and cross-discipline collaborations offered by the CCTSI. The CCTSI will support and assist with the academic promotion and career advancement of faculty but the major responsibility will continue...
to reside with the faculty member’s home department. The CCTSI has been instrumental in setting the new CU SOM 2012 promotion criteria to recognize leadership of “team science” as a key component of independence and scientific leadership. Dr. Ronald Sokol, CCTSI Director, will work with academic units at CU-D, CU-B and CSU to similarly incorporate team science into their promotion criteria. We will continue to use our expansive Website (http://cctsi.ucdenver.edu), quarterly e-newsletters, Grand Rounds and email announcements to communicate with Members. Further details of the academic home structure and functions are in Section II.

**Goal 2: Institute new Clinical Research Management strategies to strengthen quality, safety, efficiency, cost-effectiveness and innovative team science throughout our research enterprise**

A critical Strategic Goal is to ensure that research performed at CU-D and partner institutions is of the highest quality, that innovative team science is promoted, that we maximize efficiency in our operations and the conduct of clinical trials to lower cost (1), and that the safety of human research participants is the highest priority. With our challenge of a substantial NIH budget reduction over the five year grant period, this goal assumes even greater importance and urgency. We will approach this goal head-on by re-engineering and improving our Clinical Research Management through 6 new initiatives:

1. **We will ensure high quality research by expanding CCTSI scientific review of proposed study protocols beyond those protocols requesting CCTSI resources.** Our CTRC scientific review committee (SARC) will now begin to provide review of all patient-oriented non-peer reviewed research protocols prior to submission for IRB review, campus-wide. We will provide highly trained and certified research personnel at our state-of-the-art clinical research facilities (CTRCs). A new Clinical Trial Management System [CTMS] will be purchased and implemented in concert with the CU Cancer Center in early 2013, integrated with our EMR (Epic) and used by our Enhanced Research Environment program to track progress of each clinical trial (cancer and non-cancer) from planning through initiation through completion. *Details of these initiatives are in Section II.*

2. **Cost control and program income (“charge-backs”) policies and systems will be phased in over years 1-3 to shift more of the cost of research from the CCTSI budget to investigators, intra- and extramural research grants, and other sources of support, while preserving CCTSI support for trainees and junior investigators.** This new business model will utilize a new Core Laboratories Tracking and Management software system that will be purchased in early 2013 (several are currently being reviewed), with its capacity to track requests and utilization, invoice and collect charges and generate reports. (see Goal #3 below).

3. **A principal objective is to simplify and support the process for approving, implementing, enrolling and completing NIH-funded multi-site clinical studies and trials.** Many such clinical trials are currently supported by CCTSI resources and facilities, including NeuroNEXt, and large multi-site studies on type I and II diabetes, HIV/AIDS, nutrition and obesity, women’s health, cystic fibrosis, hemophilia, adult and childhood cancer, maternal-fetal medicine, autoimmune diseases, and childhood liver diseases, to name just a few. We will initiate: a) new Enhanced Research Environment Program’s regulatory support to assist investigators in preparing and completing IRB and budget submissions; b) a commitment to participate in the Central IRB model for multi-site studies; c) new processes to achieve rapid IRB and contracting approval; d) assistance with recruitment and study enrollment by our Recruitment & Enrollment Team; e) rent-free space in the CTRCs; and d) expert research nursing and bionutrition support. *Details are in Section II.*

4. **A new effort to maximize our efficiency and effectiveness of research will be the creation of the CCTSI Quality and Process Improvement Program (QPIP) in year 1 to complement our Tracking and Evaluation Core (T&E Core). David West PhD, a health outcomes and comparative effectiveness investigator at CU-D with vast experience in LEAN system redesign and quality/process improvement, will direct QPIP, which will map and redesign processes to become more efficient and eliminate unnecessary variation in procedures, and reduce cost. *Details about QPIP and T&E Core are in Section II of this application.*

5. **To accelerate innovation and Team Science, a new Incubator Studio Program (ISP) will be initiated in yr 1.** Based on the Vanderbilt Studio Model (2), the ISP will bring together an interdisciplinary panel of 4-5 experts to assist an investigator or team with a specific research question, such as hypothesis generation, study design, research team building, grant review, implementation advice, analysis interpretation, or manuscript review. The goal is to offer multidisciplinary input and develop new collaborations and ensure high quality research at critical times in a research project trajectory. A T1-T2 (Jane Reusch, MD) and a T3-T4 director (John Steiner, MD, MPH) will assemble the studio teams and 90 minute sessions will be held. Ongoing evaluation will assess the program’s value.

6. **Team science will be further promoted and facilitated through our four Pilot Grant Programs, each of which uses development of new collaborations as a major criteria for scoring of the proposals. Complete**
details of this program are in Section II of this application.

**Goal 3: Centralize and enhance the delivery of our resources, services and technologies to promote innovation and quality science.**

We have re-organized our considerable core resources and services into a single CTR Resources and Services (CTR R&S) Pillar Program under one administrative governance structure (see Section III) under the direction of Associate Director Dr. Wendy Kohrt. We believe this restructuring will maximize our ability to provide, manage and track these services to become more efficient over coming years. The philosophy of the CTR R&S is to provide broad access to high quality research support and expertise for disease-agnostic CTR within all of our partner institutions in a cost-effective manner. Our intent is to complement and leverage, but not duplicate, other infrastructure investments at our institutions. For example, we support a number of shared core resources in NeTT that are also supported in part by our NIH-funded CU Comprehensive Cancer Center. We will continue to emphasize as our highest priorities the facilitation of NIH multi-site and research network studies, other NIH and federally funded research, and junior investigator-initiated research. However, we will also facilitate research supported by foundations, industry and the private sector, with appropriate program income procedures in place. Innovative Child and Maternal Health Research, our CE&R program and a new Practical Trials & Dissemination/Implementation Research programs will be incorporated into this Pillar Program. Further details are in Section III.

**Goal 4: Infuse key concepts of community engagement into the full spectrum of translational research.**

The CCTSI Community Engagement & Research Core (CE&R) will infuse and elevate patient-centered, community-engaged research concepts throughout CCTSI programs. Our innovative and extensive CE&R structure and programs are fully described in Section III. In addition to our current innovative programs, transformative new initiatives over the next 5 years will include: 1). Boot Camp Translation for Patient Centered Outcomes, a newly developed innovative methodology for communities to translate evidence-based recommendations into language and programs understandable to their members with the goal of increasing uptake and implementation of these recommendations in the community to improve patient outcomes. Based on its success, we will disseminate this methodology throughout the CTSA Consortium, focusing on best practices developed at CCTSI. 2). Community Consults. This program will be initiated in year 1 with the goal of infusing community input into the early design of T1-T2 clinical studies or trials to be conducted at clinical research units (CTRCs) within the medical centers. Community members will provide feedback about the value of the research to their community, suggestions about patient-centered outcomes that would have meaning to them, comments on study design and ways to make the study more attractive to participants, ethical issues that may come up, etc. Further details about our Community Engagement & Research programs are in Section III.

**Goal 5: Increase the translational research workforce capacity through a broad curriculum of education and training opportunities.** Ensuring a superbly trained translational research workforce is a major objective of the strategic plan of the CCTSI. During the first 4½ years, the Education, Training, and Career Development (ETCD) Pillar Program has expanded and fortified the clinical and translational research educational and mentoring portfolio at CU-D and its partners, and ensured its alignment with the 14 NIH CTSA Core Educational Competencies in translational research training. In essence, we have built a clinical and translational educational pipeline that spans the continuum from high school students to our university leadership. As a result, we have transformed the educational landscape across the University and our affiliate institutions. In Section IV of this application we will fully describe our educational strategic goals for the next five years: 1) to strategically build a robust clinical and translational research workforce for the future; 2) to enhance the effectiveness of our ETCD programs; and 3) to enrich the recruitment and retention process of the most promising and diverse students and junior faculty to careers in clinical and translational research.

E. **INSTITUTIONAL COMMITMENT**

The CCTSI programs described in this application have a budget that exceeds that which would be provided by the NIH CTSA grant funding alone, particularly in view of our contracted NIH CTSA grant budget by year 5. Based on the success of the first 4½ years of the CCTSI and its critical importance to the research and training environment at CU-D and its partners, all stakeholders have agreed to expand their level of institutional support to achieve the Strategic Goals in this grant application. This enthusiasm is embodied by expansion of
major ongoing commitments from the CU-D Schools, the CU-D Chancellor’s office, CU-B and CSU, and each of the participating Hospital Affiliate (Table 2).
A total of $31,718,188 has been committed for ongoing operations support over the 5 year grant period. In addition, over $11.9 million has been invested in affiliated programs and shared technology cores that are essential to the success of the CCTSI. Thus, the total institutional commitments and investments for the 5 year period of this CTSA award equal $43,642,424.

### F. EXTERNAL ADVISORY COMMITTEE (EAC)
An EAC in place for the first cycle of the CCTSI has provided annual review of progress, guidance to challenges that have arisen and helpful recommendations. For the new grant cycle, many members of the EAC will be reappointed and several new members added. Appointments are approved by the Vice Chancellor of Research (VCR) and Vice Chancellor of Health Affairs (VCHA) under the recommendation of the PI and the Executive Committee. The EAC will consist of 6 to 8 nationally renowned CTR scientists (including several CTSA PIs or co-PIs). Individual expertise will include: 1) T1 translational research, 2) community engagement and implementation research, 3) clinical research management and industry collaborations, 4) biostatistics and study design, 6) research informatics and data sharing, 6) education, training, and career development, and 7) child and maternal health research. The EAC will meet annually at CU-D with the Executive Committee to be updated on achievements and progress, challenges, obstacles, and proposed solutions. The EAC submits a detailed report to the PI which will be shared with the VCR and VCHA. The current EAC has been instrumental in providing recommendations which have spawned new initiatives. For example, in yr 3 of the current award, EAC identified that translational informatics lacked an academic home at CU-D. Upon these recommendations, Dr. Sokol and Informatics Director Dr. Michael Kahn led a major initiative at CU-D that culminated in 2012, with the SOM Executive Committee approving a new Center for Biomedical Informatics at CU-D and a Division of Biomedical Informatics and Personalized Medicine in which academic appointments will be made. A search is being conducted for the Director of both of these programs with a commitment of substantial resources. In year 3, the EAC identified the need to more formalize data sharing and clinical data warehousing among our partner institutions. Begun in 2012, Dr. Kahn is leading a major initiative to develop a single shared enterprise data warehouse for CU-D, UCH, CHCO and University Physicians Inc. The EAC advised the CCTSI to expand its quality and regulatory responsibilities beyond only those studies supported by CCTSI resources. CCTSI responded by a) making REDCap available across all campuses and hospitals for all studies, now totaling over 1400 projects using REDCap, b) developing the Clinical Research Support Center in the Regulatory Core to assist all translational investigators, and c) requiring SARC to perform scientific review for all clinical research studies of more than minimal risk across CU-D.

### Table 2. Institutional Funds Supporting CCTSI

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<th>I. Infrastructure Support for CCTSI Cores or Programs*</th>
<th>Source</th>
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<th>Years</th>
<th>Funds</th>
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<td>Baby Blanket Program</td>
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<td>Bioinformatics Core Support</td>
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<td>Dean, SOM and Vice Chancellor of Research</td>
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| **TOTAL** | **Five Year Budget** | **$43,642,424** |

*Infrastructure funds are committed to support the CCTSI Allied Programs or CCTSI cores co-funded by other CU-D Centers or Schools. This infrastructure support is not specifically committed as cost-sharing to the CCTSI.

PHS 398/2590 (Rev. 06/09)  Page  528  Continuation Format Page
Research Plan

II. Integrated Home Leadership Section

Specific Aims
1 page

Integrated Home Section
30 pages

- Organization and Governance
- Clinical and Translational Research Environment
- Informatics Coordination and Research Data Security
- Tracking, Assessment and Evaluation
- Translational Pilot Program
II. INTEGRATED HOME LEADERSHIP SECTION

NOTE: Commonly used abbreviations in this section are defined in page 516 of this application.

A. SPECIFIC AIMS

The integrated home for the CCTSI (Fig. 10) provides an infrastructure to support the broad range of T0.5 to T4 research across the partnering institutions and as the foundation for training and developing the next generation of clinical and translational investigators. The over-arching goal is to provide a robust and supportive governance structure and research environment to enable and ensure safe, high quality, highly efficient and cost-effective research to flourish.

The purpose of this section is to detail the vision for the integrated home for the CCTSI that is distinct from but integrated into the infrastructure of the various partner institutions. Each specific aim corresponds to one of the five subsections of this Section (as outlined in the FOA). The Specific Aims are to:

1. Provide an integrated organizational governance structure that engages participating institutions and constituencies to promote the vision of the CCTSI.
2. Promote a responsible and safe research environment across the lifespan of each study and improve the research enterprise to ensure a streamline, efficient, and cost-effective system.
3. Implement systems to coordinate the access, delivery, and sharing of data resources in a secure and compliant environment for translational researchers and communities.
4. Catalyze quality and process improvement and ascertain key program impacts through responsive tracking, assessment and evaluation.
5. Expand our comprehensive pilot grant program to catalyze and promote new, high quality, collaborative T1 – T4 investigation throughout the CCTSI.

The CCTSI informs and partners with the university to ensure researchers’ needs are met through an integrated research support structure. Many of the new initiatives in the research environment were developed by the CCTSI or will be beta-tested on the CCTSI. The CCTSI was also the catalyst for the establishment of an academic home for bio-informatics and the expansion of an integrated data network to facilitate the conduct of research. Similarly, institutional progress to improve and streamline processes will be in large part instigated and developed by the CCTSI. In collaboration with the Tracking and Evaluation Core, metrics will be established and reported every 6 months to the CCTSI Director/PI, the Executive Committee and the Clinical Translational Research Advisory Committee of the SOM to monitor progress and evaluate potential areas of focus for the CCSTSI quality and process improvement team.

Our overall aim is to ensure that all federally-funded research and research without funding is conducted to the same high standards of quality and safety, and as efficiently, as industry sponsored research.

Figure 10. Organizational Structure of CCTSI
II.1. ORGANIZATION AND GOVERNANCE

SPECIFIC AIM 1: Provide an integrated organizational governance structure that engages participating institutions and constituencies to promote the vision of the CCTSI.

A. BACKGROUND AND SIGNIFICANCE:

The CCTSI was created in 2008 at CU-D as an institute with the authority and broad reach to forge relationships within the CU system and with outside partners, communities, affiliated hospitals, and industry. The Director/PI of the CCTSI has programmatic authority and autonomy to implement the programs and functions of the Institute, manage the space assigned to the CCTSI, and hire and fire personnel within the Institute. Buy-in has been obtained from CU-D, CU-B and CSU leadership, the Deans of each health profession school, CEOs of each Affiliate Hospital and Health Care Organization, community members, corporate leaders, officials at each campus, and most importantly, the faculty, investigators and trainees. The CCTSI is actively involved in breaking down silos and obstacles, introducing new software and technologies and establishing data sharing infrastructure and agreements that have transformed the Colorado biomedical enterprise and its relationship to communities throughout the state. The CCTSI provides the highest quality research support services, state-of-the-art facilities, translational technology cores, pilot funds and training programs used by a diverse group of investigators across the partner institutions.

B. APPROACH

B.1. Organizational Structure. The CCTSI has been a formal Institute since 2008 within the University of Colorado, based at CU-D Anschutz Medical Center campus (AMC), and governed by an Executive Committee chaired by Ronald Sokol, MD, the Director and Principal Investigator in the current application (Fig. 11). The Director reports to the Vice Chancellor for Research (VCR), Richard Traystman, PhD, and the Vice Chancellor for Health Affairs (VCHA), Richard Krugman MD, the Dean of the School of Medicine, who in turn report to the Executive Vice Chancellor of the AMC, Lilly Marks, who reports to the Cu-D Chancellor, Donald Elliman, Jr. As Executive Vice Chancellor, Ms. Marks oversees the campus of the AMC and all of its Schools and programs. The Deans of the other health sciences schools report to the VCHA. The VCR and VCHA work closely to integrate and support educational, research and clinical programs at AMC, thus the dual reporting of the CCTSI Director to both of these individuals will ensure the campus-wide integration of CCTSI programs.

The PI/Director (Dr. Sokol) will have institutional responsibility and authority for all aspects of the implementation and function of the CCTSI and will have daily involvement with the activities of the CCTSI, including: 1) oversight of all administrative, strategic, academic, operational, and financial functions, 2) control over assignment of space and allocation of resources assigned to the CCTSI, 3) relationships with the partner institutions, 4) collaboration with other CTSAs through the National CTSA Consortium Steering, 5) interaction with NIH Project Scientists and NIH Program Officer providing information concerning progress, and 6) maintenance of career development opportunities to encourage new investigators in clinical and translational sciences. The PI/Director will work with Department Chairs throughout the Health Profession Schools at CU-D, and appropriate departments at CU-B and CSU, to help recruit outstanding investigators and ensure their protected time for research, and with Promotion Committees to ensure promotion of worthy investigators. (Note: The CCTSI does not have authority to directly hire faculty, who must have an appointment within a department within a school or college). The PI/PD is viewed as the campus leader in CTR research and training and sits on important committees at CU-D, including the Executive Committee of the SOM, the Clinical and Translational Research Advisory Committee to the VCR and VCHA, the Enterprise Data Warehouse planning committee, the Research Advisory Committee to UCH, the Strategic Planning Committee of the SOM, and others. The PI/PD will be an established well-funded clinician scientist who is a recognized academic leader at CU-D, with a funded research program, excellent administrative, fiduciary and communication skills, highly regarded by the partner institutions, and with extensive experience in translational research infrastructure and training programs.

The CCTSI Administrative Director/Chief Financial Officer (Tim Lockie, MS, MBA) will work closely with the PI/Director to prepare the budget for each year; develop and implement a program income system in yr 1;
B.2. Integration of CCTSI within Partner Institutions.

Theoretically, one might expect the existence of major disparities in institutional culture among the CCTSI partner institutions that would create competing institutional perspectives and would be a challenge for implementing a CTSA academic home across four university campuses and six academic hospitals. However, in reality these institutions have worked collaboratively for decades and are well aligned in missions and actions. For example, all research and clinical faculty in each of the six hospitals are faculty in the CU School of Medicine, Pharmacy, Public Health, Dentistry or Nursing, as CU-D is the only Academic Health Center with health profession schools for 500 miles. Thus, scientists interested in research have sought and received appointments at CU, regardless of their hospital affiliation, for 40 years. Establishing a central IRB (COMIRB) on record for 5 of the institutions further demonstrates the willingness to work together to achieve efficiency and cost savings. In a state with poor support of higher education, it is essential that the major public universities (CU-D, CU-B and CSU) collaborate and share core facilities and other resources to be successful, and this is certainly the case in Colorado.

Leadership at each of the six hospitals is also committed to the mission of the CCTSI and the CU Health Profession Schools in order to achieve their own missions. Thus, the Vice Chancellor of Health Affairs of CU-D meets regularly with hospital Presidents and CEOs of all the partner institutions, further ensuring open communication channels for challenges that may arise. It also should be emphasized that faculty at CSU, CU-B and CU-D collaborate on literally hundreds of projects each year across institutions, co-mentor graduate students, publish together and are co-investigators on grants, demonstrating the collegial relationships between the academic institutions themselves. Finally, the many rich educational programs of the CCTSI are available to trainees and faculty at all of the partners. For example, two of the KL2 awardees have been based at National Jewish Health and two of our CCTSI Translational Technology Laboratories are located at CU-B and two at CSU. Thus the national reputation of our institution as a highly collaborative environment in which to work permeates through the CCTSI programs and partnerships. To continue to ensure effective integration across the partner institutions, representation on the CCTSI Advisory Council (which meets biannually) includes high ranking leadership from each partner hospital and university campus, as well as the health profession school Deans.
B.3. Leadership of Programs. (Please see Biosketch for academic and professional achievements of each individual listed below)

Ronald J. Sokol, MD, the Principal Investigator and Director of the CCTSI (responsibilities are described in B.1) since its inception in 2008, will continue in these roles in the current proposal. Dr. Sokol will have the responsibility and authority for all aspects of the implementation and function of the CCTSI and will have daily involvement with the activities of the CCTSI. He will oversee the 5 Associate Directors, the Executive Committee and the Administrative Core, including the Administrative Director for Finances and Operations, as well as all operations. Qualifications for this position include Dr. Sokol’s leadership, administrative and organizational experience as prior Program Director of the Pediatric GCRC for 10 years prior to becoming Director/PI of the CCTSI in 2008. He has a long investigative career in childhood liver disease, and has been PI on NIH funded basic, clinical and translational research grants and a T32 training program grant in pediatric gastroenterology. Dr. Sokol has chaired a national 16-site NIDDK-funded pediatric liver disease research network (ChiLDREN) for the past 10 years, providing him with additional high-level administrative and scientific experience, as well as collaborative experience across a consortium. Dr. Sokol will devote 50% of his effort (6 months) to the PI/Director position.

Tim Lockie, MS, MBA, Administrative Director and Chief Financial Officer (responsibilities are described in B.1), has functioned in this position for the past 4 ½ years following the same position in the Adult GCRC for 4 years. Mr. Lockie has a scientific background (MS in Medical Genetics) and finance background (MBA) as well as years of operational, grants management, clinical research infrastructure development, and fiscal management experience at CU-D. Mr. Lockie has forged strong relationships with senior administrative and finance leaders of CU-D, each of the schools, and all of the CCTSI affiliated hospitals and institutions. His training in basic science and extensive administrative and financial experience provide Mr. Lockie with the abilities to undertake the role of Administrative Director and CFO for this large program. Mr. Lockie will devote 100% effort (12months) to this position.

The following five CCTSI Associate Directors will be responsible for the operations and functions, implementation, and oversight of one of the Pillar Programs, Chair the Steering Committee for that Pillar Program, manage its budget, report to the PI/Director, and sit on the CCTSI Executive Committee:

Marc Moss, MD, CCTSI Associate Director overseeing the Research Education, Training and Career Development Pillar Program, is Professor of Medicine in Pulmonary and Critical Care and an active NIH funded critical care investigator. Dr. Moss has been dedicated to education and mentoring throughout his career and has been the director of Education & Training Program for the CCTSI since 2008, building an outstanding program that has grown from 4 to 11 separate educational programs in the course of 4 years. Dr. Moss possesses the leadership; educational, research and mentoring knowledge, skills, and experience; personal qualities; and administrative experience to direct this key program. As Associate Director, he will Chair the ETCD Steering Committee, oversee the directors of each education program, approve program curricula, manage the budget, review evaluations of each program, sit on the CCTSI Executive Committee, and recommend changes to the Director/PI. Dr. Moss will devote 25% of his effort (3 months) to this position.

Alison Lakin, RN, LLB, LLM, PhD, CCTSI Associate Director for the Enhanced Research Environment Pillar Program, has extensive experience in research regulatory science, and has been the CU-D Assistant Vice Chancellor for Regulatory Compliance since September 2011. In this position, she has overall responsibility for CU-D’s human research protection program (HRPP) and works closely with the HRPP programs at the affiliated hospitals to develop consistent policies and processes to facilitate research. Dr. Lakin was Director of the Institutional Review Board (COMIRB) from 2005-2011, as well as the director of the CCTSI Regulatory Knowledge and Support Core and the Champion of Change of the CCTSI since early 2011. In January 2012, she established the Clinical Research Support Center (CRSC), which encompasses the new proposed Enhanced Research Environment Pillar Program. The goals of this program are to increase the efficiency and effectiveness of the regulatory approval process, contracting and research management and improve the quality of protocols submitted for regulatory support. Dr. Lakin will sit on the CCTSI Executive Committee. Dr. Lakin will develop policies and procedures, oversee the budget, activities and personnel of this program (see specific aim #2 for details) and devote 10% of her effort (1.2 months) to this position.

Wendy M Kohrt, PhD, CCTSI Associate Director for the CTR Resources and Services Pillar Program is a tenured Professor of Medicine in the Division of Geriatric Medicine at CU-D. Dr. Kohrt is an NIH supported clinical investigator, continuously funded for more than 20 years, whose research focuses on lifestyle and pharmacologic interventions to mitigate metabolic and functional declines with advancing age. She is the Director of the Energy Balance Core Laboratory for the NIH-sponsored Nutrition and Obesity Research Center, and the Chair of the CCTSI SARC and PCIR Oversight Committee for the past 5 years. Because of her
knowledge of CTRC operations, management skills and administrative experience, she will direct this Pillar Program, chair the Steering Committee, implement the Program Income System, monitor and evaluate productivity metrics of each resource and service, recommend to the Director/PI changes in services to be supported, sit on the CCTSI Executive Committee and devote 20% effort (2.4 months) to this position.

**Michael Kahn, MD, PhD**. CCTSI Associate Director for the Translational Informatics Program, currently holds the same position and has done an outstanding job the past 4 ½ years establishing the CCTSI informatics program. Dr. Kahn, Associate Professor of Pediatrics, developed the translational informatics infrastructure and services across the CCTSI campuses and affiliated hospitals. He is a National Library of Medicine trained Informaticist, past co-Chair of the CTSA Consortium Key Function Committee on Informatics, and an expert in data security, data sharing, data standards and ontologies and clinical trials data acquisition. Dr. Kahn will be responsible for all personnel, operations, data storage and sharing and budget aspects of the Translational Informatics Program. Dr. Kahn will oversee the existing three CCTSI informatics project directors (systems infrastructure, data management, and education/research), and will provide strategic and technical guidance with weekly one-on-one team meetings and monthly project directors’ meetings. Dr. Kahn will remain active in national IKFC activities. He will sit on the Executive Committee and devote 25% effort (3 months) to this position.

**Mark W. Geraci, MD**. CCTSI Associate Director leading the CCTSI Pilot Grant Pillar Program and the Network of Translational Technologies (NeTT) program, is a tenured Professor of Medicine and Head of the Division of Pulmonary Sciences and Critical Care Medicine at CU SOM. He has led these two CCTSI programs since 2008. He is an NIH funded basic and translational investigator who focuses on prostanooid metabolism and lung disease and lung cancer. He is the Director of the Genomics Shared Resource, supported by the CU Comprehensive Cancer Center and the CCTSI. Through Dr. Geraci’s efforts, the technology and expertise offered through this resource have had an enormous impact on research throughout CU and the region. His qualifications for this position include his scientific expertise, project management and administration skills, clinical and research productivity and his demonstrated outstanding performance since 2008. Dr. Geraci will oversee the administration of our Pilot Grant programs including developing the application, writing the RFAs, directing the review of applications and monitoring of awardees. He will choose the review panel, chair the review committee, make recommendations to the EC for approval of pilots and oversee Sandy Chalmers. He will also monitor the productivity of the 13 translational technology labs, assist with implementing the Core Management System, and make recommendations to the EC about changes in funding of cores. He will sit on the Executive Committee. Dr. Geraci will devote 25% of his effort (3 months) to these two programs.

*Each CCTSI program, core or service will employ portions of other faculty effort; these will be described in detail in Sections II and III of this application.*

### B.4. Advisory Committees

Three advisory committees will play important roles in providing input and advice to the Director/PI:

1. **The CCTSI Advisory Council** will consist of Deans of each of the CU-D health science schools; a high ranking research official from CU-B, the Downtown Denver Campus of CU-D and from CSU; CEOs or their designates of each Affiliate partner Hospital/Health Organization; the Director of the Technology Transfer Office of CU; 2-3 members from the business/corporate community; and 2-3 representatives from lay communities including underserved populations. This committee will be chaired by the Director/PI and the VCR and VCHA will be *ex officio* members. This Council will provide the opportunity for leadership from each of the collaborating institutions to be informed about CCTSI functions, discuss important issues, and provide input to the CCTSI leadership and devise thoughtful strategies to deal with challenges that may arise. The Council will receive an annual written report from the Executive Committee describing each institution's performance from the COMIRB Protocol Tracking Database with suggestions for improvements. This Council will meet bi-annually as the vehicle to assure strategic discussions, integrations and collaboration among the major Universities, Schools, campuses, affiliated Hospitals and communities of the CCTSI.

2. **The External Advisory Committee (EAC)**, as fully described in Section I, will provide objective review of CCTSI programs and structure will offer recommendations for achieving the goals of the CCTSI.

3. **The Clinical and Translational Research Advisory Committee (CTRAC)**. As CCTSI’s goal is to stimulate interdisciplinary research among the collaborating schools and partner institutions, direct input from faculty representing each of these constituencies is essential. The CTRAC guides and advises the CCTSI Executive Committee in addressing issues relevant to faculty across all involved institutions. The CTRAC includes 12-15 senior and junior investigators, with representation from each University, the health science schools, from each campus, and from major Centers (e.g., CUCCC). The membership includes basic, clinical, and population scientists. This committee has already been instrumental in shaping CCTSI initiatives over the past 4 years.
The CTRAC has been, and will continue to, meet with members of the Executive Committee monthly. **B.5. Organization and Functions of the CCTSI Academic Home.** As the Academic Home for Clinical and Translational Sciences at CU-D and its partners, the CCTSI will a) develop a new generation of investigators with advanced degrees, interdisciplinary and collaborative skills and a team approach to scientific investigation; b) provide outstanding resources, services and infrastructure; c) insure efficiency and cost-effectiveness in our research processes and remove barriers to achieve these; and d) integrate novel technologies, services, and community research infrastructure to stimulate and support the highest quality research. The CCTSI is structured to include membership from a wide range of academic and community stakeholders and to provide career development support to trainees and faculty at all levels. The following describes how the CCTSI will meet its responsibility as the Academic Home for clinical and translational sciences:

**Membership:** The CCTSI will be inclusive in its membership policy, reaching out to all faculty and trainees who express an interest in, or have experience in, clinical or translational research. This includes basic scientists who are searching for collaboration to translate their discoveries into diagnostics or therapeutics. CCTSI Individual Membership will include faculty members, research associates, trainees and students, public/private members, and community members involved in activities related to clinical and translational science. Members will be derived from the six Health Science Schools of CU-D; non-health science Schools, Colleges and Departments of CU-D, UCB and CSU; faculty and trainees at the six partner hospitals; community physicians, government officials and laypersons; and representatives from Industry. During the first 4 ½ years of the CCTSI, 2,650 members have joined (greatly exceeding our initial prediction of 400-600), 57% of which are faculty, 19% research associates, 18% trainees, 6% private/public sector, and 4% community members. Benefits of membership include interactions with a community of investigators, educational programs and career development opportunities and mentoring, access to experienced and expert research personnel and facilities, support for academic promotion, discounted charges for some CCTSI services, and eligibility for funds from Pilot Grant Awards. Membership requires being available to collaborate with other investigators, being accessible and share expertise, train/mentor students and trainees, maintaining InfoEd and Colorado Profiles personal profiles, abiding by the CCTSI Data Sharing Plan, and sitting on review committees as requested. The online membership registration is simple and quick. Our inclusive membership policies encourage membership.

**Promotions, Appointments and Tenure:** The CCTSI will work to ensure that appropriate recognition is given to team science within each department, school and campus. The CCTSI has been instrumental in setting the new CU SOM 2012 promotion criteria to recognize “team science” as a criterion for independence and scientific leadership, key requirements for promotion. Dr. Ronald J. Sokol, the CCTSI Director, and other CCTSI leadership will now work with the other schools and colleges at CU-D, CU-B and CSU to similarly incorporate team science into their promotion criteria. The responsibility for appointments and promotion resides with individual departments at our schools and colleges. However, each CU-D Health Profession School has agreed to allow the CCTSI to participate during the promotions process. CCTSI leadership will submit letters of support for faculty members of CCTSI who have made strong contributions or participated in CCTSI activities. A member of the Executive Committee will attend each primary Department’s Promotion Committee meeting as needed, to speak on behalf of the faculty member. The Executive Committee will help identify prominent local and national references from the clinical and translational sciences field to write supporting letters for promotion. The CCTSI will also write a formal letter supporting the promotion or awarding of tenure, which will be included in the promotions packet delivered to the University’s Promotion Committee.

**Faculty Recruitment:** When appropriate, the CCTSI will participate in the recruitment of new clinical and translational science faculty in all Health Profession Schools and other appropriate non-health related schools at CU-D, CU-B and CSU. The Executive Committee members will participate in faculty recruitment by 1) sitting on search committees, 2) nominating candidates, 2) making recruiting phone calls and visits as needed, 3) emphasizing the rich resources and services and training programs available from the CCTSI, and 4) interviewing and evaluating potential candidates. We anticipate that this function will build closer relationships between Dept. Chairs and the CCTSI and encourage development of interdisciplinary collaborative programs.

**Faculty Mentoring and Career and Leadership Development:** The CCTSI leadership will provide ongoing career mentoring of faculty as part of the process of career development. In addition, the Leadership in Innovative Team Science (LITeS) and the Colorado Mentor (CO-Mentor) programs provide high quality training in these important aspects of career development for groups of 30-40 faculty and mentees per year. These programs are outlined in detail in the ETCD (Section IV) of this application.  

**B.6. Distribution of Resources, Decision Making and Conflict Resolution.** The Executive Committee (EC) has worked very collaboratively over the past 4½ years while implementing the CCTSI at CU-D and at its...
partner institutions. For decisions resting with the EC, we anticipate a continued collegial consensus will be the mode of decision making. Many decisions reside with the PI/Director and Administrative Director who obtain input as needed before decisions are reached. If issues arise that cannot be decided through consensus, the Program Director/PI will discuss them with the VCR and VCHA and come to a final decision. The CCTSI Advisory Council will be an additional venue for open discussion of issues that cut across institutional boundaries. With the reductions in our NIH budget that will be phased in during the next five years, CCTSI resources will be prioritized for NIH-funded or other federally funded investigators, trainees and investigator-initiated research projects. After funding source is considered, allocation to Member investigators and trainees will be based on merit and need and not on their location or academic affiliation. The decision making processes for allocation are transparent and fair. If conflicts arise between the major CCTSI institutions that cannot be resolved at the PI/Director level, CU-D highest leadership (Executive Vice Chancellor, VCR and VCHA) will become involved.

**B.7. Physical Space of the CCTSI Available To Faculty And Trainees.**

The CCTSI has been assigned space in all of the partner institutions. The CCTSI occupies the entire third floor of the Leprino Building (Fig. 3), including the offices of the CCTSI Administrative Core, Informatics Program and ETCD program as well as the UCH outpatient CTRC clinic, the Metabolic Kitchen, the UCH Core Laboratory and the Exercise Research Laboratory, all totaling over 35,000 ft². The Leprino Building is located on the CU-D AMC campus and is connected to UCH via a bridge. UCH also houses the inpatient CTRC unit, whole room calorimeter and sleep lab (total of 8 rooms, 7,204 ft²). CHCO houses an outpatient CTRC research clinic (12,000 ft²), an inpatient CTRC unit (6 beds, 6,000 ft²), a Core Laboratory (10,000 ft²) and offices. NJH houses an outpatient CTRC unit, offices, and Core Laboratories (4,475 ft²). The mobile Perinatal CTRC unit covers CHCO and UCH. Investigators at CU-B conduct patient-oriented research at the CCTSI CTRC (2,790 ft²) located on the 3rd floor of the Waardenberg Student Health Center on campus (full details about CTRC facilities is in Section III, page 568). This CTRC physical space is provided for investigators and trainees to perform research visits and procedures, store research records and materials, and hold mentoring sessions, meetings and conferences. CSU investigators may use shared clinical research space and Core Lab space in the Veterinary Teaching Hospital in Ft. Collins, in which clinical trials in natural animal models of human disease are conducted (1,300 ft²). Shared research space for CCTSI investigators is available at DH, the DVAMC and KP. The CCTSIT leadership has authority over the CTRC physical space. All individual faculty members have office space and individual laboratory space provided by their home departments; trainees will have space provided by their mentors or teachers.

**B.8. Evaluation and Replacement of Directors of Program Components.**

It is essential that the Program Director and Associate Directors undergo a rigorous annual evaluation with input from stakeholders, and that replacement be considered if performance does not meet objectives. The Director will undergo an annual performance review by the VCR and VCHA. This annual review will be based on 1) an annual self-review, 2) information gathered by the VCR and VCHA, and 3) a written evaluation by the CCTSI Advisory Council. A 360 evaluation of the Director will be performed each 2-3 years by the Evaluation and Tracking Center, the results presented to the Program Director, VCR and VCHA. The Program Director will evaluate performance of the Associate Directors, using objectives and specific criteria developed by the Director in consultation with the Tracking & Evaluation Center. The Core and Program Directors who report to the Associate Directors will be similarly evaluated by the Associate Director by criteria developed by the Evaluation Center. Replacement of the Director or any Associate Director will be considered if they have not capably carried out the job responsibilities, if they are unable to perform all of their duties because of other responsibilities, or if they leave the institution or resign from their position. In the 4 ½ years of the CCTSI, two Associate Directors have been replaced; one left our institution and the other resigned because of illness. The VCA and VCHA will make the final decision on replacing the Director and the Director will decide on the Associate Directors. If replacement of the Director is required, the VCR and VCHA will assign an interim Director from the Executive Committee. The VCR will be the signatory for the Program Director in his/her absence. The Search Committee for a new Director will be chaired by the VCR and VCHA, and including Deans of the 6 health science schools (or their designee), CEOs (or their designee) from the six affiliated Hospitals/Health Care Organizations, a high ranking representative from the CU-B, CSU and Downtown Denver CU-D campuses, and 5 faculty involved in translational research. The Search Committee will forward a single name to the VCR and VCHA for approval. For replacement of an Associate Director, the Director will consider replacements after consulting with the other Associate Directors, the IAC/CTRAC, and the Deans of the 6 health science schools, with final sign off by the VCR and VCHA. For replacement of Core Directors, the Director and the appropriate Associate Director will make a selection with the advice and input from Executive
Committee and the VCR and VCHA.


Dr. Sokol, the Program Director will be accountable for the structure, function, operations, budget, and expenditures of the CCTSI. The Administrative Director (who has the delegated authority from Dr. Sokol to manage the budget and expenditures on a day-to-day basis) and his staff will manage the budget and have monthly meetings with Dr. Sokol to review expenditures and budget projections. Each program, component or shared resource will be reviewed annually by the Director and Administrative Director. Data collected by the Associate Directors, Core Management System and Tracking & Evaluation program (based on objectives and metrics for each Core/Program) will be submitted to the Administrative Core in the fourth quarter of each year. Using these data as performance measures, the Director/PI and the Admin. Director will determine the appropriate budget and resources for each program for the coming next year. Actions taken may include increased support for a component, re-allocation of resources to a more utilized component, instituting strategies to increase utilization, termination of a program or component director, etc. **This activity attains particular importance given the mandated NIH grant budget reductions each year based on the new NIH CTSA budget formula.** Factors under consideration for allocation of resources will include 1) the value of the Program/Core to the mission of the CCTSI, 2) utilization of the resources and the performance measurement for the prior year, 3) potential negative impacts if the function were to be scaled back or eliminated, 4) the proposed budget for the next year and 5) the availability of funds either from the NIH grant, program income or institutional support. The final decision on the distribution of resources and the budget will be made by the Director and will be shared with the CCTSI Advisory Council, the IAC and the EAC.

**B.10. Recruitment of New Investigators and Research Programs, Including Underserved Minorities.**

The lifeblood of any academic enterprise depends on its ability to attract new investigators, stimulate creative ideas and new collaborations, and promote transformation of programs, positioning itself to respond quickly to new opportunities. The CCSTI has built its structure and programs to ensure that new investigators are aware of CCTSI resources, expertise, training, and services that will benefit their research and careers. **General Recruitment:** Recruitment of new investigators and programs will be performed through the following efforts, which have successfully attracted 2,650 CCTSI members during its first 4½ years: The CCTSI Website Portal will be widely advertised at all CU-D, CU-B and CSU websites and partner Hospitals as the preferred site for obtaining up-to-date information about CCTSI funding opportunities, resources and services, and training and career development. The Website is user-friendly and allows easy identification of useful collaborations (through the new Colorado Profiles portal), consultants, and shared resources. Several emails and announcements will be sent each year to all faculty, researchers and trainees, and potential community and industry members, outlining the process of applying for CCTSI membership, announcing new programs and requests for funding opportunities, important seminars, education programs, etc. Dr. Sokol will continue to conduct annual Town Hall meetings at each hospital and university campus to update on CCTSI resources and programs and answer questions. Medical Directors of the five CTRCs will serve as ambassadors for the CCTSI and actively recruit investigators to use CCTSI resources and services. Dr. Sokol also presents an annual update at Division Director Meetings for Departments of Medicine and Pediatrics and to CTRAC. Finally, stories about investigators who used CCTSI services and resources and training programs will be distributed to CU and CSU and external media outlets to demonstrate how the CCTSI benefits investigators, the institution and research. **Training and Education programs** will be actively announced by academic email announcements and on our website, and presented by Dr. Sokol during Town Hall meetings. **Pilot Grant Funding Opportunities and other internal granting programs** will be announced by blast emails and emails to our Membership, as well as posting on the CCTSI and affiliate websites, and presented by Dr. Sokol during Town Hall meetings.

**Underserved Minority Recruitment and Efforts to Enhance Diversity:** CU-D, CU-B and CSU and the CCTSI are strongly committed to recruit, retain, and support investigators and trainees from underserved minorities and of diverse backgrounds. We will make all efforts to recruit and retain faculty and trainees who are individuals from under-represented racial and ethnic groups, individuals with disabilities, and individuals from socially, culturally, economically, or educationally disadvantaged backgrounds. Efforts are underway across all CU and CSU campuses to increase minority trainees and faculty in educational and research programs. The CCTSI ETCD program leadership will continue to work with the Office of Diversity and Inclusion and with programs that guide minority high school and college students into health and research careers (e.g. the Summer Minority Student program of the CCTSI [SUMMiT] - see Section IV), and will attend several internal and external recruitment meetings with minority students and residents. American Indian/Alaska Native clinical translational investigators and trainees will be encouraged to participate through the Native Investigator
program. All CCTSI programs announcements will specify that we encourage minorities, those disabled and those from disadvantaged backgrounds to apply for membership, trainee positions or faculty appointments. Senior faculty from minority groups will serve as role models and individual mentors for these students/trainees to enhance career development. This program is detailed in the ETCD Section (Section IV) of this application. In addition, we have designated specific CCTSI Pilot Grant Award funds for investigators from minority groups or disadvantaged backgrounds (see Pilot Grant Program section below.)

Women in Leadership Positions. We also believe that it is critical to promote and support women in academic careers. CCTSI will work with several current CU-D initiatives to promote women in academic leadership positions (e.g. nominations for ELAM program). When it is time to replace CCTSI leadership, women will be actively recruited for these positions and given high priority. Currently two of the five CCTSI Associate Directors are women, and numerous core and other program directors are women.

B.11. Point of Contact for Industry, Foundations, and Community Physicians
CCTSI will welcome and encourage involvement of the private sector and will follow CU-D, CU-B and CSU procedures regarding conflicts of interest and other policies. The two main points of contacts for those in industry will be through the relatively new CU Office of Corporate Alliances (Dr. Laura Simon, Director, partially funded by the CCTSI) for collaboration and business opportunities, and the Technology Transfer Office (TTO) related to filing, licensing and commercialization of intellectual property. The CCTSI Director is in close contact with both of these offices on a biweekly basis. CSU has two similar offices as do several of our hospital affiliates. The CCTSI is an active member of the Colorado BioScience Association, a not-for-profit organization that provides services and support for Colorado’s biotechnology and medical device industries. Through this organization, we will interface with biomedical companies in Colorado, promote collaborative research and licensing of CU-D inventions, and be involved in state-wide programs and opportunities. Community physicians will be encouraged to become CCTSI Community Members and to work with the Community Engagement Core leadership to develop plans for involvement and collaboration.

The CCTSI will infuse into the National CTSA Consortium our particular expertise in the areas of child and maternal health research; community-based participatory research; health care implementation in rural communities; Native American and Alaskan Native health research, training and leadership development; use of natural animal models for T0.5 translational research; experience with a central IRB for multiple local institutions; graduate clinical science education and training programs; and our experience in integrating several Universities and hospitals into a single successful academic home. The CCTSI is fully committed to remain very active in the National CTSA Consortium, to cooperatively address impediments to research and science, to work towards adopting and implementing agreed-on best practices and standards to advance clinical and translation research and training. We are committed to each of the national Strategic Goals and have representation on three of the SG committees as well as other Consortium leadership positions by Drs. Sokol, Hay, Kahn, Westfall, Eckel and others. Furthermore, we are strongly committed to creating a national networked CTSA infrastructure in which clinical and translational studies and clinical trials can be expedited through more rapid contracting, streamlined and cooperative IRB approval models (such as the central IRB of NEURONEXT) and provision of efficient and compliant resources and services. Furthermore, we are committed to adopting software developed by Consortium members that will increase efficiency and apply standards for better data sharing. Each of our academic institutions and hospital affiliates have pledged to work towards adopting and implementing the agreed on policies, procedures, best practices, and other measures established by the National CTSA Consortium and the NIH, including the data and software sharing plans described in this application (see Letters of Support).

II.2. CLINICAL AND TRANSLATIONAL RESEARCH ENVIRONMENT SPECIFIC AIM 2: Promote a responsible and safe research environment across the lifespan of each study and also improve the research enterprise to ensure an ethical, efficient, and cost-effective system
A. OBJECTIVES AND SIGNIFICANCE
In our Enhanced Research Environment Pillar Program, the CCTSI in collaboration with its partner institutions, is committed to ensuring that there is a broad culture of responsibility for safe and ethical conduct of human subject research with the appropriate resources in place to conduct only high quality studies and to facilitate multi-site trials. We have built a centralized approval process for our partner affiliate hospitals and CU-Denver, streamlined our approval and contracting processes to enable funded research to be conducted in a timely manner, and are in the process of further establishing processes and methodology to facilitate
recruitment, enrollment and retention and to appropriately manage failing studies. The components of this
Pillar Program are outlined in Fig. 10. In the following section of this application, we will first describe several innovative programs established as the foundation for the Enhanced Research Environment, followed by preliminary data demonstrating metrics and enhancements already achieved, and then followed by new initiatives for the next 5 year funding period. This will be followed on page 543 by Table 6 summarizing our plans outlined in this section to track and ensure high quality, efficiency, safety and effectiveness in clinical research studies and clinical trials.

B. INNOVATION

1. Centralized IRB: Since 1991, CU-D has had a centralized IRB (Colorado Multiple Institution Review Board; COMIRB), thereby allowing a single human research protocol application and approval process for the following sites: the CU-D, CHCO, Denver VAMC, Denver Health (DH), and UCH. This approach set a historical precedent as one of the first centralized IRBs in the nation. Additional memorandums of understanding (MOUs) have been developed with CSU, University of Northern Colorado and CU-D to establish a partnership approach to IRB review; a similar approach will be used with the newly formed University of Colorado Health System (Memorial Hospital, Poudre Valley Hospital & UCH). A reciprocity agreement is in place with the CCTSI partner, NJH, to further limit duplication of review. In addition, COMIRB is frequently the IRB of Record when faculty members at CU-D collaborate with other institutions regionally and nationally. Currently, COMIRB has IRB authorization agreements with over 160 separate institutions. COMIRB is also the IRB of Record for several large Practice-Based Research Networks, including the State Networks of Colorado Ambulatory Practices and Partners (SNOCAP) and High Plains Research Network (HPRN), both associated with the CCTSI Community Engagement & Research Pillar Program. CU-D has also developed a MOU for use of a central IRB for NeuroNEXT and has written letters of support for several other NIH initiatives using a central IRB for consortium research. Thus, the CCTSI is well positioned to centralize and streamline IRB review. CCTSI is also an active participant in IRB Share, a National CTSA consortium initiative to share IRB reviews and reduce needless duplication among institutions for multi-site trials.

A Centralized IRB also ensures a consistent approach to safety and quality of review across the research enterprise. For example all COMIRB protocols are required to have an appropriate data management and security plan utilizing such resources as REDCap as a HIPAA compliant management system. Currently 1,321 protocols are utilizing the CU-D REDCap database, supported by the CCTSI. Denver Health also has an instance of REDCap and the DVAMC is in the process of establishing its own instance.

2. Clinical Research Support Center (CRSC): CRSC was established in spring of 2012 at CU-D (co-funded by CCTSI and Chancellor’s office) as an integrated regulatory and support resource for clinical researchers. It builds on the efficiency of a centralized IRB and on the expertise of the current CTRC protocol scientific review (SARC) process. The goal is to develop a centralized pre-review of protocols prior to COMIRB submission to include: feasibility assessment and budget, FDA regulatory support review, integrated hospital research committee review and approval, and a centralized scientific review. CRSC will facilitate these multiple simultaneous reviews and ensure that the protocol submitted to COMIRB is of high quality and ethically sound, thus reducing cycle time not just with the IRB but the overall process review time to approval. A director will oversee the personnel listed below and report to Dr. Alison Lakin, CCTSI Associate Director. The CRSC consists of 3 specialized, but integrated, teams that address the entire clinical study/clinical trial process.

   1) The Protocol Specialist Team provides regulatory guidance to research teams during protocol development to ensure compliance with all internal, external and federal policies. The team also conducts a pre-review of protocols prior to submission to COMIRB to ensure quality and accurate submissions. A Consent Writer provides training and advice on consent writing; poorly written consents are one of the leading reasons for IRB deferral. Requests to write the consent will be managed as a fee-for-service option for investigators. A Budget Specialist assists in clinical trial budget development to ensure all research expenses are included and site-specific requirements are met. The new FDA Coordinating Center facilitates initial FDA IND/IDE and COMIRB submissions, maintains all FDA communication, and ensures appropriate follow-up and compliance. The Protocol Specialist Team will coordinate with SARC, TTO, partner hospitals, Office of Corporate Alliances and COMIRB to ensure an integrated, efficient and compliant process for the researcher.

   2) The Study Support Resources Team conducts quality assurance and quality improvement through periodic oversight of on-going studies to ensure compliance and efficiency. This Team will also train divisions or departments, research centers and/ or individual research teams on best practices to improve their clinical research management and feasibility assessment capabilities. In close collaboration with the clinical trials curriculum developed by the CCTSI, the CRSC Education Team will augment existing education programs,
establish mandatory minimal training for all research coordinators as well as continuing professional certifications (in coordination with our hospital partners), provide venues to discuss ethical issues that arise and establish a tool to make research set-up more efficient. Research Specialists will ensure that ethical and safe research is conducted by CTRC studies and trials, through the provision of consultative services to investigators, safety monitoring oversight and educating investigators, research coordinators and CTRC staff. The main function of these specialists is to coordinate the Study Monitoring Committees (SMC) of the CTRC Network (see Section III, page 567). A Research Subject Advocate (RSA) will focus on the involvement of subjects in the research process; discuss and mediate questions, concerns or complaints by research participants in a safe and confidential manner; serve as an objective witness to the consent/assent process if requested by any person involved in the research; and provide educational information to help participants better understand the research experience. Such work will involve close collaboration with the Recruitment Liaison, research bioethics program and the Community Engagement liaisons to ensure that there is an integrated resource for research participants. This resource will no longer be limited to participants who are involved in research on the CTRCs, but will be expanded and available to all subjects involved in research at CU-D and its affiliates with prioritization to the needs of vulnerable populations.

3) The Recruitment and Enrollment Team, led by the Recruitment Liaison, was originally developed to establish and facilitate recruitment into ResearchMatch, which is a centralized recruitment database for CTSAs nationally. However, recruitment of subjects locally has been poor via that system (453 subjects in 18 months) despite devoting resources to the effort. The CCTSI leadership has decided that a better approach to assist investigators with recruitment is to partner with the affiliate hospitals to establish a compliant mechanism for subject recruitment making use of hospital registration of patients combined with the electronic medical record (EMR) system. Discussions with CHCO, DH, and UCH are well underway to establish an “opt-in” or “opt-out” process by which patients (or parents) are asked for permission to be contacted by researchers if they are found to be eligible for research studies; this permission to be contacted process will occur at the time of hospital registration and consenting to the delivery of care. If the patient does not give permission, this will be recorded in their EMR and they will not be “searchable” for research studies. Investigators will use i2b2 or similar systems to identify cohorts of patients for IRB-research studies. An oversight committee will be set up at each hospital to screen requests for cohort identification, grant permission to investigators to contact eligible patients, address complaints, and remove patients from the eligible list if they so desire. Similar “Opt-in or Opt-out” processes are currently used successfully at NJH for recruitment into studies. KP and DVAMC also have centralized mechanisms to facilitate recruitment. CU-B and CSU recruit primarily through advertising and do not have clinical care facilities. The Recruitment Liaison will work with each institution and hospital along with the Research Ethics program, to develop policies and best practices as well as align implementation across the hospitals and institutions. Additional training in recruitment and retention methods is available in the CCTSI Clinical Research Education Program for investigators and research coordinators (see Section IV, page 598). A tool kit for investigators will be developed by the Recruitment Liaison to include templates for flyers, newspaper and media advertisements, brochures for display in clinics, letters to referring investigators or physicians, laminated charts with inclusion/exclusion criteria, a primer on subject recruitment, primer on consent process, primer on subject retention and options for subject handbooks based on material developed by the National CTSA consortium. The success of these recruitment initiatives will be carefully tracked.

CCRO - Children’s Hospital Clinical Research Organization. The CCRO coordinates with the CRSC to streamline and optimize research process at CHCO and to assist CHCO investigators with protocol design, participant safety, feasibility assessment, budget development and recruitment plans. CCRO provides centralized, comprehensive research services and personnel to facilitate the life cycle of research studies conducted at CHCO. The CCRO provides services and a study coordinator pool that the CCTSI traditionally did not provide, thus both organizations have been complementary in the services they offer to investigators. The CCRO has been restructured in the past 2 years to streamline clinical trial conduct/oversight to avoid redundancy and maximize efficiency and cost effectiveness. CCRO works closely with the CRSC to provide integrated resources to investigators. For example, applications for use of CTRC and CCRO resources are now fully integrated into a single process. The CCRO, in collaboration with CRSC, the CHCO CTRC and UCH, is currently working with the CCTSI Quality and Process Improvement Program (QPIP) to further enhance streamlining of processes for feasibility and pre-review of protocols.

DVAMC Research Liaison role. Additional regulatory and operational requirements at the Denver VA hospital add to the challenges to timely approval and early recruitment into clinical research. A Research Liaison role has been established between the VA and SOM to focus on integrating processes and facilitating reviews between the VA and CU-D. The first key integrations are to facilitate the VA’s use of the electronic
system for submission of protocols for review by COMIRB and the establishment of a VA REDCap instance.

3. **Centralized Scientific Review**: The Scientific Advisory and Review Committee (SARC) performs thorough scientific and feasibility review of new research protocols proposing to use services or facilities at one of the five CCTSI CTRC units (described in Section III, page 570). To improve and standardize the quality and safety of all investigator-initiated, non-peer-reviewed clinical research at CU-D, SARC will now expand its role to perform scientific review of all such protocols (whether CTRCs are used or not) submitted to COMIRB to ensure that all research is of an appropriate scientific quality to be conducted safely and ethically. It is estimated that this will add a net of only 30 new protocols per year for SARC review, given the re-assignment of many CTRC protocols to an expedited review process that will not require SARC review (see Section III, page 570). NIH-funded studies (including multi-site) will receive expedited scientific review (not full committee) in view of the multiple peer review approvals that have already been performed on these protocols.

4. **Perinatal Research Triage Committee**. This committee of the CCTSI Child Maternal Health Research program 1) determines the feasibility of all proposed research protocols involving pregnant women and newborns, 2) establishes priorities among the protocols submitted, 3) assures that investigators are fully aware of existing data and biobank resources that may preclude the need to enroll new subjects, and 4) directs investigators to alternative resources and/or research sites when necessary. The feasibility assessment involves using the perinatal Baby Blanket database to estimate the number of available subjects, validating that the study can be accomplished within the specified timeframe and ensuring that the study does not compete for enrollees with other approved studies. This review is now required for all clinical research on perinatal subjects (pregnant mothers, their fetuses, and/or mothers and their newborn infants) across the CCTSI. This process has facilitated collaboration and effectively reduced the competition for these vulnerable populations. (See Section III.2.A for more details)

C. **PRELIMINARY DATA**

1. **IRB Protocol Volume and Time to Approval**. Currently, COMIRB (AAHRPP accredited) has 3,272 active studies and averages approximately 1,230 new approvals per year. COMIRB consists of five review panels: two adult biomedical review panels (mainly investigator-initiated protocols with mean time to approval of 74 days) and one oncology panel (mainly NIH multi-site with mean time to approval of 25 days) that meet every two weeks, one pediatric panel that meets weekly (both PI initiated and NIH multi-site with mean time to approval of 56 days) and one social and behavioral panel that meets weekly (mainly investigator initiated with time to approval of 48 days). The average number of days to approval, including PI response time, for full board reviews is 57 days with 25% of protocols approved on the first review, 45% requiring minor modifications, and 30% requiring more than one full board review. **These approval times have been significantly shortened by a variety of process improvements instituted over the past 4 years (Fig.12)** for multi-site federal grant-funded protocols and for Industry sponsored studies. There still remains room for improvement, especially for investigator-initiated and pediatric studies. The metric to be tracked will be the time for approval for each IRB panel.

2. **Office of Grants and Contracts (OGC) Volume and Time to Completion**. OGC administered 4,315 grants and contracts proposals and 2,146 awards during FY 2012. At any given time, OGC is administering ~5,000 active projects. A number of performance metrics (Table 3) are monitored (and will continued to be tracked) for continuous improvement in service delivery to the CU-D research enterprise. These performance metrics have shown improvement over the past 3 years.

3. **Technology Transfer Office (TTO) Volume**. The CU TTO has been consistently effective in assisting investigators with intellectual property filings, approvals and licensing over the past 4 years. **Table 4** illustrates TTO metrics for the CU system, which includes CU-D, CU-B and the Anschutz Medical Center (AMC), from 2008 to present. These metrics will be reviewed annually by the CCTSI PI and the Exec. Committee.

![Figure 12. IRB Approval Cycle Times](image-url)
D. APPROACH

D.1. Improvement in Processes to Enhance Efficiency and Quality

Through a needs assessment of CCTSI members and non-members (across all affiliated institutions) in March 2011, key informant interviews, and work flow analyses, the T&E program identified regulatory support and process improvement as priority needs of investigators and research study staff. These findings led to the development of the Clinical Research Support Center in which the CCTSI Enhanced Research Environment Program resides, and a university-wide quality improvement plan. The plan, accepted by CU-D senior administration in February 2012, was guided by a logic model for increasing the effectiveness of the regulatory approval process, improving the quality of protocols submitted for regulatory approval and increasing the efficiency of the regulatory approval process. The associated evaluation matrix detailed measures of success over the course of the next 5 years (The full plan is posted on the Regulatory Compliance website along with a baseline report that was written in August 2012 and distributed to faculty to ensure the transparent evaluation and reporting of progress to date). Future process improvement initiatives to reduce redundancy and improve efficiency of the approval process will be conducted in collaboration with the CCTSI quality improvement program.

Enhancing Study Design and Quality of Research. We will enhance the quality of research through optimizing study design. Study design assistance will be provided directly through the Incubator Studio program (Section I, page 526) in which a content expert team is assembled to meet with an investigator to address a question, including design of a proposed study. Biostatistical Consultation (BERD Core) is also encourages to assist investigators at all levels of sophistication with study design. The Responsible Conduct of Research seminar series and Biostatistical Seminar series include sessions on study design techniques and adaptation. Finally, formal coursework on study design is available in the Clinical Sciences Graduate Program. The metric to be tracked will be the percentage of protocols reviewed by SARC that are believed to be of inadequate design – these data will be reported annually by the TEC to the Director/PI and Exec. Committee.

Total cycle time to protocol approval. Negotiations are currently underway with each of the main affiliate partner Hospitals to streamline the protocol approval process further to eliminate redundancy and to improve transparency with regard to the process. The plan is to work with QPIP to map out and streamline the process to develop one portal for all protocol reviews (IRB, SARC, Hospital Research Committee, CCRO, etc.). We will work with our web-designers to develop a single portal for all research related information that is easy to follow based on the UCSF “The Hub” model. The metric to be tracked will be the time to protocol approval from submission, which will be captured in the Protocol Tracking Database (see 2. below) and reported to the PI/Director annually.

Conduct feasibility and budget review. Currently a resource and budget review of proposed protocols is conducted only at SARC and CU Cancer Center review meetings. With a centralized approach using pre-review of protocols via the CRSC, all clinical investigators will be required to submit a protocol and feasibility/ resource/ budget plan for review. These documents will be evaluated by the appropriate entities (hospital research committees, SARC or CRSC) through a centralized routing plan. QPIP is currently working with these entities to establish a single workflow based on a standardized feasibility/resources tool. This will include feasibility assessment based on research subject availability, past performance of the investigator’s team in recruitment and enrollment, resources required, etc. The metric will be the percentage of studies that do not successfully make it through the feasibility or budget review process.

Fast-track approval for clinical trials. Industry-sponsored trials at UCH using CTRC facilities can utilize the fast-track WIRB panel (UCH has been approved by WIRB as a designated site), which commits to reviewing the protocol in 5 days streamlining the approval process for the CTRC, UCH and CU-AMC. The plan is to also be able to provide regulatory approvals within 15 days; the Office of Grants and Contracts is similarly developing a fast-track process for rapid budget and contracting approval. If pilot testing of the process is successful, it will be expanded to all CTRC industry funded research and then expanded further to include CHCO trials. Initial pilot protocols have all had regulatory review in 15 days and contracting time in 40 days. Metrics to be tracked will be time to IRB approval and contract finalization and reported annually to the CCTSI PI/Director and Exec. Committee.

Recruitment facilitation. A number of mechanisms will be put in place to enhance study participant...
recruitment. 1) The afore-mentioned “opt-out” or “opt-in” registration process will be a major improvement in identifying cohorts of potential research participants in our electronic medical records and provide the investigator with a HIPAA compliant means of contacting them. The EMRs at our hospital partners now include records on over 4 million patients. 2) The CRSC Recruitment Liaison will work with the Community Liaisons and scientific staff of our Community Engagement Program (PACT) to collaboratively plan with target communities, from as early as possible in the project development process, key aspects of research projects, including strategies for participant recruitment and data sharing. PACT will serve as a resource to evaluate research materials and review protocols that connect to the community, which may further enhance enrollment (described in Section III, pages 574). 3) Specific recruitment databases have been developed for unique CCTSI programs. One example is the Baby Blanket database that identifies pregnant mothers willing to be involved in research who attend obstetrics clinics at UCH (details in Section III, page 573.)

**Failing and Troubled Studies.** However robust the feasibility modeling, there will be studies that encounter problems with recruitment and retention or other operational issues. Study Monitoring Committees (SMC) for the UCH and CU-B CTRCs currently monitor study enrollment and compare this to targets; this process will be expanded to include the NJH and CHCO CTRCs. To further facilitate consistency across the CTRCs, a recruitment plan will be developed at beginning of each study by the Research Specialists and the PI which will establish the parameters for successful, acceptable, and failing studies. The SMC will be charged with reviewing recruitment metrics for each CTRC study annually based on data entered into the Clinical Trial Management System (CTMS; see below), to be installed and implemented for all CTRC studies by year 2. If enrollment in a study is identified as only “acceptable”, the PI will be contacted by the Research Specialist to provide assistance to enhance recruitment. Where appropriate, the PACT will also advise and assist projects with recruitment and retention plans. If a study is identified as “failing” by the SMC, an improvement plan will constructively be developed with the PI. If a credible plan is not formulated or if it fails, a report of the issues will be sent to COMIRB to consider with the next continuing review. COMIRB has the authority to close failing studies. Once this process has been effectively implemented for CTRC protocols, it will be expanded to include all investigator-initiated and multi-site protocols at all partner institutions under the authority of COMIRB. Metrics will include the number and percent of studies that are closed by COMIRB and reported to PI and EC.

**ClinicalTrials.gov.** The CRSC will ensure that all appropriate studies are initially registered at ClinicalTrials.gov. CRSC resources will be developed and made available to assist investigators in meeting study registration requirements. Resources will include tip sheets and facilitators to assist with the initial upload of information. CRSC will ensure protocol information is reviewed and updated every 6 months, as a quality assurance function. The eventual plan is to automate this process through the new CTMS.

### D.2. New Infrastructure to Improve Processes

**Protocol Tracking Database.** An institutional database system for tracking the complete life cycle of human research protocols is being developed by the CRSC with implementation occurring in three phases: 1) investigator-initiated and grant-funded protocols up to time of final approval (completed September 2012); 2) industry-sponsored protocols to time of approval (due to be completed Spring 2013) and 3) the total life cycle of the human subject protocol (due to be completed Fall 2013). Wherever possible, data are pulled from the primary source database; some data points are entered manually. These metrics (Table 5) will be reported annually to the CCTSI PI, EC and QPIP for review of progress in improving metrics. Using these and other data (see below), the CCTSI Exec. Committee will develop action plans to address studies that are under-performing (examples of action plans in Table 6). In addition, the EC will develop written recommendations for

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<th>Table 5. Protocol Life Cycle Metrics to be Tracked and Reported to CCTSI Executive Committee</th>
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<td><strong>For Federally Funded Studies</strong></td>
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<td>Feasibility and budget cycle time</td>
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<td>Hospital review cycle time</td>
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<td>Other regulatory approval cycle times</td>
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<td>IRB approval</td>
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<td>Time to first subject enrolled</td>
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<td>Recruitment plan tracking</td>
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<td># of Compliance issues</td>
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<td># of Unanticipated problems</td>
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<td>Study closure date - reason</td>
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Electronic Protocol Submission. In 2008, CU procured a system-wide, comprehensive electronic research administration system from InfoEd International, Inc. This system provides a single convenient portal for researchers to interface with the main regulatory offices: 1) OGC conducted its first electronic proposal development in 2011; 2) COMIRB has implemented electronic submission for expedited and exempt human research protocols and is in the process of expanding this process to full board protocols; 3) Since August 2012, the Office of Conflict of Interest has relied on the integration between the grants module and the IRB module to ensure disclosures are on file, and to identify and manage potential financial conflicts of interest.

Electronic Clinical Trial Management System (CTMS). UCH and CU-D are in the process of purchasing and implementing an electronic CTMS system, which will be managed jointly by the CU Cancer center and the CCTSI and initially used for CTRC studies. CHCO is implementing Click Commerce, a similar CTMS, to manage the approval and tracking processes for protocols using CHOC CTRCs. Both systems will integrate with the CU-D electronic regulatory infrastructure to provide a compliant and efficient platform for investigators to manage all aspects of their clinical trials. Importantly, these systems will provide data for the SMCs, CRSC and CCTSI to monitor study enrollment, progress, and completion and will facilitate identifying failing studies.

Research Ethics Core. The Research Ethics Core consists of representatives from bioethics and humanities and the CCTSI Community Engagement, Education, Training & Career Development, and Regulatory Cores. This important Core was developed and funded in large part by the CCTSI. The Core conducts intercampus initiatives including an annual research ethics grand rounds, an annual research ethics conference (which has drawn 100-200 participants), research ethics interactive sessions for clinical research coordinators, orientation sessions for student researchers, and participation in the new campus-wide Responsible Conduct of Research classes. In addition, the Team will offer confidential research ethics consultations to facilitate safe and ethical research. One important initiative of the Research Ethics leadership in collaboration with the PACT Council of the CE&R program is the Research Ethics Committee. Formally established as a sub-committee of the PACT Council in 2012 and in collaboration with the Research Ethics Core and Regulatory Compliance Office, the mission of the Ethics Committee is to investigate and recommend best practices for the ethical conduct of community engaged research. The committee aims to create tools to support bi-directional community-academic research partnerships around such topics as power sharing with the community, consent, data sharing and dissemination of research results.

Office of Corporate Alliance. Established in 2010 with support from the CCTSI, this office has worked to realign the research management strategies of CU-D to fit the emerging landscape of academic research funding. This includes a shift into philanthropy and corporate collaborations as major sources of funding for the research enterprise while maintaining our academic vision and mission. The office is investigating and

![Table 6. SUMMARY - Tracking Methods of Clinical Research Studies and Action Plans to Ensure High Quality, Efficient, & Safe Research](image)

- **High Scientific Quality**: SARC protocol review - Reject poor quality studies; recommendations for improved study design in others
- **Ethically Sound**: SARC and CRSC review - Research Bioethics consult, reject poor studies
- **Study Design Sound**: SARC protocol review - Make recommendations for improved study design, Reject poor quality studies; suggest Incubator Studio session
- **Realistic Recruitment Goals**: SARC, CRSC, CCRO review - CRSC and CCRO assistance to establish realistic goals, COMIRB deferral of non-feasible study
- **Meet Enrollment Targets**: SMCTMS tracking - Targets not met – remediation plan by SMC or COMIRB closure of study
- **Efficient work flow operations**
  - **Prompt Data Analysis**: Protocol Tracking Database - CRSC communicates with investigator and supervisor
  - **Dissemination of Results**: Protocol Tracking Database, Clinical Trials.gov, SMC - SMC contacts investigators with delayed dissemination of results
  - **Vulnerable Populations**: RSA, CRSC, Protocol Tracking Database, COMIRB - Careful study design, monitoring and maintaining AAHRPP accreditation
  - **Decrease Cost of Research**: QPIP, CTMS, T&E - Process improvement plans for increased efficiency; closure of failing or troubled studies
  - **Identify Troubled Studies**: CTMS, SMC, COMIRB continuing review - Remediation plan recommended by SMC or COMIRB closure of study
  - **Clinical Trials.gov**: CRSC - Monitoring and assistance with registration
  - **Multi-site studies**: SMCRSC, CTMS - Monitor key metrics
  - **Speed Contracting, CTAs**: SMCTMS, Protocol Tracking Database, OGC - CRSC and CCRO to assist in budget development, CTA development, etc.
  - **Central IRB adoption**: COMIRB - COMIRB to facilitate centralized and other IRB options at all institutions
developing innovative approaches to integrate academic researchers and their scientific and medical expertise with biopharmaceutical and device company partners, whose project management-oriented, real-time decision making, early kill-no-kill milestone approach to funding research projects is an imperative to sustainably funding novel approaches to curing disease. This new office, directed by Laura Simon, MD is enhancing our abilities to develop new public-private partnerships in a compliant and ethical framework.

**Honest Broker Network - Facilitating access to repository data and/or samples:** In collaboration with the CCTSI Translational Informatics Pillar Program (see Specific Aim 3 of this section) and the CU Cancer Center, a pilot program is currently being developed to facilitate access to EMR data and biosamples from cancer patients stored in existing repositories through a mechanism of de-identification. The Honest Broker Network will ensure that data and/or samples are used in an ethical and safe manner but with limited need for formal regulatory review, thus enabling researchers to access samples with essential clinical data. The plan is to expand over the next 2-3 years the network of repositories through which this model is available and to include the Enterprise Data Warehouses (when established) outlined in Specific Aim 3 below. We believe this will succeed as piloted successfully by the Baby Blanket Program, which has facilitated perinatal research for the past 4 years by establishing a clinical database that is linked to a bio-repository, which houses data and biological samples of women (including placentas) and their newborns who receive their prenatal care and deliver at UCH. This program was set up to reduce the number of prospective studies on a vulnerable population by creating easy access to samples and data already collected in a standardized fashion within an ethical and safe framework. It is the CCTSI plan that the Honest Broker Network will create similar efficiencies and lower cost of research in a broader context.

**D.3. National CTSA Consortium Participation and Active Involvement**

The Enhanced Research Environment Director will continue to:

- participate in the Regulatory Knowledge Key Function Committee and the Clinical Research Management Task Force of the CTSA Consortium;
- act as the “Champion of Change” for the CCTSI and CU-D and participate in the 2nd IRB Pilot Project;
- be involved with several national projects looking at alternative IRB models including the Vanderbilt IRB Share initiative and NeuroNEXT;

The Regulatory Specialists will participate in the Regulatory Knowledge Key Function Committee, including the Recruitment and Retention subcommittee, Research Subject Advocacy subcommittee, IND/IDE subcommittee, and Monitoring/DSMB Affinity Group; the Clinical Research Ethics Key Function Committee; Pediatric Research Ethics Workgroup (Chair); CTSA Consortium Child Health Oversight Committee as well as the CRE Biobank subcommittee and Clinical Research Management KFC.

**II.3. INFORMATICS COORDINATION AND RESEARCH DATA SECURITY SPECIFIC AIM 3: Implement systems to coordinate the access, delivery, and sharing of data resources in a secure and compliant environment for translational researchers and communities**

**A. OBJECTIVES**

By definition, translational research seeks to transition research findings from discovery to implementation. Although the context of “discovery” and “implementation” differ across T0.5-T4 translational research, the challenges of transitioning are similar. For research informatics, the key challenges focus on integrating data across the discovery-implementation domains, where data sources, structures, terminologies, and systems are markedly different. An additional challenge unique to research informatics is managing the transition of data collected during routine clinical care to data that meet significant regulatory constraints for secondary (research) use (3). Finally, the growing presence of team science, with large, geographically dispersed collaborations, requires the use of advanced web-based collaboration platforms, secure data and document sharing mechanisms and research workflow support. (4-6)

Building on the extensive inter-disciplinary relationships built over the previous 4½ years, the CCTSI Translational Informatics Pillar Program will work collaboratively with data owners, application managers, and oversight committees on our campus and across our affiliated Universities and Hospitals to (1) assemble a rich compilation of data collection, integration and distribution resources to provide secure, compliant, and managed data services, and (2) integrate these resources with governance and regulatory oversight requirements and workflows. The close coordination between technical systems with governance and oversight bodies will ensure that appropriate processes are embedded into routine research data management activities, encouraging translational investigators to “do the right thing” within standard data
management activities rather than as separate, disconnected, and burdensome processes. This coordinated approach was extremely successful when the Translational Informatics Program worked with the IRB leadership to develop pre-approved data management language for any investigator who used the CCTSI-supported REDCap data management system.

B. INNOVATION

The diversity of data sources, data integration needs, and data oversight requirements across the multiple affiliated but independent institutions within the CCTSI and across national research networks demands diversity in the technologies deployed and in the data management processes implemented. Yet an uncontrolled “anything goes” approach results in investigator confusion, organizational inconsistencies, and poor data oversight and security. In the Approach below, we present a flexible yet robust model for data management, integration and distribution that provides investigators with multiple technical approaches that are within an overall management framework that meets institutional oversight and data security. Our approach engages a wide range of data and application owners, allowing primary responsibilities for data security and management to remain local while the CCTSI provides centralized coordinating services and oversight. At the same time, we will expand our highly successful model developed for current users of the REDCap system to integrate institutional IRB and HIPAA requirements within the CCTSI data management processes to ensure that research data oversight can be uniformly applied across disparate data systems and networks.

Our approach is innovative in its use of collaborative governance structures that cross local, regional, and national institutional barriers and physical locations. While the data-sharing resources we offer our clinical and translational investigators draw from successful large-scale translational informatics systems, such as i2b2 (7), OMOP (8), HMORN VDW (9), and OSU TRIAD (10) that are deployed throughout the national CTSA consortium, our specific innovative contribution lies in implementing workflows around these technologies that reduce regulatory barriers and support data security needs via distributed governance models and honest broker systems. With our existing experience implementing all of the above technologies at the University of Colorado and at multiple CCTSI partner hospitals and campuses and national collaborations as described in Preliminary Data, our focus on embedding optimal workflows is a logical next step in accelerating translational studies without compromising core values of data sharing, security and oversight.

C. PRELIMINARY DATA

The CCTSI Translational Informatics Program has been engaged in multiple local, regional and national data integration and sharing activities which are summarized in Table 7. The Translational Informatics Program has successfully collaborated with numerous campus and regional CTSA programs to leverage a wider range of translational informatics systems and services than could be supported by the CCTSI Informatics Program resources alone. The key insight from Table 7 is the Translational Informatics Program’s commitment to supporting a robust core set of widely-used data models, informatics platforms, and grid technologies so that translational investigators have multiple options when evaluating their informatics needs.

D. APPROACH

The CCTSI Translational Informatics Program will partner with campus data owners, systems managers, and executive leadership to create a rich, multi-faceted data sharing infrastructure that can provide services and systems to a diverse translational investigator community.

At the same time, we will expand our current Honest Broker System to facilitate data access while ensuring
appropriate regulatory oversight. Our planned technical approach is divided into a CU-D data sharing infrastructure, and a regional and national data sharing infrastructure illustrated in Fig. 13. In addition to a comprehensive technical infrastructure plan, we also describe current highly successful data governance efforts that will be expanded jointly with the multiple regulatory and oversight parties across the CCTSI community in coordination with the growing technical infrastructure.

D.1. The Anschutz Medical Campus (AMC) Translational Informatics Data Integration Strategy

Fig. 13 highlights four data systems groupings across the AMC campus: (1) operational systems, (2) research data sources, (3) data integration systems and (4) regional & national data sharing. In this diagram, multiple data sources come together in the data integration box, which contains the campus-wide clinical & research enterprise data warehouse (CREW) and i2b2 research data marts. These newly approved campus-wide initiatives are where data harmonization, common data elements, and national terminology standards will be applied to create data that can be integrated and shared within and across institutions. Processes to incorporate standard terminologies within the Research Data Sources are described in Section III under Informatics Data Services. Our experience with national i2b2 ontologies in two national pediatric clinical research networks listed in Table 7 (ImproveCareNow/pediatric inflammatory bowel disease and MiPeds/epilepsy) will be expanded across the CCTSI to create ontology-driven data integration ETL services in CREW. We will model our approach on the i2b2 and OMOP ontology-driven data representations where data are stored with an atomic concept representation and then are accessible via multiple terminologies and ontologic structures that are external to the concept representation. Externalizing concept hierarchies has proven extremely flexible and scalable in i2b2 and OMOP for incorporating new data domains rapidly while enabling data access via multiple controlled terminologies.

D.2. The CCTSI Regional and National Translational Informatics Data Sharing Strategy

During the course of this grant, the approach to collecting, securing, storing, linking, using and re-using data pertinent to health and healthcare will be dramatically expanded and transformed, into a new data stewardship framework to support multi-institutional, multi-disciplinary team science. The CCTSI anticipates that its Research Ethics, Community Engagement, Translational Informatics, and discovery resources will collaborate to assess the evolving data landscape and take steps to enable large-scale translational research that was previously impractical.

Following an approach similar to the CU-D strategy described above, Fig. 14 highlights the use of a layered technology approach that allows the Informatics Program to focus on a limited number of technologies while simultaneously providing translational investigators with multiple data sharing options. Many of the technologies proposed for the AMC campus in Fig. 14 also appear in our regional and national data integration and sharing strategies. Fig. 14 presents the available and planned data sharing technologies as functional layers (institutional data repositories, data models/terminologies, record linkage, secure networking protocols, data sharing policies and applications/projects). The CCTSI Translational Informatics personnel have been actively engaged in all of the technologies in Fig. 14. Of note,
OMOP and i2b2 use the same ontology-driven data representation model that is being proposed for the AMC data integration strategy (see previous section). The HMORN Virtual Data Warehouse is a traditional relational model that uses common definitions borrowed from existing standards to create a data sharing infrastructure that has been successfully used by the HMO Research Network and its related disease-specific networks (Cancer Research Network) (11), Cardiovascular Research Network) (12). The CCTSI and its affiliates have embraced the use of local research data management with distributed data sharing/governance. Fig. 14 highlights our use of Ohio State’s TRIAD technology and the i2b2 SHRINE technology for distributed queries. We have successfully implemented TRIAD with the OMOP data model in the SAFTINet distributed research network; we are implementing i2b2/SHRINE as part of two national pediatric data sharing networks (ImproveCareNow and MiPEDS). In addition, we are implementing TRIAD with the HMORN VDW data model to support CHORDS, a regional data sharing project across all five CCTSI affiliated hospitals.

We also highlight two nascent data sharing proposals (Fig. 14) that we will pursue over the 5-year grant period. The Colorado All-Payers Claims Database (APCD) is a state-wide claims database that by state law will capture all health-care related financial transactions on patients in Colorado. (13) At this time, the SAFTINet distributed network is in discussions with APCD to link Medicaid claims data with clinical care data. Dr. Michael Kahn, the CCTSI Informatics Program director, is the informatics lead of that effort. We intend to pursue negotiations with APCD to develop a grid-based data sharing model for access to claims data. CORHIO is Colorado’s state-designated regional health information exchange organization. CORHIO is implementing a state-wide master patient index to support clinical data exchange. We have initiated discussions with CORHIO to extend their master patient index capabilities to include a trusted third party record linkage service using random research subject identifiers. This service will also be grid-enabled to allow participants to obtain random subject IDs from CORHIO. These two services are represented by asterisks in Fig. 14 because of the early stage of negotiations with APCD and CORHIO, respectively.

D.3. Data Security

The CCTSI has worked closely with institutional HIPAA officers, IT security experts, and COMIRB, the centralized IRB for most CCTSI institutions, to ensure close coordination and approval of data security and management processes. The CCTSI hosts its research data management systems in the Colorado School of Public Health (CSPH), which maintains a secure, modern data center that utilizes a state of the art virtualized server environment. CSPH employs a layered defense-in-depth approach in protecting the integrity, confidentiality and availability of the data and ensures best possible compliance to the National Institute of Science and Technology (NIST) SP800-53 security controls. The CSPH data center is NIH approved as FISMA compliant and maintains numerous HIPAA and FERPA-compliant projects.

The CSPH in-house full time Security Administrator holds certifications in ITIL v.3 and Global Information Assurance Certification, GSEC Analyst #32459. The GSEC certification is based heavily on hands-on real world expertise. The Security Administrator role is involved not only in managerial and theoretical security administration and compliance, but also in application aware firewall configuration (Palo Alto), vulnerability scanning (Wireshark, Nessus), penetration testing (Backtrack Linux Suite) and system security assessment (CIS, MBSA). CSPH utilizes independent third party consultants for network resource development and white-box penetration testing. The frequency of scans and what types of scans are needed are determined by the profile of each system, sensitivity of the data held by the system, and compliance requirements. Vulnerabilities are assessed for exploit potential. Exploit potential is then assessed for risk by the Security Administrator, developers and other stakeholders. Risk is then either, mitigated, transferred or documented as acceptable. CSPH is scheduled to complete a comprehensive Risk Assessment and Security Plan by summer 2013 based on the NIST SP800-53 security controls used to assess FISMA compliance. These documents will drive the leadership decision making process, future budget and security planning. The CCTSI, in collaboration with its partners, are pursuing distributed research network architectures across its affiliated clinical institutions. In this model, operational data systems’ and the distributed research networks’ technical security are under the control of the IT organization at each data sharing partner institution. This model ensures that all data sources meet each institution’s specific data security requirements since all data sharing components are housed and maintained by the institution. Inter-institutional security and access control is assured in the OSU TRIAD grid technology by the extensive caGRID GAARDS certificate-based infrastructure.

D.4. Data Governance / Honest Broker

In view of the extensive collaboration amongst the CCTSI Translational Informatics Program, the IRB and all institutional HIPAA and Security Officers, current users of the REDCap Data Management System have
pre-approved data management language that meets all regulatory and security requirements. We will replicate this successful partnering to create data governance structures and processes in collaboration with all key parties to ensure that the new systems deployed exceed regulatory and institutional requirements. DH already has their own instance of REDCap and the DVAMC is in the process of establishing the same system for their researchers.

Our efforts will also focus on extending data governance to include an expanded AMC Honest Broker process. Honest Broker services (HBS) support data sharing by assembling information from existing sources and providing it to researchers in a de-identified manner that complies with the HIPAA Privacy Rule (14-16). Specifically, HBSs address two requirements of the HIPAA Privacy Rule which sometimes present impediments to clinical research: 1) researchers who are not directly responsible for the care of a patient are not permitted to contact that patient directly for enrollment in a study and 2) clinical data may be used without patient consent only if all protected health information has been removed.

Data sharing governance will occur at two levels: AMC campus and CCTSI Regional/National Data Sharing Collaboratives (Fig. 13). At AMC, an existing HBS is being established at the CU-D Cancer Center that is modeled on the HBSs deployed at the University of Pittsburgh and NJH, the latter a CCTSI affiliated site. After seeing the benefits of an automated HBS that was built into the NJH research data warehouse, NJH extended that service to include certified honest brokers who could: (a) broker de-identified or coded data or biosamples that were not in the data warehouse, (b) make determinations of whether research is non-human subjects research, and (c) facilitate coordination between researchers and providers on contacting patients about study participation. This free-to-investigators service is structured as an IRB-approved protocol, and coordinates with three other service protocols for the NJH research data warehouse, the institutional biorepository, and the human live cell core.

The AMC Honest Broker/Data Sharing initiative will address four use cases. It will determine whether a specific request constitutes non-human subject research (NHSR), thus decreasing the administrative burden on both the IRB and investigator. For requests deemed to be NHSR, it will provide data to determine study feasibility by calculating counts of candidates meeting study eligibility criteria, and will provide access to de-identified biospecimens linked to de-identified clinical data. The HBS also will provide identified secondary data extraction from participating data sources for IRB-approved human subject research. The HBS will certify honest brokers at each of the participating data sources who will extract the required data and ensure that only those data approved by the IRB are shared with investigator. Although individual investigators could develop this functionality for each study, a centralized service will provide economies of scale and a nexus of expertise.

Because the CU-D HBS project was initiated by the CU Comprehensive Cancer Center, the current alpha version includes a number of cancer-specific data sources -- the Tumor Registry, the Cancer Center Tissue Banking and Pathology Shared Resource, and Radiation Oncology -- as well as more general ones such as the UCH and CHCO Epic EMR systems, and the Surgical Pathology Archive. In the future, other sources, such as diagnostic radiology, specialized biomarkers, and molecular biology assay results will be added, in coordination with an AMC-wide Enterprise Data Warehouse. Ultimately, any data source that contains direct identifiers is potentially within scope, so the HBS will eventually accept long-term responsibility for sharing de-identified data from completed studies, an NIH directive which most investigators do not have the technical expertise to fulfill. Alternatively, the HBS may coordinate de-identified data submissions to the NCBC-funded, UCSD-hosted iDASH repository, which has the objective to be a national resource for secure, compliant access to high-quality, annotated de-identified data sets. Wherever such data sets are housed, the HBS service will submit descriptions of these data assets in a national resource discovery tool such as Eagle-I.

For regional data sharing we will develop policies and procedures for the simultaneous review and approval of regional data sharing projects based on the existing centralized IRB model. We will establish a standing approved protocol that will allow Honest Brokers at all facilities perform cohort counts to support study feasibility queries during preparatory research. A CCTSI-wide Data Governance Committee will be jointly established with the Informatics and Regulatory Programs, with representatives from all data-sharing partners to ensure executive and regulatory oversight of regional and national data sharing projects.

D.5. National CTSA Consortium informatics Activities

Many of the national CTSA Consortium Informatics activities have focused on inter-institutional data sharing initiatives, including our work with Ohio State University on TRIAD and the University of Alabama Birmingham on FACE. We have been highly active in the REDCap Consortium, including hosting the annual REDCap Days meeting in Breckenridge, Colorado in 2011. Our institutional deployments of Profiles and i2b2 also include participation in their related national user groups and activities. In the future, we will extend our consortium activities to include increased activities in defining common data elements to support data
exchange and reuse. Our efforts to date have also focused on a leadership role in the REDLOC library of structured forms. Dr. Kahn also functioned as the co-Chair of the Informatics KFC from 2009-2011.

D.6. Institutional Commitment

In November 2011, in response to the recommendations of an internal SOM committee, the Dean of the SOM approved the creation of a new campus-wide Center for Biomedical Informatics along with a linked academic Division of Biomedical Informatics and Personalized Medicine in the Department of Medicine. Funds to recruit a Division Head/Center Director and 5-7 new faculty have been secured and recruitment for a Director position is in progress. Included in the new academic Division is the creation of a campus-wide clinical and research data warehouse (CREW – Fig. 13). In June, 2012, executive leadership from four independent legal entities – UCH, CHCO, CU-D and University Physicians Inc. - formally endorsed the creation of a shared combined data resource to support innovative clinical predictive modeling, personalized medicine, and basic biomedical informatics research. Funding has been secured to develop a 10-year capital and operating budget. All four institutions have agreed to share the development and staffing costs for CREW. An initial project plan would have CREW providing limited data queries within 18 months of project launch, with significant additional functional milestones every 6 months thereafter. Dr. Kahn is leading the efforts to set up the governance and implementation structure of CREW.

Additional research-oriented data systems (Table 7) have received institutional funding commitments and are in early stages of planning or implementation. During the next 5 years, all of these systems will be fully operational. Similar systems are also being acquired or developed at CCTSI affiliated sites.

II.4. TRACKING, ASSESSMENT AND EVALUATION  SPECIFIC AIM 4: Catalyze quality and process improvement and ascertain key program impacts through responsive tracking, assessment and evaluation.

A. OBJECTIVES AND SIGNIFICANCE

Efforts related to tracking, assessment and evaluation of the CCTSI are being conducted by The Evaluation Center (TEC), CU Downtown Denver Campus, in coordination with the new Quality and Process Improvement Program (QPIP) in the CCTSI Administrative Core. The TEC external program evaluation thus represents a unique way in which the CCTSI leverages the expertise and resources of another campus of the CU system. As the external evaluator, TEC will be chiefly involved in examining and documenting the impact of the CCTSI on: 1) promoting translational research across the spectrum and across all phases of the research process, 2) establishing a sustainable, efficient, cost-effective, highly-responsive infrastructure and environment for translational research, and 3) engaging diverse investigator communities to leverage these resources to emerge as leaders in cutting-edge translational research. The results of Tracking and Evaluation (T&E) will inform the Director/PI and Executive Committee on priorities for process improvement initiatives to be conducted by QPIP. The evaluation of the ETCD component is outlined in Section IV of the grant. In this section, evaluation plans related to assessing CCTSI’s impact on CTR, including the establishment of a responsive and cost-effective resource-service infrastructure, are described.

Needs Assessment: TEC last administered a needs assessment survey to researchers and trainees in early 2011 to determine the resources/services that investigators consider essential and to what degree these needs are being met effectively. Six hundred thirty nine individuals responded. The results informed a number of new initiatives reflected throughout this proposal, which include: 1) more rigorous support for training and retaining high-quality research study coordinators; 2) efforts to establish enhanced access to EMRs and biological data/samples through biobanks; 3) more frequent solicitations for pilot funding; 4) enhanced support for meeting regulatory requirements and streamlining the interface with regulatory entities; and, 5) expedited processes to enhance capacity to participate in NIH Network and industry-sponsored clinical trials. Annual Needs Assessment surveys are planned for the 5 year grant period (see Approach below).

B. INNOVATION

Since the CCTSI’s inception in 2008, TEC has demonstrated both innovation and an enduring commitment to keeping longer-term goals in the forefront through robust evaluation processes and by communicating resulting findings through frequent face-to-face meetings, a web-based dashboard showing progress toward achieving defined metrics for each program and core, formal reports and presentations, and quarterly briefs to specific Pillar Program Directors. Examples of innovation include: 1) process mapping and workflow analyses of the regulatory review process within and across partner institutions to identify redundancies and inefficiencies and opportunities to streamline and capitalize on unique strengths/capacities; 2) case study analysis of team
D. APPROACH

CCTSI (identifying, engaging, enrolling, and retaining research subjects is a critical and challenging function of the essential success factor for a research unit of production. Revising them to be more efficient is essential for success of the CCTSI. TEC undertook two comprehensive workflow analyses, one focused on investigator-initiated studies and the other necessary to track related metrics systematically and reliably. From November 2011 through June 2012, TEC and retention pilot study of CTRC-supported protocols that revealed current gaps in the infrastructure more important to support the longitudinal tracking of trainees and scholars; and 3) the design of an enrollment programs; 2) development of a searchable, centralized awards management system, which will become even more important to support the longitudinal tracking of trainees and scholars; and 3) the design of an enrollment and retention pilot study of CTRC-supported protocols that revealed current gaps in the infrastructure necessary to track related metrics systematically and reliably. From November 2011 through June 2012, TEC undertook two comprehensive workflow analyses, one focused on investigator-initiated studies and the other on industry-sponsored studies. Results led to recommendations to enhance the quality, efficiency and cost-effectiveness of human subject research and the capacity and competitiveness of CU-D and partner institutions to participate in clinical trials.

Based on T&E results and recommendations, the CCTSI Executive Committee has prioritized the following three process improvement initiatives as priority areas for the QPIP to address during Grant Year 1:
1. Clinical Research Support Center (CRSC): CRSC will focus on developing and implementing work flows and support for pre-study checklists, document preparation, pre-IRB review/critique, and processing of documents required for project start up and monitoring of ongoing compliance. Mapping current processes and revising them to be more efficient is essential for success of the CCTSI.
2. Regulatory Approval: Securing regulatory approval is often considered a significant rate limiting step in translational research. Developing and documenting processes for the incorporation of regulatory compliance into grant/project planning processes is essential, as is assuring that IRB, CTRC, Hospital Research Committees, HIPAA, and other approval processes are clearly understood, streamlined, responsive, relevant, serve to protect subjects, and meet the requirements of process stakeholders, including funding agencies.(17)
3. Subject Recruitment/Retention: Developing, disseminating, and putting into practice clear processes for identifying, engaging, enrolling, and retaining research subjects is a critical and challenging function of the CCTSI (18). An efficient and workable framework to support investigators through this critical process is an essential success factor for a research unit of production.(19)

D. APPROACH

D.1. Needs Assessment Surveys. Over the 5 year grant period, TEC will conduct needs assessments of investigators and trainees annually and focus on trends emerging about the cost, level of utilization, and value of the resources/services for CTR research at our institutions. In addition, utilization-focused reports will be provided and discussed with the Director/PI and Executive Committee. The executive leadership and QPIP will utilize these data, as well as the financial reporting generated by the program income system, in annual data-informed decision making regarding resource allocation and the strategic reallocation of any resulting cost savings. This evaluation will attain particular importance in years 3-5 when NIH CTSA grant funding reductions are greatest.
D.2. Tracking and Evaluation of Targeted Key Programs. Three areas of focus for the evaluation of CCTSI’s impact on CTR will include: 1) the portfolio of CCTSI-supported pilot projects, 2) the quality, enrollment, retention and completion of studies supported by the Resources and Services infrastructure, including the CTRCs, and 3) the research of trainees and KL2 scholars. (Evaluation plans for the latter are presented in Section IV of the grant [ETCD]).

1. Evaluation of the Translational Pilot Program. In order to assess the efficiency of start-up, completion and outcomes of newly awarded CCTSI Pilot Grants, TEC will track the timely completion of regulatory requirements for each new pilot, time of first subject enrollment, interim (6-month) and final (12-month) enrollment and progress reports, and annual follow-up for three years of data analyses, publications and subsequent grant submissions and successes, using the CTMS system and other standardized electronic data capture and survey mechanisms. These data will generate reports that will document timely progress in accomplishing specific aims, identify barriers to timely completion of pilot studies, explore how the experience of conducting the project has supported the development of CTR core competencies, and track follow-on external funding support, patents, publications and presentations that are direct outgrowths of the pilot award. These outcomes, as well as sustained collaboration among awarded investigators, serve as the focus of longitudinal tracking and return-on-investment (ROI) estimates. As new CCTSI Enhanced Research Environment initiatives are implemented (see Specific Aim 2 above), we will be able to track their effect on the efficiency and productivity of Pilot Grant awardees. In addition, TEC will conduct a comparative analysis to determine how the CCTSI Pilot program impacts the research productivity of investigators. Specifically, Pilot awardees' research productivity will be compared to that of the group of applicants who, although not funded, received the next best scores on their pilot grant applications. An initial analysis, conducted with the first cohort of CO-Pilot, Child and Maternal Health Pilot and KL2 awardees (2008-2009), examined the number of grant proposals submitted and the number of grant dollars awarded in the subsequent two years. Results revealed that CCTSI awardees submitted more grant applications than their unfunded peers (4.1 vs. 1.8 per investigator) and received more annual grant dollars than non-awardees ($137,327 vs. $49,485 per investigator). This analysis will be expanded to include additional cohorts and will examine the impact of the pilot program on different types of investigators (e.g., mentored junior versus more senior investigators).

2. Evaluation of Studies supported by the CCTSI Resources & Services Infrastructure: This evaluation will focus on examining the effectiveness of providing a comprehensive array of resources and services to support CTR projects. We will examine a stratified random sample of studies at different phases of development or implementation to explore how each is benefiting from the unique suite of services available in the Resources & Services program: study design and analysis, study implementation, and technology and laboratory analyses. The evaluation will explore how these resources/services enhance the quality, efficiency, cost-effectiveness, innovation and safety of each study included in the sample. In addition to study phase/stage, the sample will be stratified based on type of study (i.e., investigator-initiated versus industry-sponsored), faculty rank of PI for investigator-initiated studies and, for those studies in an analysis phase, whether high-throughput technologies are required for analysis. This stratification will help to elucidate what type of study/investigator may benefit the most from the various resources and services provided to overcome some of the more challenging aspects of the process, such as regulatory review/approval, designing studies that meet the necessary standards of rigor to be clinically significant, accessing sufficient study populations/biological samples, and disseminating results (positive or negative) in a timely fashion. Studies in the earliest (design) phase will be followed to document their evolution over time and how resources and services expedite or otherwise enhance the CTR process. For those studies that have completed data collection and analyses, the evaluation will document evidence that the Population-based Translational Research Programs support timely and meaningful dissemination and expedite the initiation of clinical trials. TEC will examine the research productivity metrics associated with studies receiving support from CCTSI Resources & Services. Bibliometric analyses of resulting publications will be used to determine the relative impact of studies supported at different points of the process through the Resources & Services infrastructure.

D.3. Resource-Service Infrastructure as a Key Feature of the CTR Environment: To promote an environment that fosters CTR and adequately assists investigators, the Resource & Service infrastructure must efficiently and cost-effectively support high-priority projects across their life cycle – from idea generation through dissemination. This infrastructure and capacity must also be sustainable and responsive to an increasingly fiscally-constrained context, locally and nationally. To assess the effectiveness of the CCTSI in meeting the goals of providing quality (client-centered) and cost-effective resources/services, the evaluation will address the questions: 1) What resources/services are most critical to supporting CTR at AMC and partner institutions? 2) To what degree is the CCTSI meeting the resource/service needs of CTR investigators?
3) What standards of quality and cost-effectiveness do the resources/services meet? 4) How satisfied are stakeholders (e.g., investigators, research study coordinators, departmental administrators and research study participants) with existing CTR resources/services? 5) What is the impact of the CCTSI Resource & Service infrastructure on CTR? What opportunities does this infrastructure create that would not be available/possible otherwise (at these or other institutions)? 6) To what degree is the Resource & Service infrastructure sustainable within an increasingly resource-constrained environment? and 7) In what ways do the Program Income System and QPIP work synergistically to support fiscally-sound decision making related to resource allocation? Comprehensive CCTSI Needs Assessment surveys will continue to serve as the primary mechanism for regularly assessing the resources/services that investigators (representing all partner institutions) consider essential to the CTR enterprise, as well as the degree to which these needs are being met effectively.

**D.4. Development of Indicators of Success and Metrics.** During the first year of the current grant cycle, TEC worked closely with each CCTSI program and key function to develop logic models and associated immediate, intermediate and long-term outcomes. These logic models informed the development of detailed evaluation matrices, organized by key evaluation questions and domains of interest, which led to development of indicators of success, metrics and methods/data sources. A similar process has informed the development of this proposal and will guide T&E activities over the course of the next five years. Table 8 presents examples of key indicators of success that have emerged from this process, which involved the Director/PI, Executive Committee, key function directors and the QPIP director. Key indicators of success (i.e., evidence of meeting the goals of the grant) are organized by cross-cutting themes: quality, efficiency, cost-effectiveness, innovation and safety. **Study life cycle metrics.** Specific metrics have been developed for Protocol Tracking (see component D under Enhanced Research Environment above) which will be monitored on at least an annual basis by the PI and the Executive Committee in coordination with the T&E core. Examples of action plans in response to poor study performance are in Table 6. Implementation milestones and timelines have been developed for each program and are located at the end of each grant Section.

**Table 8: Key Indicators Guiding Tracking and Evaluation**

<table>
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<tr>
<th>Quality</th>
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<tr>
<td>Support/services, processes undergo continuous quality improvement to achieve coherence, optimize resource allocation and utilization, and meet investigator needs for quality and cost-effectiveness</td>
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<tr>
<td>Expanded data infrastructure and innovative informatics solutions support more robust monitoring, tracking and reporting for enhanced accountability, transparency</td>
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<td>Standardized, validated tools support feasibility assessments and the disclosure review process (to enhance objectivity, efficiency and transparency)</td>
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<td>Public trust, engagement is fostered through strategic outreach and the safe, ethical conduct of research (including engagement of diverse study participants and timely, meaningful dissemination of results/findings)</td>
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<tr>
<th>Efficiency</th>
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<tr>
<td>Increased efficiency of study start-up (scientific review, regulatory approval, recruitment) is achieved</td>
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<td>Central IRB is expanded to new strategic partners; WIRB expedited process is adopted for rapid response to clinical trials</td>
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<tr>
<td>Investigator and research study coordinator interactions with regulatory entities are streamlined</td>
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<tr>
<td>Prioritized/targeted processes are integrated/consolidated across departments/institutions; redundancies eliminated</td>
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<td>Censuses of industry-sponsored and multi-site clinical trials increases over time</td>
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<th>Cost-Effectiveness</th>
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<td>Proactive support is provided to failing studies; unresponsive studies are closed within a specified timeframe</td>
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<td>Processes and support services are centralized and integrated to achieve economies of scale, enhance access to support</td>
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<tr>
<td>Key transitions across the translational spectrum are expedited through strategic partnerships (e.g., enhanced T0 capacity makes early-stage translational research less costly and expedites process of identifying promising new methods, models, approaches)</td>
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<tr>
<td>Cost-savings (achieved through QPIP) are reallocated/reinvested to sustain robust translational research infrastructure</td>
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<th>Innovation</th>
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<tr>
<td>CCTSI actively promotes creativity in the policies, approaches, and resources/services established to support CTR</td>
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<td>Systems-level initiatives position CCTSI to participate in national consortia projects</td>
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<tr>
<td>New partnership with Colorado State University (CSU) advances translation of basic discoveries from NIH-supported laboratories to support development, testing, and adoption of novel therapeutics, diagnostics</td>
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<tr>
<td>QI and program evaluation expertise is synergistically applied to address initiatives and position CCTSI to remain viable as a comprehensive infrastructure and environment for CTR</td>
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<th>Safety</th>
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<tr>
<td>Safe and ethical conduct of research is proactively supported across spectrum through internal audits and courses/trainings (including RCR requirement)</td>
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<tr>
<td>Internal and external monitoring programs promote compliance and safety monitoring of clinical trials</td>
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<tr>
<td>Data sharing plans adequately address the safe and secure handling of PHI and other sensitive data</td>
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<tr>
<td>HIPAA-compliant data collection and storage systems (e.g., REDCap) are supported for all investigators and are required for IRB approval</td>
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<tr>
<td>“First in human” studies have decreased potential for risk due to increased T0 capacity, achieved through CSU partnership</td>
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**D.5 Quality and Process Improvement Program (QPIP).** To maximize the effectiveness of T&E Core and enhance the Institute’s ability to respond robustly to the priorities of quality, efficiency, cost-effectiveness,
innovation and safety, the CCTSI established a formal QPIP in 2012. Recognizing that increased quality, decreased waste, and transparent processes are hallmarks of contemporary translational research organizations (20), the CCTSI transformed its organizational structure to incorporate the QPIP in a way that was strategically aligned with T&E functions and was directly linked to management (the CCTSI Director and Executive Committee). QPIP is intentionally positioned to leverage existing evaluative capacity (including logic models, indicators and metrics, evaluation findings and recommendations) and develop structured process improvement strategies for priorities determined by the Executive Committee. The leadership of the CCTSI and partner institutions are committed to be fully engaged in the decision-making processes and the resulting needed re-designing of processes to ensure a more efficient and cost-effective operation. The CCTSI QPIP will, through direct interaction with CCTSI management, work to:

- Identify and remove obstacles to efficiency and process improvement in priority areas
- Form clearly identified and empowered process improvement teams
- Link with evaluators to ensure efforts are complementary rather than redundant, and
- Integrate quality and process improvement into CCTSI governance and decision-making structures.

The T&E team. The T&E team is comprised of Ph.D.-credentialed evaluation professionals who collectively bring more than four decades of experience with conducting large-scale evaluations for NIH, NSF, CDC and the U.S. Department of Education with senior-level support staff. The team includes evaluators with specialized quantitative and qualitative expertise who have applied their skills to develop rigorous quasi-experimental designs, engage in policy analysis, and support broad-based organizational change and capacity-building initiatives. As an academically-based center at CU-D Downtown campus, TEC also has a history of effectively engaging colleagues to support economic analyses.

The QPIP team and goals: QPIP is made up of seasoned quality and process improvement medical professionals, directed by David West, PhD, whose research and efforts have focused upon quality improvement activities in both operational settings and in advancing Design-and-Implementation Science. The QPIP team will apply its expertise to improve processes that are considered critical to a successful and efficient CTR enterprise. Specifically, QPIP will be engaged in the innovative application of LEAN (21,22) techniques within a biomedical research setting to achieve the following goals for the CCTSI:

- Efficient use of resources, streamline processes and eliminate of waste (23) (e.g., by CCTSI service centers)
- Elimination of unnecessary variation (24) (to maintain the high-quality and client-centered delivery of services and support, and to maintain high standards of rigor in conducting CTR)
- Achieve cost-savings that can be reinvested in mission-critical aspects of the infrastructure and environment for CTR.

By the end of Year 1, the QPIP will carry out a ten-step process for three priority areas identified above (see C. Preliminary Data). These efforts will culminate in a formal report to the CCTSI PI/Director and the Executive Committee on the findings, process revision recommendations, and lessons learned for each of the three priority areas. The QPIP will ask the Executive Committee to take formal action to adopt revised processes and to fix responsibility/accountability for their maintenance (including the establishment of ongoing metrics for T&E) and future revision/improvement. Additionally, the QPIP will establish a CCTSI Process Improvement Toolkit for use by the QPIP team and CCTSI process owners to initiate and complete their own process improvement activities with a minimum of facilitated assistance from the QPIP.

The QPIP will also propose priorities for process improvement beginning in Year 2 to the PI/Director and the CCTSI Executive Committee. The basis for the efforts undertaken will derive from priorities already identified, and those stemming from ongoing T&E efforts. Already slated for Year 2 and beyond are the following: 1) ensuring safety and protection of human subjects, 2) acceleration of hospital approval processes for research, 3) criteria and process for closure/discontinuation of futile studies, 4) budgeting and contracting/linkage with and streamlining processes with CU office of grants and contracts, and 5) developing/improving processes for networking with other CTSAs and conducting consortium-wide projects with shared/published performance metrics.

II.5. TRANSLATIONAL PILOT PROGRAM  SPECIFIC AIM 5: Expand our comprehensive pilot grant program to promote high quality collaborative T1–T4 investigation throughout the Institute

A. OBJECTIVES AND SIGNIFICANCE

The CCTSI developed a strategic operation to enhance collaborative translational and clinical studies and provide for the cost-effective execution of research projects. The Translational Pilot and Collaborative Studies program (Pilot Program) of the CCTSI is a vital mechanism for facilitating the collaboration and team science
necessary for improved disease prevention, diagnosis, and treatment. The Pilot Program funds people and projects for one year, awarding grants to faculty and trainees under the administration of the CCTSI. The Program provides the infrastructure to organize funding opportunities, prioritize funding opportunities for collaborative efforts in translational medicine, and broaden the reach of the funding opportunities to facilitate integration across Discovery (T1-T2) and Community-Population (T3-T4) Translational Research. To achieve this goal, the Pilot Program seeks to identify areas for potential collaboration, and supply both targeted and open funding opportunities to address specific CCTSI priorities and to open routes for new ideas.

Assurance: The Translational Pilot Programs will not, under any circumstances, support clinical trials beyond Phase IIa in accordance with NCATS guidelines.

The Pilot Program targets four distinct pilot categories of research (Fig. 15), each with its own program:

1) The Colorado (CO)-Pilot Program encompasses funding for trainees through senior investigators, prioritizing interdisciplinary team collaboration on innovative or high risk T1 through T2 research questions, in a disease-agnostic manner. The CO-Pilot Program represents the broadest category of Pilot funding, as well as the highest number of grants funded. This program includes four levels of funding: Mentored Pilot Awards ($30,000) are for beginning investigators (including post-docs and assistant professors in tenure or research tracks) who will partner with two senior mentor investigators. The award is made to the Mentee as the PI of a Mentored Pilot application. Junior Faculty Pilot Awards ($30,000) are for junior faculty who have not attained associate professor rank or above. Independent Investigator / Career Transition Awards ($60,000) are for independent investigators (usually associate or senior assistant professors with independent funding) looking to incorporate a new clinical translational direction into their research. The Team Science Award ($100,000) is for groups of researchers proposing an efficient plan for cross-disciplinary collaboration. A total of $400,000 of annual funding (supported by the CU SOM) is devoted to this program.

Newly added to the CO-Pilot program in 2013 are the CSU-CU Pilot Grants. These will have the same criteria, application and review procedure as the CO-Pilot program, up to $30,000 per award (total of $130,000 per year) and be conducted primarily on the CSU campus. These grants will encourage CSU-CU collaboration and use of Natural Animal Models of Human Disease as well as other unique CSU resources.

2) The Child and Maternal Health (CMH) Pilot Program awards one-year grants to encourage cross-disciplinary and collaborative T1 through T4 clinical and translational research focused on pediatric and maternal health and disease. Emphasis is placed on research in children of all ages as well as pregnant women and mothers that will ultimately improve child and maternal health and prevent diseases that begin in early life. These awards are designed to:

- Promote innovative research teams capable of interacting across disciplines, schools, institutions
- Promote research in children of all ages
- Promote investigation of the mother-child pair to achieve prevention-oriented, life-course outcomes.

This program includes two levels of funding: The Mentored CMH Pilot Award ($25,000) represents an opportunity for a beginning investigator to benefit from strong mentorship and cross-disciplinary training in clinical and translational research. Co-mentorship is required for this award with a primary mentor as the direct supervisor for the candidate and a secondary mentor adding expertise in a related, but different discipline. The Junior Faculty Pilot Award ($25,000) is an opportunity for faculty at the Instructor or Assistant Professor level. While this award carries no mentoring requirement, the proposed project should emphasize collaborations and interactions. A total of $100,000-$180,000 of annual funding (supported by CHCO) is devoted to this program.

3) Community Engagement (CE) Pilot Program: Community Engagement is critical to increase the reach, effectiveness, adoption, implementation, and maintenance of clinical and translational research efforts. Accordingly, the goal of the CCTSI Community Engagement & Research (C&E) Core is to build capacity in community-academic partnerships and transform the existing community research infrastructure using community-based participatory research (CBPR) principles to translate established efficacy into effective implementation at the community or clinic level. The CE Pilot Program is intended to support community-academic partnerships to perform pilot studies that will strengthen relationships and produce preliminary data for future competitive grant applications. Funded projects will encompass partnership development, project planning, capacity building (i.e., data collection and management, recruitment and outreach, etc.) as well as implementation of research projects within specified areas of emphasis chosen by communities (e.g.,
cardiovascular disease, childhood chronic conditions, social emotional health). Applicants must propose work conducted within a partnership between academic researchers and community organizations or individuals. Researchers should employ a community based participatory approach that involves key stakeholders, including persons affected by disparities in health outcomes, as full participants in the proposed research from conception to the design; implementation, analysis, interpretation; and dissemination of research results. Applications focus on T3-T4 translational research, which includes research evaluating the translation of evidence-based interventions or practices into real-world, clinical and community sites. The focus may be clinical, and/or focused on health promotion and disease prevention strategies; or more policy-oriented. A total of $200,000 of annual funding ($100,000 from CTSA grant and $100,000 from the SOM) is devoted to this program. There are two types of one-year CE Pilot Awards:

Joint Pilot Project Awards (up to $30,000) are appropriate for experienced researchers, or junior investigators who demonstrate appropriate mentorship, who have an established community-academic partnership in place and seek funds for a well-defined joint research project that produces preliminary data for future competitive grant applications. Ideally, collaborative proposals will be based upon partnerships that have demonstrated working success in the past. Activities for joint projects may include a) data collection and/or analysis of community-specific information or other quantitative and qualitative data, b) disseminating and translating research findings (e.g. development and implementation of appropriate dissemination tools, such as, fact sheets and policy briefs, to community and academic audiences and to policy-makers), and c) studies of the community translation process, including studies of dissemination methods.

Partnership Development Project Awards (up to $10,000) will support new or potential partnerships. The projects require a two-year commitment: the first year of funding is dedicated to relationship building, exploration of shared areas of interest, creation of a partnership structure, identification of a specific research collaboration, and leading to a research project to be submitted for a one-year Joint Pilot Project Award to be funded in the second year. Partnership Development activities may include a) building relationships between partners, b) exploring shared research interests and identifying capacity building needs, c) developing an Advisory Committee and/or other appropriate partnership infrastructure mechanisms, d) evaluating the partnership process and e) developing a research plan for a Joint Pilot Project.

4) Novel Clinical and Translational Methods Development Program (NCTM). The development of novel methodologies takes at least three steps: (i) identification of a specific research question for which current methodologies are insufficient and for which novel methodologies are needed; (ii) analysis of what resources in individuals, knowledge, and equipment are already available to support the development of any specific novel methodology; and (iii) a process to facilitate the transformation from a need to a functioning novel methodology. These stages are outlined in Fig. 16. The purpose of the NCTM Pilot Program (NCTM) is to develop a process to respond to the needs of researchers in need of the development of novel clinical and translational methodologies. Stage 1 of this process will be an RFA seeking requests from investigators for a novel method needed for their research. These requests will be reviewed by the NCTM Steering Committee, which will generate a list of 3-5 needed methods of highest priority. A second RFA will then be issued seeking competitive applications by other investigators to develop these methods. The Steering Committee will review these applications and award up to $25,000 one-year grants for the development of the method. Finally, these novel methods will be implemented within the CCTS program locally and nationally (where appropriate).

B. INNOVATION

The Translational Pilot Program has initiated a number of innovative operational procedures that will be shared with the CTSA consortium:

1) Electronic Submission / Review: The Translational Pilot Program developed an automated electronic submission and review program for applications. This program enables applicants to access information,
including Frequently Asked Questions (FAQs), regarding every aspect of the application process. Submission of mandatory Letters of Intent and full applications, as well as the review process, is completely electronic, with reviews modeled after the NIH standard review templates and scoring system (1-9 Scale). The applicants receive full written reviews of their applications from two reviewers (primary and secondary). A Review Panel (akin to a Study Section) is held in which the most meritorious applications receive full discussion while applications deemed less meritorious have a full written review but are not discussed. A separate Review Panel for each category of award ensures appropriate peer review. All scores are then forwarded to the Executive Committee of the CCTSI for final decisions regarding funding.

2) Broad program encompassing T1-T4 research: The Translational Pilot Programs are designed specifically to encompass and support T0.5-T4 research, leveraging our new Naturally Occurring Animal Models Core at CSU, Special Populations Programs in Child and Maternal Health Research as well as our expertise in Community Engagement. In addition, by convening selected panels for review of each of the Pilot Award focus areas, the reviewers are deemed to have the requisite expertise.

3) Resource to assist allied Pilot Programs: The success of our Translational Pilot Program has been a model to other Pilot Programs across our Institution and its Affiliates. In this regard, we have partnered with other Pilot programs (e.g., Emergency Medicine and Neurosciences) to provide our electronic templates for submission and review. We have also leveraged the considerable infrastructure for our review process and have aligned the submission, reviews and review panels of these other Awards to the Translational Pilot Program timeline; this has greatly enhanced the efficiencies of these other Pilot Programs.

4) Funding source is primarily from the Institution: The funding source for almost all Translational Pilot Awards is from Institutional funds, leveraging the support to the CCTSI and optimizing the flexibility of funds. This mechanism minimizes the difficulties often encountered with the UL1 grant funding of Pilot Awards at other CTSAs, particularly related to carry-forward requests at the end of a grant year. Since Pilot awards have proven vital to our membership, and have a profound return on investment, having our Pilot program primarily funded by Institutional monies obviates the limitation of having the Pilot program limited to 10% of the total CTSA award budget and enables the expansion of Pilot funding to be unencumbered by the carry-forward limitations of the UL1 grant.

C. PRELIMINARY DATA: Accomplishments during CCTSI funding years 1-4

1) Number of Pilot Awards funded during first grant cycle. One hundred fifty two pilot grants have received a total of $4,287,124 of funding in the first four years of this program (Table 9).

2) Source of funds. In addition to the Institutional funding provided on an annual basis, the CCTSI was awarded ARRA funding directly for the purpose of Pilot Grant funding. The total ARRA award for Pilot funding was $588,815 for a project period of September 2009- September 2011. The funding for other awards of the Translational Pilot Program are from Institutional resources and represent a component of the Institutional Commitment to the CCTSI. Only $100,000 of the CE Pilots and $80,000 of the NCTM grants are derived from NIH CTSA funds.

3) Publications and patents generated

The Translational Pilot awardees average 0.75 publications per Pilot award. There have been several patents applied for and generated from this program.

4) Return on Investment – follow on grant funding. Obtaining subsequent grant funding as the result of data generated from a pilot award generally takes 2-3 or more years. Thus, this measure of return on investment (ROI) for a grantee is best illustrated for our initial cohort of Pilot Awardees from 2008-2009. The overall ROI for this cohort has been 11.3 to 1, with over $12.6 million of funding achieved from an initial
awarding of $1.11 million of pilot awards, with significant ROI for each of the four individual Pilot categories (Fig. 17). Therefore, the return on investment has been highly significant.

Our T&E Core has performed an analysis of funded investigators and the next level of investigators (based on score of the proposal) not funded by the Translational Pilot Program. The Pilot Program funded investigators maintained a greater degree of follow-on funding. A case study of one successful investigator is presented below.

**Case Study:** Steven Moulton, MD, a pediatric surgeon based at Children’s Hospital Colorado, received a $50,000 pilot award in the first year of the CCTSI. This pilot has led to the development of a medical device called CipherOx, which utilizes feature extraction and machine learning techniques to estimate and predict hemodynamic changes related to any form of central blood volume loss, whether it be due to bleeding, dehydration, epidural anesthesia or hemodialysis. CipherOx is currently being developed for use on trauma patients under a $2.1 million grant from the Department of Defense. Dr. Moulton and Dr. Greg Grudic co-developed the technology. They have licensed the technology from the University of Colorado and started a company, Flashback Technologies, Inc., which has secured over $7 million in outside, follow-on funding support, including a $750,000 Phase II STTR/SBIR award from the Department of Defense and a Business Development award from the State of Colorado.

**D. APPROACH**

This section will describe our policies and procedures for the submission, review and oversight of Pilot Grants.

**D.1. Solicitation of applications.** Solicitation of applications to all Translational Pilot Award categories will be synchronized to occur at the same time on an annual basis. This synchronization serves to standardize a timeframe for applications, review and awards for all of the award types. The solicitation for new applications will occur each June (Table 10) and be widely advertised on the CCTSI web site, as well as through numerous email announcements to all faculty and trainees at CUD, CU-B, CSU and all partner hospitals, as well as the community organizations associated with PACT. A “Letter of Intent” by August is mandatory and serves two purposes: choose the appropriate expertise for the review panels, and enable leadership of the Pilot Program to contact individuals for clarification prior to submission of a full application. The prolonged “lag time” (four months) between release of the RFA and the due date in September is intentional and designed to enable applicants to engage in a thoughtful and collaborative effort toward the application.

**D.2. Review of Applications and decision process.** The CO-Pilot, Child and Maternal Health Pilot, and NCTM focus areas have identical criteria for review and evaluation. Each application is scored by the appropriate Review Panel and ranked according to overall impact score. The scores and ranking are then transmitted to the Executive Committee for consideration for funding. Factors that will be considered in the scoring of the applications are:

- **Innovation**
- **Scientific merit of approach**
- **Cross-disciplinary or collaborative focus**
- **Significance to the CCTSI** - Will the results further our understanding / diagnosis / prevention/ or treatment of human diseases?
- **Making use of CCTSI resources** is encouraged and will be taken into account in review, but is not mandatory.
- **Investigator integration** - Have the investigators made use of new collaborations? Are attempts made to integrate basic and translational researchers in discovery translation? Are efforts made to collaborate with community researchers or community members, if relevant?
- **Environment**

The Community Engagement Translational Pilot applications have a unique focus and design and will therefore be reviewed under a separate rubric: The PACT Pilot Grants Committee will review all grant applications, giving preference to those that have the potential to improve community translation and decrease health disparities while meeting the criteria outlined in the RFA. Scoring criteria will include: general responsiveness to the RFA requirements; quality of the study design and measurement methods within the framework of CBPR collaboration; project focus; project outcomes related to community-engagement and translational research; outcomes related to health disparities and the community engagement process; and (for Joint Pilot Projects)
probability of extramural funding, if successful. The Review Committee will present funding recommendations to the PACT Council, which are then sent on to the CCTSI Executive Committee for final funding decisions. Brief, written feedback will be provided to unfunded applicants.

**D.3. Prioritization of Applications.** Prioritization for funding occurs in two stages: The first stage is that each Translational Pilot Program category determines specific and timely areas of investigation that will be “highlighted” in the annual RFA, thus setting the stage and framing the areas of investigation deemed to be most responsive to the RFA. In the second stage, subsequent to the scoring process, the Executive Committee receives a formal report of all applications and discusses, in detail, applications that fall within the “fundable range”. Specifically, applications with widely discrepant scores, virtual “ties”, and applications which border the funding range and have more direct response to RFAs are discussed at length. The Executive Committee provides final authorization of funding based on the prioritization outlined.

**D.4. Business and cost management of funded applications.** Each awardee has an individual account established in his/her name through the Administrative Core. Invoices for services utilized, personnel costs, and other expenses will be paid out of these accounts. The applicants are provided timely reports of spending, balances, and cost management on a regular basis directly from the Administrative Core, which will ensure that accounts are in balance and not overspent.

**D.5. Tracking of progress of each pilot and their outcomes** The T&E Core will provide the tracking of progress for each pilot. (See Tracking, Assessment & Evaluation Section for details). We gauge the success of the Translational Pilot program by data such as numbers of applicants, success rate, grant applicant surveys of satisfaction with the grant process and feedback, and grant productivity as measured by publications, patents, follow-on funding and impact of the research. Career trajectory of mentored pilot awardees is also tracked. For the CE Pilots, establishment of new academic-community partnerships is also a tracking parameter.

**D.6. Process for Evaluation of Pilot Program.** Evaluation of the Translational Pilot Program will involve ongoing tracking and annual surveys of awardees. Metrics to be examined will include: 1) The timely completion of regulatory requirements to allow the pilot study to proceed, 2) Interim (6-month) and final (12-month) progress reports, and 3) annual follow-up for three years, using standardized forms. Progress reports describe progress in accomplishing specific aims including enrollment and retention of subjects, obstacles encountered, the translational potential and reach of awards, how the experience of conducting the CCTSI-supported project has supported the development of translational research core competencies, timely analysis of data and dissemination of results, and follow-on external funding support, patents, publications and presentations. The latter (external funding, patents, publications and presentations), as well as sustained collaboration among awarded investigators, serve as the focus of longitudinal tracking and return-on-investment (ROI) estimates. In addition, Annual Needs Assessment surveys of members and non-members of CCTSI will include questions about the benefits, obstacles, and potential improvements in the Pilot Project Award Program. The diverse character of CCTSI’s portfolio of supported Pilot Project Awards provides a unique opportunity for TEC to pursue more robust evaluative studies. The following vignette is an example:

**Comparative Analysis of how CCTSI Award Programs Impact Research Productivity.** The first cohort of CO-Pilot and Child and Maternal Health awardees were compared to the next group of applicants who, although not funded, received the next best scores. Analysis results revealed that CCTSI Pilot awardees submitted significantly more grant applications on average than their unfunded peers (4.14 vs. 1.81 per investigator). CCTSI awardees also brought in substantially more annual grant-dollars than non-awardees ($137,327 vs. $49,485 per investigator). This analysis will be expanded to include additional cohorts and will examine the differential impact of the program on different types of investigators (e.g., mentored junior versus more senior investigators).

**D.7. Ensure compliance of all pilots with federal and NIH policies (Human subjects, GWAS, stem cells, model organisms).** Each applicant must note, within the application, where relevant inclusion of human subjects, model organisms and animal welfare, GWAS, or stem cell. Furthermore, at the time of review, the review panel notes the appropriateness of the subjects as outlined by the applicant and particularly notes the regulatory requirements which must be met prior to the initiation of the studies, and provides this information to the CCTSI Executive Committee (in effect the “Council” for the Translational Pilot Program). Approval from other appropriate review bodies, such as COMIRB, IACUC, or any other regulatory group relevant to the proposal is required prior to the institution of the award in a “just in time” format. Applicants are strongly
encouraged to attain all relevant regulatory approvals as soon as possible upon receipt of the Translational Pilot award; however, regulatory approval is not required prior to Translational Pilot application. Awardees will be allowed up to 6 months to achieve these approvals following their notice of award. Resources within the CRSC will be available to facilitate this process. If an awardee intends to use any CTRC resources, the research protocol will also require separate SARC submission and approval. CTRC resources include: inpatient and outpatient research facilities, clinical research nursing support, nutrition research support, exercise research laboratory, ancillary funds; and CTRC Core lab support.

Table 11: Translational Pilot Program Funding

<table>
<thead>
<tr>
<th>Program Type</th>
<th>Annual Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO- Pilot Program</td>
<td>$400,000</td>
</tr>
<tr>
<td>Child and Maternal Health Pilot Program</td>
<td>$180,000</td>
</tr>
<tr>
<td>Community Engagement Pilot Program</td>
<td>$200,000</td>
</tr>
<tr>
<td>Novel Clinical and Translational Methods Pilot Program</td>
<td>$100,000</td>
</tr>
<tr>
<td>CSU/CU Pilot Awards</td>
<td>$130,000</td>
</tr>
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</table>

Table 12: CCTSI Program Integration and Interactions with THIS Subsection (Specific Aims)

<table>
<thead>
<tr>
<th>Program</th>
<th>Integration and Interactions with THIS Subsection (Specific Aims)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTR Resources and Services Program</td>
<td>Pre-IRB review of protocols by Scientific Advisory Committee</td>
</tr>
<tr>
<td></td>
<td>Regulatory support via Children’s Clinical Research Organization and Clinical Research Support Center</td>
</tr>
<tr>
<td></td>
<td>Control of data access and security through Research Data management and integration</td>
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<tr>
<td></td>
<td>Process improvement for implementation of clinical research</td>
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<tr>
<td></td>
<td>Resources to facilitate safe, ethical and cost-effective research</td>
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<tr>
<td></td>
<td>Evaluation of user satisfaction and needs</td>
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<tr>
<td></td>
<td>Develop metrics for success</td>
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<tr>
<td></td>
<td>Provides structure by which the translational pilot program can conduct research</td>
</tr>
<tr>
<td>Education, Training, and Career Development</td>
<td>Educational opportunities for researchers and coordinators in biostatistics, research design and conduct of clinical trial</td>
</tr>
<tr>
<td></td>
<td>Establish mandatory training requirements</td>
</tr>
<tr>
<td></td>
<td>Develop CTMS, as well as feasibility and recruitment assessment to facilitate training of the research team</td>
</tr>
</tbody>
</table>

Programs of the CCTSI. Table 12 illustrates many of these programmatic integrations.

F. MILESTONES AND IMPLEMENTATION TIMELINE

Table 13 describes milestones and a timeline for their implementation during the 5 year grant cycle.

<table>
<thead>
<tr>
<th>Specific Aim 1: Establish Organization and Governance</th>
<th>Active Development → Ongoing Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Establish new organizational configuration of CCTSI and new membership and duties of Executive Committee</td>
<td>→ → → → → →</td>
</tr>
<tr>
<td>Establish CCTSI Advisory Council meetings</td>
<td>→ → → → → →</td>
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<thead>
<tr>
<th>Specific Aim 2: Enhance the Research Environment</th>
<th>Active Development → Ongoing Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adopt and integrate CTMS</td>
<td>→ → → → → →</td>
</tr>
<tr>
<td>Development of a centralized clinical research support center</td>
<td>→ → → → → →</td>
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</tbody>
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<tr>
<th>Specific Aim 3: Data resources</th>
<th>Active Development → Ongoing Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development of enterprise data-warehouse</td>
<td>→ → → → → →</td>
</tr>
<tr>
<td>Development of an honest broker system</td>
<td>→ → → → → →</td>
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<tr>
<th>Specific Aim 4: Process improvement and evaluation</th>
<th>Active Development → Ongoing Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formation of QPIP</td>
<td>→ → → → → →</td>
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<tr>
<td>Establishing metrics of success for each program</td>
<td>→ → → → → →</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific Aim 5: Pilot grant program</th>
<th>Active Development → Ongoing Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program expansion to include CSU</td>
<td>→ → → → → →</td>
</tr>
<tr>
<td>Evaluation of the pilot grant program</td>
<td>→ → → → → →</td>
</tr>
</tbody>
</table>
Research Plan

III. Clinical and Translational Resources and Services Section

Specific Aims
1 page

Resources and Services Section
30 pages
III. CLINICAL AND TRANSLATIONAL RESOURCES AND SERVICES

NOTE: Commonly used abbreviations in this section are defined in the table on page 516 of this application.

A. SPECIFIC AIMS

The goal of the Clinical and Translational Resources and Services (R&S) Pillar Program of the CCTSI is to provide broad access to high quality disease-agnostic support for all phases of clinical and translational research (CTR). The R&S Program will complement other NIH and institutional infrastructure investments by leveraging existing resources and avoiding duplication of services; this will be facilitated by the centralized management and oversight of resources and services. The efficiency and cost-effectiveness of these services will be tracked carefully, including cost containment and program income strategies. We will continue to facilitate NIH network and multi-site studies and maximize the number of investigators and studies served by the CCTSI, while promoting collaborations that reduce study time and overall costs. We will provide support for our highly successful investigator-initiated clinical research activities through the CTRC Network and our unique Community Engagement and Child and Maternal Health Research programs. We will extend support through the new Practical Trials and Dissemination-Implementation (PT-D/I) Unit, as well as our new Natural Animal Models Core at Colorado State University.

The Specific Aims, (aligned with Fig. 18) are to:

1. Develop and implement a Program Income System and an evaluative process for cost-effective allocation of resources that supports planning, conduct, analysis, and dissemination of research results.

   We will phase in a Program Income System that includes methods of analyzing the costs of each resource and service, including such elements as equipment use, space, supplies, and personnel. This system will track utilization of CCTSI resources and services at the individual protocol level. We will produce an income program that also encourages and supports creative ideas for translational research, particularly for future researchers.

2. Optimize the infrastructure for implementing and tracking research and support services.

   We will expand the robust space, facilities, and scientific capabilities of the CTRC Network that support CTR across the CCTSI partner institutions. As part of this Aim, a Clinical Trials Management System (CTMS) will be implemented to track resources and services utilization and productivity. This information will be used to meet NIH reporting requirements and inform decision-making on the distribution of CCTSI funds.

3. Integrate and expand our distinctive cross-cutting population-based translational research programs to facilitate research with diverse communities and populations.

   Our three population-based translational research support programs complement and are integrated into all of our resources and services. Our Child and Maternal Health Research Program (CMH) supports multidisciplinary, translational research programs focused on problems that begin early in life, but adversely impact health over the life course. Our Community Engagement and Research Program (CE&R), through community-academic partnerships, provides community-based research assistance, training, and evidence-based practices to support studies aimed at reducing adverse health outcomes and health disparities across Colorado and the Rocky Mountain region. Our new Practical Trials and Dissemination/Implementation Unit supports research to determine the most effective diagnostic and therapeutic strategies in real world settings.

4. Provide a network of services to support investigators in designing, conducting and disseminating the highest quality research.

   High-quality clinical research requires broad training and fundamental support in such areas as study design, sample size calculation, data management, and statistical analysis. We will work with our other CCTSI Programs to provide services that enable investigators to develop successful grant applications and comprehensive research protocols that incorporate optimal study design, patient safety considerations, data management, timely data analysis and lead to the effective dissemination of study results.

5. Strengthen our integrated Network of Translational Technologies (NeTT) and laboratories that provide state-of-the-science services for comprehensive clinical and translational research.

   We will implement a Core Laboratories Tracking & Management System to centralize tracking of the broad range of translational technology resources available to CCTSI members. A major focus is to accurately track utilization to improve cost-efficiencies and prioritization of resource allocation.
B. OBJECTIVES AND SIGNIFICANCE

The overarching goal of CCTSI Clinical and Translational R&S Program is to maximally support our CTR environment by integrating, streamlining, and making the provision of resources and services more cost-effective, efficient, and safe, both within and across sites. The R&S Program will encompass resources and services in four clusters: Study Implementation, Population–based Translational Research Support Programs, Study Design and Analysis, and Laboratory Analysis and Technology (Fig. 18). Objectives for improving the provision of resources and services to CCTSI investigators include:

- Our well established and very successful CTRC Network will continue to promote high quality research through robust scientific review of research protocols, provision of trained and certified personnel to deliver services, specialized research facilities and clinical phenotyping services, and proven technologies. Through implementation of a CTMS and a Core Laboratories Tracking and Management System, there will be rigorous evaluation of processes, cost and resource utilization.

- CCTSI resources and services will continue to be accessible to a wide spectrum of investigators representing diverse research disciplines and levels of seniority, ensuring broad access across CCTSI partner institutions, centers, schools, departments, divisions, hospitals, clinics, and communities.

- A Program Income System will be developed during the first year and phased in to shift the costs of research from the CCTSI budget to investigators, intra- and extramural research grants, and other sources of institutional support (subsidized facilities, pilot support, and personnel).

- A new central management structure of our comprehensive CTR R&S infrastructure (Fig. 18) will serve to complement and avoid duplication of other NIH investments in CCTSI institutions.

- A principal objective is to leverage the extensive breadth of research resources (facilities, equipment, and personnel) at CU and affiliated partners (CHCO, UCH and UC Health System, NJH, DH, DVAMC, CU-B, CSU, and our unique state-wide community research networks) that have a long-standing track record of and commitment to excellence in CTR and successful development of future investigators. A high priority is to optimize the process for approving, implementing and completing NIH network and multi-site studies.

- Rigorous evaluation of the degree to which the R&S Program meets its objective to achieve high standards (e.g., safety, quality, cost-effectiveness) will be supported by the metric-level data available through the CTMS and Core Laboratories Tracking and Management system. Areas that require improvement will be identified and the QPIP will be engaged to address process deficiencies (see Section II).

C. INNOVATION

The new organizational structure for the CCTSI R&S Program represents a major step in innovation by bringing all of the previously separate, and in some cases autonomous, services and resources into a centrally managed structure. This alignment of R&S will enhance the ability to track utilization and costs of all R&S, thereby improving efficiencies of operation and enhancing the ability to respond more quickly to shifting needs of investigators and to make budgetary adjustments. The R&S program will promote innovation by stimulating the incorporation of leading-edge technologies into clinical and translational research. A recent example of this was the support of the CCTSI in the acquisition of a new PET/CT instrument dedicated to research use and the establishment of a radiochemistry lab to synthesize non-commercially available radiopharmaceuticals for use in clinical research. New approaches for the delivery of R&S will be adopted in the proposed award period. One example is the Micro-Grant program, which is a research support strategy that is expected to stimulate novel translational science, particularly among junior investigators.

A broad goal of the CCTSI is to enhance the translation of emerging knowledge from basic laboratories to the development, testing, and adoption of novel clinical discoveries, therapeutics, and diagnostics in appropriately defined populations. As one example of T1-level translation, Drs. Robert Eckel (Endocrinology) and Dennis Roop (Regenerative Medicine) have collaborated to treat a rare genetic disease (lipoprotein lipase deficiency) using human stem cell technologies. These studies are poised for the translation to first-in-human studies, which will use CCTSI facilities and resources. The new partnership with CSU is expected to expand what we refer to as T0.5 translational research (i.e., pre-clinical trials in natural animal models of human disease), which will enhance our capacity for bench-to-bedside translation.

An innovative new feature of the CE&R program that will be adopted in year 1 will be “Community Consults”, which will infuse community input into the early design of T1-T2 clinical research to be conducted in the CTRC Network. PIs preparing new research projects will be invited to meet with community members or patients whose interests are aligned with the proposed research. Community members will provide feedback
about the value of the research to their community, suggestions about patient-centered outcomes that would have meaning to them, comments on study design, ways to make the study more attractive to participants, and ethical concerns. This will provide community and patient input into a research study early in its process so that it may be most responsive to the needs of the patients and community.

D. APPROACH

In this section, we describe the leadership and governance structure of the R&S Programs, followed by policies and procedures governing this Program, a description of the Program Income System and Micro Grant program, and then a description of each resource and service, based on the functional clusters in Fig. 18.

D.1 LEADERSHIP: The CTRC R&S program will be directed by the CCTSI Associate Director, Wendy Kohrt, PhD. Key leaders of each R&S Core and program are identified in Fig. 18. The R&S Management Committee will be chaired by Dr. Kohrt, and consist of each Core Director and administrative staff. This Committee will meet monthly to review usage and productivity of each core and program, progress in the implementation of the Program Income System and address issues that may arise. Before the end of each grant year, Dr. Kohrt and the Committee will review the progress and metrics of each core/program, which will be reported to the Director/PI. Dr. Kohrt, Dr. Sokol and Mr. Lockie will review these metrics and, taking into consideration the funds available, determine the appropriate funding level for each core/program for the next grant year. Qualifications and responsibilities of Drs. Kohrt, Kahn, and Geraci are described in the Integrated Home Leadership section (section B.b.3b). The qualifications and responsibilities of other leaders of the R&S programs are (see Biosketches for further details):

Robert Eckel, MD, will serve as the Director of the CTRC Network, which oversees human CTRC research operations at UCH, CHCO, NJH, and CU-B. From 1993-2008, he was the Program Director of the Adult GCRC and from 2008-2012 he served as the Director of Discovery Translation in the CCTSI. Dr. Eckel will oversee all aspects of CTRC protocol submission, review and implementation and Program Income System implementation, and will work closely with the medical, nursing, bionutrition and core laboratory directors across the entire CTRC Network to ensure coordinated, efficient, and cost-effective efforts.

William Hay, Jr, MD, will direct the CMH Research program and the Perinatal CTRC and will be responsible for those aspects of the CCTSI and the CMH Program that involve life course research. He is Scientific Director of the Perinatal Research Center, with extensive experience of over 35 years conducting and directing continuously NIH funded basic, translational, and clinical research in perinatal medicine and biology. He has been Director and PI of a NICHD T32 Training Program for over 20 years and also is the Program Director of a NICHD K12 Child Health Research Career Development Program.

Jack Westfall, MD, Associate Dean of Rural Medicine in the SOM, will serve as the Director of the CE&R Program. He is the Founding Director of the High Plains Research Network (HPRN), a PBRN, and the Director for the Colorado Area Health Education Center Program Office. For the past 2 years, he has been the Director for the CCTSI Community Engagement Core.

Elaine Morrato, DrPh MPH, is a health services researcher with over 20 years of experience focused on the diffusion and clinical translation of medical innovation and policy. She is a member of the FDA Drug Safety and Risk Management Advisory Committee, which advises on issues of risk management implementation. She is also the Education Leader for an AHRQ-funded Center for Research in Implementation Science and Prevention. Dr. Morrato will lead the PT-D/I Unit and serve as co-investigator in the QPIP.

John Kittelson, PhD, is a biostatistician with expertise in the methodologic aspects of clinical trial design and analysis with particular emphasis on statistical methods related to monitoring clinical trials and is the lead trial statistician on several NIH and industry-sponsored randomized-controlled clinical trials. He has directed the BERD program since 2008. He will continue in the role and oversee the infrastructure for biostatistics consultation and collaboration across the CCTSI.
Frank Accurso, MD, will serve as the Co-director of the CTRC Core Laboratories, with primary responsibility for oversight of the CHCO lab. He has been Child Health/Pediatric Core Laboratory Medical Director for more than 10 years and has been a Principal Investigator on more than 30 CCTSI protocols.

Lisa Maier, MD, will serve as the other Co-director of the CTRC Core Laboratories, with primary responsibility for oversight of the UCH and NJH labs. She is the Director of the CCTSI Inflammation and Immunology Core Laboratory and the Medical Director of the Beryllium Lymphocyte Proliferation Laboratory, which provides diagnostic testing at NJH. As Director of these two laboratories, she has an interest in biomarker and clinical, translational and basic science assay development.

D.2. POLICIES AND PROCEDURES GOVERNING THE CTR R&S PROGRAM

1. Process for Selection of R&S Components. The key components of the R&S Program were selected by the CCTSI Executive Committee to provide both fundamental and specialized support for our strong investigator-initiated CTR programs, and to support NIH multi-site and industry-supported clinical trials. Criteria for selecting CTR R&S to be supported by the CCTSI include the number of investigators who require the resource or service and their source of grant support (NIH is priority), the importance of the resource or service in meeting the needs of investigators across our institutions, the appropriateness of requests for support (e.g., sufficient scientific priority; cost considerations) and whether the resource or service is already available across partner institutions. Special consideration will be given to leveraged co-support of resources and services. For example, the NIH-supported Nutrition and Obesity Research Center (NORC) provides technical expertise for the management of the whole room calorimeter located in the UCH inpatient CTRC and the CCTSI provides personnel support required for this resource. In addition, the CUCCC shares support of several of our Translational Technology laboratories, thereby reducing the cost to the CCTSI.

2. R&S Not Selected. Some resources and services were not selected for support based on low demand, inappropriate requests for services (e.g., low scientific priority, too costly) or duplication of existing services. For example, requests for the establishment of a CTRC unit at DH were not approved due to the lack of a sufficient numbers of investigators to justify extending the CTRC staff to another location and anticipated reductions in NIH CTSA grant support. Similarly, requests for CTRC units at the Barbara Davis Diabetes Center and the Health & Wellness Center at CU-AMC were rejected because the services would duplicate those available in the UCH and CHCO CTRCs, which are in close proximity to these Centers.

Historically, we have demonstrated flexibility in supporting R&S that meet the needs of investigators. In 2008, the CCTSI Translational Informatics Core proposed to expand an internally developed web-based data collection system. In 2009, Vanderbilt released a version of REDCap that was less functional than our home-grown system. However, REDCap allowed for “self-service” forms creation, had a rapidly growing national (now international) user community, and committed significantly more technical resources to its development. The Informatics leadership, with approval of the CCTSI Executive Committee, terminated further development of the local system and reallocated resources to adopt and expand REDCap. More recently, usage metrics highlighted persistent low utilization of the Secondary Database Library and Analysis Center (SeDLAC) despite multiple efforts to promote its use, thus it will no longer be supported. The resources devoted to SeDLAC are being redeployed to focus on Epic-to-REDCap data integration, which has received high priority ratings in recent investigator needs assessments.

3. Tracking, Evaluation and Process Improvement. The mutually-reinforcing mechanisms of tracking, assessment and evaluation, and quality and process improvement will guide the centralized management of the CTR R&S infrastructure.

a. Tracking. R&S utilization will facilitate the development and administration of the Program Income System. However, it will also support assessment of the more global value of the R&S program, which will take into consideration such factors as consumers, process, fiscal responsibility, and sustainability (Fig. 19).

Tracking of R&S utilization will be supported by a robust data collection infrastructure, including a CTMS and a Core Laboratory Tracking and Management System. Guiding metrics will examine: 1) R&S costs, including such elements as: equipment, operations, space, supplies, and personnel; actual vs. projected costs; 2) R&S utilization at the individual protocol level and across the research community that spans CCTSI partner institutions; and 3) productivity, with respect to both proximal (e.g., recruitment, enrollment, attrition) and more distal indicators (e.g., publications, patents, follow-on funding, etc). Tracking at the protocol level will support objectively and proactively identifying failing studies, thereby improving quality, safety, efficiency, and cost-effectiveness. Given the scope and complexity of the tracking necessary to support the integrity of the R&S program, and the importance of these data to other CCTSI components (e.g., inform ETCD programs and...
Clinical Research Support Center [CRSC] services), tracking will be an integrative and collaborative effort involving the T&E Core, Informatics, CRSC, and pillar program leaders and administrators.

b. Assessment and evaluation will be informed by tracking data and by additional data collected from the annual CCTSI Needs Assessment survey of users. External evaluators of the T&E Core will examine data trends and use a balanced scorecard approach (i.e., as represented in Fig. 19) to prepare an annual utilization and needs report that incorporates both quantitative and qualitative indicators. The CTR R&S Director and Steering Committee will annually review these reports as considerations of cost to develop recommendations regarding the continued support for the next year of the individual R&S component cores and programs. These recommendations will be sent to the PI/Director and the Executive Committee for their review and discussion. The Director/PI and the Administrative Director will have final authority for decisions on funding levels of individual CTR R&S components prior to each grant year.

c. Quality and process improvement will be essential to achieving cost effective delivery of services to investigators. Since the R&S program is supported by the largest portion of the CTSA Award, process mapping by the QPIP program of identified R&S priorities is expected to lead to improved efficiency and cost savings through the identification of duplicative or overly tedious structures, systems, processes, resources, and services (Section II, pages 552 for QPIP Approach). These efforts will be particularly important in the early stages of the proposed grant cycle, during the transition to centralized management of R&S and during the development and implementation of an efficient Program Income System. Fig. 19 represents how the T&E Core and QPIP will synergistically inform quality and process improvement to drive positive trends in metrics and indicators associated with consumer needs and satisfaction, business processes, fiscal responsibility, and sustainability of a sound program.

4. Potential problems and alternative approaches

a. To address evolving trends in translational research, we will assess relationships to scientific priority and service needs to determine whether trends justify service requests. As we bring the CTMS and Core Laboratory Tracking and Management systems online in Year 1, the systems will be augmented and customized to address oversight requirements as the need arises. Strategies will be collaboratively developed to streamline sharing and integrating data from the different CTMS platforms. We will develop policies and strategies to project and meet future needs when demands exceed capacity and services available. As an example of how this has been accomplished in the past, the Perinatal Triage Committee (described below) was developed in response to the high demand for services of the Perinatal CTRC that could not be met.

b. We will examine the steps of SARC protocol review and approval to determine areas requiring process improvement if targets in time to protocol implementation are not realized. Particular attention will be directed to accelerating the regulatory and contracting approval of NIH network and industry-sponsored multi-site trials.

5. Metrics for success (Table 14) will be assessed annually and directed toward: a) quality (e.g., enhanced access to R&S that meet the needs of the research community); b) efficiency (e.g., streamlined process for accurately tracking R&S utilization); c) cost-effectiveness (e.g., leveraging R&S support to expand extramural research base); d) innovation (e.g., use of CE&R and PT-D/I key concepts and new technologies to catalyze T1-T4 research); and e) safety (e.g., identifying factors that distinguish successful vs. failing trials).

D.3. PROGRAM INCOME SYSTEM (AIM 1) AND “MICRO GRANT” PROGRAM:

A comprehensive Program Income System will build upon existing systems and will be implemented during Year 1 and phased in completely by Year 3. Funds generated will support personnel, operating supplies, and instrumentation that were previously directly supported by the CTSA grant. As revenues increase, personnel and other core operating expenses will be shifted off of CTSA grant funds and into program income funds. This process will allow the CCTSI program to achieve its goal of increased efficiency and effectiveness, thereby decreasing the overall grant budget in response to the new NCATS funding formula, while retaining...
investigator access to specialized R&S.

**Service Center Model.** CU-D, CU-B, and CSU operate Service Centers to compliantly manage the charging of services within the Institution (e.g., internal users are charged the same rates). The service center program requires a comprehensive cost analysis of the operation to identify all expenses embodied in each service, including overhead for the core. The cost analysis studies must be completed annually and approved by the University. The result of the cost analysis ensures that proper rates are set and charged back to users in a manner compliant with state of Colorado regulations. The system allows for profits to be earned from outside users of a resource but ensures that profit making is not embodied in rates charged to internal users. Profits from external utilization can be used to upgrade and replace instrumentation. The CCTSI Program Income System will be expanded across the network of CCTSI-supported service center accounts, which will be monitored by the University for financial compliance. The CCTSI will purchase and employ a Core Laboratory Tracking and Management system to track activity and to bill investigators or grant accounts for resource and service utilization. The CCTSI Administrative Core will oversee the billing and collection process for each core service center within R&S. The policies and processes by which services will be charged to investigators will be implemented consistently throughout the CCTSI and its affiliated partners. Tiered cost structures will be developed for industry- versus investigator-initiated research. Charge-back systems at each affiliate will be compliant with the specific financial systems at each institution, but efforts will be directed to harmonize the cost structures across institutions as much as possible. Systems will be developed to import utilization metrics into the tracking system from the affiliates for centralized tracking. The implementation of the charge-back system could potentially introduce financial barriers to conducting early pilot research programs across the spectrum of CTR.

**Phasing In of Program Income System.** Historically, utilization of the CTRC Network and BERD services has been provided at no charge (within reasonable boundaries of utilization) to CCTSI members. Over the past year, the CCTSI has established a Program Income System (service centers) for the CTRC Core laboratories; utilization of services over a threshold of $7,000 per year (for up to 3 years) per protocol has been re-charged to investigators. This implementation of re-charge for services for new protocols will be phased in over several years by expanding the types of services included in the Program Income System each year (CTRC core laboratory, biostatistics consultations and hospital laboratory services Year 1, bionutrition Year 2, & CTRC research nursing Year 3). Investigators are being informed of new CCTSI support policies and instructed to include the costs of previously subsidized resources and services in new grant applications or be in a position to cover the costs. To facilitate such planning, costs of services are posted on the CCTSI website. Obligations to currently approved projects, which extend 2 years into the next award period, will be fully honored under the approved protocol budgets, however these will not be extended beyond year 2 of the award.

The revenue generated through the Program Income System will help to offset declining CTSA grant funds, which will occur gradually over 5 years. Table 15 summarizes projections for the major revenue-generating CTR R&S programs in grant year 1 compared to year 5.

**“Micro-Grant” Program.** A new program of “Micro-Grants” will be instituted in Year 1, whereby institutional funds will provide up to $5,000/protocol/year in year 1 (for up to 3 years) to pay for CCTSI resources and services that will be charged to investigators in the new Program Income System. As more

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<tr>
<td>- Access to resources and services that address identified needs of diverse researcher communities</td>
<td>- Centralized system to request and access resources and services</td>
<td>- Program Income System supports tiered fee structure for effective recharge</td>
<td>- Centralized and integrated management of R&amp;S components to achieve economies of scale</td>
<td>- R&amp;S Program proactively promotes and addresses patient safety, biosafety, and data security</td>
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<td>- R&amp;S Program adequately supports the full spectrum of CTR and all phases of the process, including idea generation, study design, start up, implementation, analysis, dissemination</td>
<td>- Streamlined process for tracking utilization</td>
<td>- Adequate infrastructure capacity to support NIH-funded studies, including Network trials</td>
<td>- Innovative models and processes adopted across affiliates to achieve cost-effective delivery and allocation of resources and services</td>
<td>- Ongoing protocol monitoring to support identification of successful, troubled, and successful studies</td>
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<td>- Strategic partnerships to leverage multiple sources of support (NIH, institutional, other) of R&amp;S</td>
<td>- Strategic partnerships that enhance access to and ensure continuity of resources and services that facilitate research translation</td>
<td>- Maintenance or growth in utilization to achieve economies of scale</td>
<td>- Implement key concepts from population-based translational research programs across the spectrum of CTR</td>
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CTRC services are included in the Program Income System, the size of the Micro Grants will be adjusted up to a maximum of $10,000 per year by grant Year 3. The Micro Grants (from institutional funds) will be prioritized to junior investigators with investigator-initiated CTRC protocols and will be based on need, scientific merit, and availability of funds. Each Micro Grant will be administered as an individual account with a defined budget; all expenses will be reconciled on a monthly basis, with reconciliation reports sent quarterly to the investigator. At the time an investigator submits a CTRC protocol application, an option for Micro-Grant funds to support the project can be selected. Requests will be reviewed by Dr. Kohrt (R&S Director) during protocol feasibility assessment to determine if adequate funds are available to support the proposed study. The decision for awarding Micro-Grants will be made jointly by Drs. Kohrt, Eckel, and Sokol and Mr. Lockie (Administrative Director) during monthly meetings. Decisions for funding will be based not on only junior vs. senior status but on need (a pilot study with no or limited funds to support the project), scientific merit (excellent to outstanding score), and availability of funds. The funds dedicated to these Micro Grants will increase each year up to a maximum of nearly $450,000 per year by grant year 5. The outcomes of studies supported by Micro-Grants will be carefully tracked by the T&E Core.

D.4. INDIVIDUAL RESOURCES AND SERVICES

The following description of individual resources and services will follow the format of Fig. 18 and will include the following Clusters of Resources: 1) Study Implementation; 2) Population-based Translational Research Programs; 3) Study Design and Analysis; and 4) Laboratory Analyses and Technologies.

CLUSTER 1: STUDY IMPLEMENTATION

Aim 2 is to optimize the infrastructure for implementing and tracking research and support services. This will be accomplished through the CTRC Network, which supports five clinical and translational research units at four different institutions. The CTRC Network will also contribute to accomplishing Aim 1, through integration with the Tracking & Evaluation plans and Program Income Systems (described in D.2 and D.3).

1.A. CLINICAL TRANSLATIONAL RESEARCH CENTERS (CTRC) NETWORK – Robert Eckel, MD, Director

1. Objectives and Significance: The CTRC Network (clinical research units, research personnel, and support services) evolved from the foundation of two General Clinical Research Center grants that had 45 and 46 continuous years support. The CTRC Network (inpatient and outpatient CTRCs at UCH and CHCO, perinatal mobile CTRC unit, outpatient units at NJH and CU-B) provides investigators with the resources needed for innovative clinical and translational research. The Network fosters a disease-agnostic approach to translational research that meets the needs of over 1,000 PIs and co-investigators from all of our participating institutions. The Network does not duplicate, but rather complements, other NIH infrastructure investments such as centers and institutes (e.g. CU Comprehensive Cancer Center (CUCCC), Nutrition and Obesity Research Center, and NeurNEXT). Clinical resources for multicenter industry- and NIH-sponsored clinical trials are accessed through the CTRC Network to maximize efficiency and enhance subject safety.

2. Innovation: The CTRC Network will create new ways to enhance the safety, quality, and efficiency of clinical and translational research beyond measures in place for clinical research conducted outside the CTRC.

a. Innovations to enhance research participant safety. The CTRC Network will enhance research participant safety through a requirement that all research studies conducted on the CTRCs have a formal safety monitoring plan and regular oversight by the CTRC Safety Monitoring Committee (SMC).

Data and Safety Monitoring Plans (DSMP). All studies using the resources of the CTRC Network are required to have a DSMP. The CTRC Network Study Monitoring Policy is based on overall requirements of the NIH and the monitoring requirements are commensurate with the risk posed to research participants. High risk studies are required to have a DSM Board as part of their DSMP, while participant safety in lower risk research is often monitored directly by the PI directly or by an appointed Safety Officer. Because the requirements for safety monitoring may not be readily apparent for a particular study, and not all investigators are familiar with the design and implementation of research safety oversight procedures, the CTRC Network will assist

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investigators with design and implementation of DSMPs specifically tailored to their studies. The DSMP may also illuminate issues related to efficiency and cost effectiveness. For example, one required element of the DSMP is to provide assurance that adequate funds are available to achieve the specific aims, thereby ensuring that volunteers do not undergo undue risk and resources are not invested in studies unlikely to be completed.

**Study Monitoring Committee (SMC).** The UCH SMC meets monthly to oversee the safety of protocols carried out on the UCH CTRC. The SMC is currently comprised of Barbara Hammack, PhD (chair; research subject advocate), Christine Acquilante, PharmD (investigator), David Badesch, MD (investigator and Research Subject Advocate), Thomas Campbell, MD (investigator and Medical Director, UCH CTRC), and David Weitzenkamp, PhD (biostatistician). All UCH CTRC protocols are reviewed by the SMC before they receive final SARC approval and then undergo annual review by the SMC. The SMC assists investigators with the development of data and safety monitoring plans (DSMP). They review unanticipated problems for all active protocols and make recommendations for updating DSMPs, when necessary. *In Year 1 of the proposed new CTSA grant period, the SMC will be expanded (with addition of appropriate personnel from CHCO, NJH and CU-B) to monitor all CCTSI-supported protocols that involve human subjects.* The responsibilities of the SMC will be expanded to include the review of annual progress reports that include metrics that reflect whether a protocol is proceeding successfully (e.g., recruitment, enrollment, attrition). The SMC will submit a report to the IRB regarding studies that are troubled or failing.

**b. Innovations and assurances to enhance research quality.** The CTRC Network will enhance research quality by participation in national quality assurance programs and providing highly trained and experienced staff to conduct research with CTRC investigators.

*Participation in national quality assurance programs for support of multicenter clinical trials.* When needed, services provided to investigators by the CTRC Network will be certified by national quality assurance programs to allow CCTSI investigators to participate in multisite clinical trials. For example, the UCH CTRC Vascular Imaging Core is certified through the University of Wisconsin Atherosclerosis Imaging Research Program for measurement of carotid artery intima-media thickness and brachial artery flow-mediated dilatation. The availability of quality-certified vascular imaging has allowed UCH CTRC investigators to participate in NIH-funded multicenter investigator clinical trials (ClinicalTrials.gov identifiers NCT00851799, NCT01426438). *A centralized, highly trained and experienced clinical research staff to support clinical investigation and clinical phenotyping in diverse scientific areas.* The CTRC Network research staff are trained to provide investigators with clinical phenotyping services that are not available in other units including: assistance with bronchoscopy for collection of research specimens (NJH), use of metabolic carts (PARVO/VMAX), measurements of insulin sensitivity (CHCO, UCH, CU-B), use of room calorimetry for direct measurements of energy expenditure (UCH), or conduct of exercise testing or training in clinical research (UCH, CU-B, CHCO).

**c. Innovations to enhance research efficiency and cost effectiveness.** The CTRC Network will enhance the efficiency of conducting research by providing investigators with access to dedicated research facilities that have streamlined research review and approval.

*Mobility research units.* In addition to dedicated IP and OP research facilities, the UCH and CHCO CTRCs have mobile research nursing units. Regular hospital or clinic staff who focus on patient care are often not trained in the conduct of rigorous clinical research and divert their attention to busy clinical care commitments rather than investigation. Implementation of the mobile unit brings trained personnel to the bedside and expands the capabilities for conducting research in hospitalized patients in specialized units (e.g., emergency departments, ICUs, operating and post-operative suites).

*Efficient research implementation.* Streamlined research review and approval is a goal for those who seek to conduct research on the CTRC Network. QPIP is currently mapping the process for protocol approval and will oversee process improvement. After scientific review (described in Item 4 below), the various steps of the review process (i.e., human subjects’ protection, administrative and budgetary review) will take place in parallel rather than sequentially. Parallel approval processes through the CTRC Network are expected to provide PIs with shorter regulatory approval times and thus enhance their research efficiency. This is particularly important for investigators who are participating in multicenter clinical trials with competitive enrollment across sites, wherein the ability to begin enrollment sooner allows one to compete for limited enrollment slots.

*Streamlined approval process for NIH network and industry-supported clinical trials.* Attention has been directed to ensuring that NIH-sponsored and industry-sponsored multi-site trials can achieve expedited implementation. CU-D and its affiliates were among the first institutions to implement a multiple institutional IRB (in 1991). Although COMIRB is the institutional IRB for NIH Network trials, investigators have the option of...
using the Western IRB (WIRB) for multi-site industry-sponsored trials. The Assistant Vice Chancellor for Regulatory Compliance, Dr. Lakin, developed and implemented a streamlined process for protocol review and approval that can be completed in 15 days. This administrative efficiency enables CCTSI investigators to compete effectively for participation in trials that limit the number of study sites.

3. Preliminary Data: Choice and justification of resource

A centrally managed R&S program is needed to optimize the safety, quality and efficiency of the CTRC Network. Over the initial CTSA grant cycle, the CTRC program established a track record of providing a resource that meets these needs in both inpatient and outpatient settings. In our view, there is no alternative to the CTRC Network to accomplish the objectives of this CCTSI. The outstanding productivity of all the units in the CTRC Network justifies their continued support. In Year 4, CTRC-supported research generated 256 peer-reviewed publications. Table 16 summarizes CTRC activity in Year 4. Moreover, as shown in Figure 20, the level of productivity of the CTRC Network relative to other CTSAs across the country is remarkable. The number of outpatient visits was >3-fold higher than the majority of other CTSAs (reported at the CTSA Administrator Key Function Committee annual meeting, Oct 2010). The number of inpatient visits (not shown) was also among the highest.

4. Approach

a. Description of Dedicated CTRC units. The UCH CTRC includes an 8-bed inpatient unit and a 17-room outpatient clinic in the Leprino Building (Fig. 3), adjacent and connected to UCH. The inpatient unit includes 6 rooms, a room calorimeter, and a sleep laboratory. The outpatient unit consists of 11 exam rooms, 3 metabolic testing rooms, an exercise physiology room, a vascular imaging room, a 5-chair infusion center, a strength testing room, a research exercise training facility, a cognitive testing room, an imaging room (qPCT, DXA), and a phlebotomy room. The facilities are staffed by research nurses and health technologists. This unit does not offer study coordinator services.

The CHCO CTRC consists of 3 units: an inpatient unit with 5-7 research beds; an outpatient unit with an infusion center; and a mobile unit that can move throughout different departments in CHCO to conduct research visits (essential when medical conditions require specialized clinical care), including inpatient units, outpatient clinics, ER, OR, Procedure Center, PICU, CICU, Surgery, and Dental Clinic. The outpatient unit facilities include 2 research dedicated outpatient halls (pods); one is designed for visits lasting all day, including medication infusions. The CHCO CTRC also shares space with the CHCO Wellness Center, including a dedicated ultrasonography room, an exam room, a shared workroom, and a body composition lab.

The Perinatal CTRC is an entirely mobile unit that provides safe, efficient, and high quality research nursing services (all former NICU nurses) at UCH and CHCO, with the capacity to also perform studies at Exempla St. Joseph Hospital and DH. CTRC Lab space is adjacent to the UCH NICU and in the CHCO NICU. With the addition of the new Maternal Fetal Care Center at CHCO, the Perinatal CTRC has expanded support capabilities to include more complex maternal and fetal research with a new state-of-the-art laboratory. In addition, a REDCap database was developed to better track research nursing staff hours and study visit hours and more accurately identify the scope of the staff capabilities. This will be a valuable resource for calculating workforce requirements and identifying areas for process improvement.

The NJH CTRC specializes in translational research in pulmonary disease, immunology, and allergy. The unit offers research nursing services and special clinical phenotyping in an outpatient setting. Research
Nurse Practitioner services available are history and physical exams, spirometry, allergy skin testing, skin biopsies, EKGs, blood collection, pharmacokinetics, sputum induction, and assistance with bronchoscopies. The subjects are seen in the CTRC outpatient clinic, consisting of 3 exam rooms, 1 interview room, and 1 procedure room. The clinic is staffed with a Nurse Practitioner and RNs.

The **CU-B CTRC** was created in 2000 to meet the growing needs of clinical and translational investigators on the flagship undergraduate campus of the CU system. The CU-B CTRC is located in the Wardenburg Student Health Center and includes a Bionutrition Core, an Informatics Core, a Sample Processing Core, Integrative Physiology Core Laboratory (IPCL), Pharmacy Core and 4 exam/procedure rooms. MDs supervise research performed by NIH-funded PhD scientists.

**NOTE: Clinical Trials Office Services.** Currently the UCH, NJH and CU-B CTRCs do not offer study coordinators or regulatory support personnel on a fee-for-service model, although these services are offered by the Children’s Clinical Research Organization. A Working Group was recently formed at UCH to determine the need and feasibility of a clinical trials office at UCH.

**b. Research Base:** The CTRC Network provides space and safe, efficient, and high quality research nursing services for nearly 417 active protocols of which 95 are multi-site. The protocols are led by 329 PIs at the various CTRCs and span a broad spectrum of disciplines (Fig. 21). Dedicated research facilities and clinical staff ensure data quality and integrity by providing trained and experienced nurses who understand the importance of timely and precise data collection. The staffing for the units will be based upon activity levels that are assessed annually. Staffing details are in the budget justification for each site of the CTRC Network.

**c. Unique Clinical Phenotyping Services.** Unique services offered by the CTRC Network that serve the needs of investigators include: the whole room calorimeter, sleep laboratory, and pQCT at UCH; exercise testing/training, ultrasonography, and DXA at UCH and CHCO; PeaPOD at the Perinatal CTRC; TodPod and BodPod at CHCO; Behavioral Medicine Assessment Core, skin testing, and bronchoscopy at NJH; and vascular physiology and nutrition services at UCH, CHCO, and CU-B.

**Nutrition Core:** The Nutrition Core, led by Janine Higgins, PhD, provides nutrition research expertise and infrastructure. It consists of a team of scientists with extensive experience in nutrition and metabolism research and a food service staff trained to prepare and distribute meals. Services include: dietary intake assessment; measured ad libitum feeding; metabolic meal preparation, design, measurement, and dispensation; growth and body composition measurement in children; resting metabolic rate measurements in children; consultation on study design; dietary counseling; and protocol-specific education and data-collection materials. Of note, this Core is among the most active of all CTSA Nutrition Cores in the country, both in the sheer number of services it provides and number of services per FTE. The Nutrition Core supports over 75 protocols per year.

The Nutrition Core runs a Nutrition Internship Program that trains a diverse range of students interested in pursuing a health care career, from high school students participating in CU SOM Office of Diversity pipeline programs (e.g., Aurora LIGHTS) through college undergraduates studying Nutrition and graduates enrolled in Academy of Nutrition and Dietetics accredited Dietetic Internship programs that are a prerequisite for a Registered Dietician. In 2013, the program will supervise 280 days of trainee activity (9 interns), which will increase to 340 days (14 interns) in 2014.

With the phased reduction of CTSA grant funding in Years 2-5, further cost efficiencies, staff restructuring, and fee-for-service will be introduced as part of the Program Income System. As fee-for-service is introduced, the number of protocols utilizing Nutrition Core services may decline. Using cost projection models, it is anticipated that cost reductions and charge-backs will reduce reliance on CTSA funding by 40% by 2015.

**Integrative Physiology Core Laboratory (IPCL):** The CU-B CTRC IPCL provides highly technical clinical phenotyping measurements of autonomic nervous system-cardiovascular physiology, body composition, exercise testing/intervention and indirect calorimetry, as well as venous occlusion plethysmography, flow-mediated dilation, aortic pulse wave velocity, carotid applanation tonometry, microneurography, and baroreflex sensitivity. A critical objective of the IPCL is to provide opportunities for students, fellows and junior faculty to acquire clinical research skills. Implementation of the newly developed Program Income System will begin in
Year 1. Currently, 30 of the active 35 CU-B protocols use the IPCL.

**Behavioral Medicine Core Lab (BMCL):** The BMCL at the NJH CTRC provides investigators with unique, specialty services in five areas: 1) Psychiatric Diagnosis and Assessment (including structured psychiatric interviews and assessments of psychological adjustment); 2) Interpersonal Assessment (including observational coding and questionnaire based measures of marital, family, parent-child, and patient-provider interaction); 3) Treatment Adherence Assessment (including support for electronic adherence monitoring for pill bottles, respiratory inhalers, and CPAP machines); 4) Health Outcomes Assessment (e.g., quality of life and illness severity); and 5) REDCap-based and other web-based standardized behavioral medicine questionnaires, using copyright protected and other instruments not in the public domain. Since 2008 the BMCL has supported 16 CTRC protocols from 14 different PIs.

**Case Study:** An example of a CTRC protocol that highlights collaboration between multiple CTRC investigators (CU-B and AMC) and unique CTRC resources is the protocol "Impact of insufficient sleep on daily energy balance" directed by Kenneth Wright, Jr., PhD from CU-B. This study examined the effects of sleep, sleep deprivation and recovery sleep on whole-body total daily energy expenditure and during the habitual day and nighttime. Small differences in energy expenditure were observed among sleep stages, but wakefulness during the sleep episode was associated with increased energy expenditure, and therefore supports the hypothesis that sleep conserves energy and that sleep deprivation increases total daily energy expenditure in humans.(25) This study could not have been completed without integrated nursing, nutrition, core laboratory, sleep lab, and metabolic chamber support.

**Undergraduate/Postdoctoral Education:** The CU-B CTRC site provides unique training opportunities in translational research for undergraduate, graduate and post-doctoral fellows. By exposing students to "hands-on" clinical research experience, it is possible to establish an intellectual interest that will, at least for some, lead to a career as a clinical scientist. In this regard, undergraduate and graduate students receive academic credit through the campus Independent Study, Laboratory Rotations, and Research Projects course offerings. These mechanisms allow students to identify satellite faculty investigators of interest, develop a mutually agreeable research training plan, and perform research training in the CU-B CTRC while obtaining up to 3 hours per semester of academic credit. This is a terrific "pipeline" program for clinical researchers of the future.

d. **Organization and Governance, including medical and nursing directors at each institution:** The organizational structure for the CTRC Network is described in Fig. 22, including the Medical Directors and Nurse Managers of each unit.

e. **Approval process for use**

The **Scientific Advisory and Review Committee (SARC)** is a committee of experienced investigators, biostatisticians, and other key personnel who: 1) evaluate the scientific merit of research protocol applications that request use of CTRC resources, 2) evaluate the feasibility of the request in terms of demand on the units and availability of participants, and 3) assign a priority score for resource utilization. SARC meets bi-weekly. Protocols can be either investigator-initiated or industry-initiated and the review process is either expedited or a full review. The expedited review is for multi-site clinical trials, peer-reviewed for scientific merit by the sponsoring agency (e.g. NIH, DOD, foundations) and typically are accompanied by a detailed statistical analysis plan and/or oversight by an independent DSMB or the equivalent (e.g., NIH monitoring committee); or protocols with a finalized research protocol that cannot be changed. For the latter, reviews are rapidly conducted electronically (expedited review) by a SARC co-chair, a biostatistician, and the Research Subject Advocate. SARC full review is typically completed within 7-10 days of submission for electronic reviews and 14-21 days for full board reviews. After approval by SARC, the protocol is sent for review by either COMIRB or WIRB. Hospital Research Committee review occurs simultaneously with SARC review or IRB review.

Once a protocol is approved by SARC and COMIRB (or WIRB), the initiation of the research protocol within the CTRC is the responsibility of the PI with CTRC staff collaboration. The CTRC staff liaison for that particular study meets with the PI and other multi-departmental staff involved in the study to facilitate the implementation of the research plan for the study. Resources and budgetary issues are discussed at this PI meeting as well as ethical and safety concerns and a plan and order sets are created for that protocol.

f. **Tracking of utilization and appropriate distribution of grant funds to individual CTRCs.** All
protocols will be evaluated for financial feasibility by Administrative Core staff before approval. By generating an expanded administrative oversight process, including Drs. Kohrt, Eckel, and the Medical Directors and Nursing Managers, we will expand the current policy of tracking of utilization and appropriate distribution of grant funds to the entire CTRC Network. Implementation of a CTMS will enable the gathering of metrics related to protocol success, including screening and accrual rates, active and completed participants, compliance with the approved budget, and protocol completion.

**g. Cost recovery plan.** An increasing need to accommodate the diminishing CTSA grant support over the ensuing 5 years is cost-containment. For all new protocols, PIs are now told to request support for all costs that relate to CTRC utilization, other than facility fees, from the funding agency or other sources available to the PI. The existing policy during the first CCTSI funding cycle allowed for a stipend of up to a $7000/protocol/year to pay for non-CTRC services required. This policy was instituted to maintain an atmosphere that encourages translational research on the CTRC, particularly for junior investigators, and allowed protocols that are funded by outside agencies to be executed when approved budgets are deficient. This policy will now be replaced by a new “Micro-Grants” program (see D.3 above), which will competitively award small grants to help (preferentially) junior investigators to buy CCTSI services and cover other costs of the research. The decision for awarding Micro-Grants will be made jointly by Drs. Kohrt, Eckel, and Sokol and Mr. Lockie (Administrative Director) during monthly meetings. Letters of approval for CTRC resources will explicitly state the cost and level of funding for all resources to be used, including the Micro-Grants.

The CTRC Network supports both industry- and federally-sponsored research. Industry-sponsored trials operate on a fee-for-service rate structure that provides full cost recovery. The reduced costs to investigators conducting federally sponsored research are enabled by subsidies from the institution and NIH infrastructure grants. In no case will a clinical study or trial be initiated until funding is secured. We expect that demand for these services will steadily increase and sufficient revenue will be generated to support the costs.

**h. Potential Problems and Alternative Approaches**

*Reduction in investigator-initiated research:* The reduction in the CTSA grant support may reduce utilization of CTRC units and consequently lower the need for research nurse support. Thus, a cutback in 24/7 coverage for the IP CTRC unit at UCH is one change that may prove to be necessary. Another alternative is to close the IP CTRC units on weekends. This modification in research support may pose a challenge to investigators and their clinical coordinators in sustaining the existing research atmosphere, recruitment of participants, and scheduling. Continued and integrated cross-training of staff from the CHCO and Perinatal CTRCs will provide flexibility in nursing staff coverage. This strategy may also serve to address outpatient coverage, if necessary, at not only UCH and CHCO but also the NJH and CU-B sites. Another concern for CTRC investigators is the increased emphasis on a fee-based system, a policy that may be a disincentive to investigator-initiated research. The Micro-Grant program aims to mitigate the impact of declining CTSA grant support.

*Scheduling and Tracking of research subjects:* The database used by the CTRCs is the Center Administrative Management Program (CAMP) system originally developed by the Cornell University GCRC to track Center activity related to active protocols, research subject visits, nursing acuity, and ancillary costs. The CAMP database has continued to be supported by the Cornell program and further adapted to CTSA programs. The program does not integrate scheduling functionality and protocol budget vs. actual tracking of protocols. With the high level of outpatient activity by the CTRCs and the inability of CAMP to “communicate” with our EMR (Epic), continued utilization of the existing database is labor intensive and inefficient. In addition, the “mobile” nature of the Perinatal CTRC operation embodies a complexity of nursing hours and activities that are not adequately tracked in the CAMP database. A REDCap database has been developed by the Perinatal CTRC and is currently being evaluated as a better method of tracking acuity and hours devoted to each protocol. In addition, CU-D and UCH are jointly evaluating and planning to purchase a CTMS to provide enhanced capabilities to manage clinical research protocols. Patient visit information and budget vs. actual financial data will be automatically fed from Epic to the CTMS through direct data connections. These new approaches will be valuable resources for calculating workforce requirements and identifying areas for process improvement for the CTRC Network.

**i. Metrics for Success** will be based on quality, efficiency, cost-effectiveness, innovation, and safety:

- Quality of services provided: utilization by a diverse research community and user satisfaction. Assuring full spectrum CTRC support for all phases of the research process.
- Efficiency of protocol implementation: tracking enrollment and utilization by protocol (by the CTMS).
- Cost-effectiveness: Program Income System and tracking systems to inform decisions for equitable
distribution of CTSA grant funds.

- Innovation: effectiveness of the new Micro-Grant program to sustain a high level of clinical research in a cost-effective manner.
- Safety: maintain a high level of surveillance to assure participant safety in CTRC studies.

**CLUSTER 2: POPULATION-BASED TRANSLATIONAL RESEARCH SUPPORT PROGRAMS**

**Aim 3** is to integrate and expand our distinctive cross-cutting population-based translational research support programs to facilitate research with diverse communities and populations. These programs include the Child and Maternal Health Research Program, the Community Engagement Research Program, and the Practical Trials and Dissemination/Implementation Unit. Some services within these programs will also contribute to accomplishing **Aim 1**, via integration with the tracking and charge-back systems (section D.3).

**2.A. CHILD AND MATERNAL HEALTH (CMH) RESEARCH PROGRAM** - William Hay, Jr, MD, Director

1. **Objectives and Significance:** The overall goal of the CCTSI CMH program is to develop a new generation of CMH researchers trained in the complexities of translational research involving pregnant women, their newborn infants, and children of all ages by providing unique services and expertise to investigators and trainees. The CMH program raises awareness of: CMH investigators within the CCTSI of ongoing CMH research; mechanisms for assistance to participate and succeed; pilot grant opportunities; and potential collaborations with on-going research programs and CMH Working Group initiatives. The CMH Research Program emphasizes the maternal-infant dyad, but all aspects of child health (pediatric) and pregnancy-related research are included, allowing expansion into life course research (**Fig. 23**). Within the CCTSI framework, the CMH program integrates our outstanding child health and maternal-fetal research programs and provides a scaffold for initiating new collaborations among basic, clinical, and translational scientists in multiple disciplines in the medical center and the community, and a streamlined infrastructure for longitudinal studies to accommodate life course research. The infrastructure in this program provides a national model for other CTSA centers engaged in life course research.

2. **Innovation.** The use of adult models for the study of diseases of infancy and childhood is not appropriate as a basis for CMH research because of the importance of the developmental trajectory that encompasses fetal and neonatal life, infancy, childhood, and adolescence and life course events including conception, birth, immune development, school performance (motor, mental, social), marriage, career performance, and pregnancy. An additional essential consideration is that maternal health and disease have a direct, life-long impact on the health of the child and, particularly for female offspring, may be transmitted from one generation to the next. For these reasons, research and training in CMH cannot be solely encompassed within research programs focused on adult diseases. We have developed our innovative CMH program with these unique attributes in mind, to address the special complexities of life course and prevention-oriented research. **This approach was used to establish the CTSA Consortium Child Health Oversight Committee (CC-CHOC) Adult-Pediatric Life Course Working Group.** Our innovative program provides a model for NCATS and the other CTSA programs and could serve as a basis for development of best practices for research, training, infrastructure, and regulatory processes in child and maternal health search throughout the CTSA Consortium and provide links with major national NIH-supported studies, such as the National Children’s Study.

3. **Preliminary data:** **Choice and justification of resource:** Because of its focus on research across the life course, the CCTSI CMH Research program bridges across many research programs at CU-D and its partner hospitals (including CHCO), such as the Center for Global Health Section on Global Maternal Child Health Research, the Obstetrics-Pediatrics Center for the Prevention of Prematurity, the Program in Maternal and Developmental Origins of Obesity, the Colorado Program in Nutrition and Developmental Health, and the Children’s Outcome Research Program. The CCTSI is a logical home for CMH research resources, given the reach of the CMH program across numerous departments, colleges, schools, and institutions. The prior robust utilization of the Perinatal and CHCO CTRC services (see utilization **Table 16**) and the major impact of studies...
conducted in this unit further justify retaining this program in our new 5 year CCTSI grant cycle. Our Institution has produced many of the top leaders in pediatric and perinatal research for decades, with seminal programs in maternal, placental, and fetal physiology and campus-wide collaborations in medical, behavioral, outcomes, and community-based research. Many of these leaders used the CMH research resources, and the Perinatal and CHCO CTRCs for support of their investigations. Recent expansion of our CU-D, CHCO and UCH programs in pregnancy and fetal research have further enriched our research and training opportunities in CMH, such as the Baby Blanket Program (described below), and fetal diagnostics and fetal surgery in the new Colorado Institute of Maternal Fetal Health (at CHCO and UCH) and the Perinatal Research Center.

4. Approach

   a. Description of CMH Resources: The CMH Research program provides important R&S to members of the CCTSI that promote and support life course research in pregnant women and children of all ages.

   1. Colorado Baby Blanket Research Program: This CMH priority research program, directed by Anne Lynch MD, MSPH (Co-director of the CMH Research Program), promotes and facilitates perinatal research through the Perinatal Clinical Database and a directly linked Biospecimen Repository, which provide unique and rich sources of longitudinal clinical data and biological samples. The perinatal database includes information on maternal risk factors, events during labor and delivery, pregnancy complications, and neonatal outcomes. It now holds information from over 20,000 women who delivered their babies at UCH. The program is expanding to collect data and samples from women in labor and at the time of delivery (mother, placenta, cord blood, neonate) and on select groups of neonates (e.g., preterm), infants, and children. One year into the project, 50% of the women who receive early prenatal care at the UCH pregnancy clinics are part of the program. This novel program has already consulted with over 55 investigators and has generated over 10 published manuscripts (with at least 7 in preparation) and 37 abstracts. One NIH R21 grant currently uses the longitudinal samples and data, with several projects in the pipeline from the CSPH and the SOM. This program was recognized at two national meetings in 2012 (AAHRPP and the Clinical Research Management Workshop at Yale) and has provided consultations regarding the infrastructure necessary to conduct clinical translational research in perinatal subjects to many researchers across the U.S.

   The Baby Blanket program provides several services for investigators. Its Clinical Service provides research nurse/midwife coordinators who recruit pregnant women into available clinical protocols. Every woman attending the UCH clinic for her first prenatal visit is invited to be part of the program. They are consented (REDCap supported Research Recruitment Form) to be part of the program and clinical data are collected and repeated during the second and third trimester. Pregnancy outcomes are collected on Labor and Delivery by the data management team. All records are reviewed by Dr. Lynch and, if necessary, an MFM Specialist to ensure the data are of high quality and that there is no misclassification of the pregnancy outcomes. The Data Management and Analytic Service provides consultation for researchers across CU-AMC on the availability and use of the Perinatal Database (and other databases), the linked Biorepository, study design, biostatistics, data analysis, and abstract and manuscript preparation unique to the perinatal subject population and clinical research requirements. The Data Management Core interacts with other databases: the Colorado Kaiser Permanente Perinatal Database, the Birth Certificate Dataset from the Colorado Department of Public Health and Environment, and the NICHD-Colorado MFMU Network datasets. The Biorepository Service provides access to the data-linked biological samples (up to ten aliquots of serum and plasma and aliquots of the buffy coat for DNA) that are collected from each subject and stored in the CCTSI freezer bank and tracked with the CCTSI-supported Freezer Works sample management software.

   2. Perinatal Research Facilitation: The Perinatal Triage and Research Facilitation Committees were developed in 2011 in response to campus-wide concerns to protect the vulnerable patient population of pregnant women and their newborn infants and provide a fair approach to allocation of this limited patient population among investigators. These committees assist investigators who are establishing studies that involve recruitment of pregnant or postpartum women and their infants. If the Perinatal Triage Committee identifies a problem with the protocol (e.g., unrealistic sample size expectations), it is directed to the Perinatal Research Facilitation committee, which includes senior leaders from the CCTSI (Drs. Hay, Sokol, and Eckel), the Department of Ob/Gyn (Dr. Santoro) and the Office of Regulatory Affairs (Dr. Lakin). These committees and this review process have garnered acceptance among investigators and established campus-wide awareness regarding protection of this vulnerable population of subjects. With over 40 protocols reviewed in the past 18 months, the review process has streamlined perinatal recruitment, facilitated investigator collaborations, and protected these volunteers from “research fatigue.”
3. **CMH Pilot Grant Program.** Described in more detail in Section II page 554, this program funds up to 9 pilot awards of up to $20,000 per year for research in CMH.

b. **Organization and Governance:** The Program Director for CMH is Dr. William Hay. The **CMH Planning and Oversight Committee** is chaired by Dr. Hay and includes broad representation across the entire CCTSI, including representatives from Pediatrics, ObGyn, Medicine, Surgery, Psychiatry, Psychology, Pharmacy and Pharmaceutical Sciences, the SOD, the CON, the CSPH, Engineering, Native American affairs, and community partners. The committee meets monthly and addresses operational issues and assists investigators with planning of studies.

c. **Tracking of utilization and appropriate distribution of grant funds:** Currently, all tracking of R&S utilization occurs internally within the CMH program and is overseen by Dr. Lynch and Christine Reed, Perinatal CTRC Research Nurse Manager. This activity will be merged into the new Core Laboratory Tracking and Management System to facilitate tracking and evaluation by the R&S Management Committee.

d. **Cost recovery plan:** Program income will be generated through a fee-based system for use of data and biological samples from the Perinatal Clinical Database and Biospecimen Repository. These funds will be used to offset the reduction in NIH CTSA grant support, allowing maintenance of all offered services.

e. **Potential problems, alternative approaches:** Developmental origins and life course research in humans is difficult due to their longevity and the later-life development of chronic conditions that begin early in life. Key to successful research in this area, therefore, is broad engagement of investigators who study problems of similar origin and nature at different stages of the life course. The CMH program has specifically involved researchers engaged in studies of pregnant mothers, the fetus, the newborn, infants, children, adolescents, and all ages of adults. Collaboration among such researchers and their studies are fundamental and a major emphasis for successful CMH Pilot Grants. To assist with this type of research, the Perinatal Database and its linked Biorepository must be expanded to later stages of life; new funding will be necessary to realize this. Furthermore, most of the life course is spent outside of the hospital and at home in communities, requiring new and innovative ways to track individuals who enter the research programs at early stages of life (as part of the pregnant mother/infant dyad, for example) but then move to their home and community settings.

f. **Metrics of success.** Indicators of success (Table 14) of this program include:

- Quality: utilization of services and specimens and user satisfaction.
- Efficiency: appropriate centralized process for tracking utilization by protocol (e.g., CTMS).
- Cost-effectiveness: Program Income Systems and tracking systems to inform decisions for equitable distribution of CTSA grant funds.
- Innovation: use of services and resources to generate novel hypotheses
- Safety: maintain high level of surveillance to assure safety of pregnant women, infant and pediatric subjects.

2.B. **COMMUNITY ENGAGEMENT & RESEARCH PROGRAM (CE&R)** - John (Jack) Westfall, MD MPH, Director

1. **Objectives:** The goal of this Program is to infuse and elevate patient-centered, community-engaged research across the translational research spectrum to strengthen the links among research discovery, bidirectional translation, and implementation. By engaging the community in the continuum of medical research, new discoveries can be efficiently and safely translated to provide the right care, to the right patient, at the right time. (26) The CE&R Core utilizes innovative community-academic partnerships to optimize and mobilize individual and collective capacity to promote facilitation of quality, community-relevant science.

2. **Innovation:** Our ultimate goal is to reduce health disparities in the Rocky Mountain Region through targeted investments in community translational research, followed by wider dissemination of successful practices. We will continue to transform and support the existing research infrastructure using Community-based Participatory Research (CBPR) principles and build new capacities in our community-academic partnerships. Our dynamic Partnership of Academicians and Communities for Translation (PACT) facilitates bidirectional exchange between our communities and academic programs. The PACT Council is the governing body of the PACT and manages the work and resources of the CE Core. PACT Council members are academic investigators and influential representatives from focus communities, affiliate organizations, and academic research institutions. Community and academic members are represented in equal numbers (8-10) on the Council and are compensated equally for their time and contributions. The PACT Council has a truly shared power structure and applies this shared power and decision making to resource allocation within the CE Core programs. The PACT Council commits personnel and informatics resources to our partner communities to support our shared translational research agenda. We will adapt successful interventions and test
disseminations to the remaining PACT communities, which include more than 1,000 physician practices, 30 hospitals and 2 million individuals and includes a strong representation of rural, underserved and minority populations, including Latino, American Indian/Alaska Native, African American and Asian American/ Pacific Islanders. We believe that the PACT and the CE&R Core bring together an effective program for reducing health disparities in Colorado and can serve as a national model for addressing them.

3. Preliminary data

Choice and justification of resource: The CE&R Core elevates patient-centered, practice-based and community-engaged research throughout the translational research spectrum, from T0.5 to T4; strengthening the bidirectional links between the academic medical center, healthcare providers, and community members. Through a robust portfolio of resources, the CE&R Core provides a multitude of services including: training, community liaison services, pilot funding, consultation, technical assistance, and mentoring to increase the workforce and build the capacity of Colorado researchers, community organizations and practices to conduct mutually beneficial, community-engaged research. It was an easy choice to include this unique resource.

Utilization and Accomplishments in Years 1 to 4 of the CCTSI

- 100 community and academic partners have completed the 8-hour CE&R Introduction to CBPR training.
- 58 faculty, postdoctoral students, research team members and graduate students have completed the 6-month Colorado Immersion Training (CIT) in CE&R; 14 CIT participants have led or been key developers of 19 grant applications (including a NIH R25 and 3 NIH Career Development Grant applications) with CE&R as a core component and 14 have been funded ($3.4M).
- The PACT Council has approved 4 cohorts of pilot awards, totaling 44 projects and $881,530 in funding. An initial investment of $681,530 for the first 3 cohorts has yielded $5.2 million in additional funding support.
- The first 3 cohorts of CE&R Pilot Grantees have more than 18 publications, manuscripts and presentations.
- The CE&R program developed 3 educational courses offered at CU-D AMC for graduate school credit.
- Community liaisons have featured their work in 35 presentations/publications.
- The CE&R and PACT Council have 7 manuscripts published, in review, or in development.
- The annual Research Exchange and Poster Session has attracted 500 participants and featured more than 100 poster presentations over the past three years.
- 450 people from all over Colorado participate in the Engaging Communities in Education and Research Conference each year, co-sponsored by the CE&R Core.
- The PACT Council and CE&R Core have submitted 7 grants with our community partners, resulting in $2.1 million in funding to support community-engaged research projects.

4. Approach and Innovation:

a. Description of resources: The CE&R Core provides community engagement expertise and support in training, community research liaisons services, pilot grant funding, academic and community research consultation, technical assistance, and mentoring to increase the translational research workforce and build the capacity of researchers, community organizations and clinical practices to conduct community-engaged research studies that can rapidly improve health in our communities. Some highlights are:

CE Pilot Grant Program: The CE Pilot Grant Program supports community-academic partnerships to perform pilot studies that will strengthen relationships and produce preliminary data for future competitive grant applications. The development of innovative interventions or the adaptation and implementation of existing discoveries and evidence into the community setting is the expected long-term outcome.

Education and Training for Academic Researchers: The CE&R Core will provide ongoing, in-depth training for researchers in the principles of CBPR. Researchers must engage with communities to fully understand how the social determinants of health; stress, racism, economics, education impact individual and community health. Longitudinal, community immersion experiences will provide a context to help researchers understand how community level determinants impact health outcomes. The CE Core will provide a variety of
educational programs ranging from 1-hour seminars, to full day symposia, to our 6-month Immersion Training. Two of our educational programs provide graduate level course credit. 100 people have completed the eight-hour CE Introduction to CBPR training over three years, 58 have completed the 6-month Immersion Training.

**Education and Training for Community Members:** Community training opportunities increase understanding about the research process, build trust between University and Community, and enhance community capacity to participate in research partnerships with academic investigators. The CE Core (along with the ETCD program) has created and will make available a variety of educational opportunities suitable for individuals who simply want to know more about academic research and how they can get involved, as well as more in-depth programs that provide community-based organizations with training and technical assistance on topics ranging from grant writing and program evaluation to identification and adaptation of evidence-based interventions to improve public health. In addition, the CE&R Core is currently developing a comprehensive training program designed specifically for our Community Research Liaisons, which includes courses on clinical trials participation, research ethics in community engaged research and qualitative research methods. These courses are intended to provide Liaisons with the skills and information necessary to educate their constituents about the benefits of research and to participate in research themselves. 40 community members have attended our 1-3 day Academic Immersion program which introduces community members to researchers and their research and laboratories. Over 100 community members attended our inaugural Frontiers in Medical Science, a 6-week evening seminar on cutting-edge medical science aimed at educating community members and hearing from them about their priorities and research ideas.

**Boot Camp Translation for Patient Centered Outcomes (BCT):** The CE&R Program provides an innovative tool for communities to translate evidence-based discoveries and recommendations into language and programs accessible to diverse communities to increase implementation and improve patient outcomes. BCT was successfully pilot tested in rural Colorado and now is being used in additional PACT communities throughout the state. Through a bidirectional process, communities choose the health conditions that are locally and culturally relevant and work with the CE&R Program to identify the best evidence for addressing the locally chosen health topic and translate it into a message that the local community will understand and adopt. The PACT Council received a first-round Patient-Centered Outcomes Research Institute (PCORI) award to implement BCT because it successfully addresses three patient-centered outcomes target areas: identifying priorities, bringing together key stakeholders, and developing, refining, and translating evidence-based care in a manner that respects local and individual patient preference. This innovative translational effort will speed the time from discovery to daily community and clinical practice.

**Community Consults:** This new initiative will be launched in year 1. The goal is to infuse community input into the early design of T1-T2 clinical research. The CTRC medical directors will identify and invite participation of PIs (including KL2 awardees) who are proposing investigator-initiated CTRC projects. The CE&R Director, PACT Council, and Community Liaisons will assemble 6 to 10 community members or patients whose interests are aligned with the proposed research. The PI will provide an overview of the research field and community members will provide feedback about the value of the research to their community, suggestions about patient-centered outcomes that would have meaning to them, comments on study design, ways to make the study more attractive to participants, and ethical concerns. This will provide community and patient input into a research study early in its process so that it may be most responsive to the needs of the patients and community. It will also build a cadre of community members available for Community Consults.

b. **Organization and Governance:** The CE&R Core utilizes an innovative community-academic partnership overseen by the Director, John Westfall MD, MPH, and is comprised of five key components:

**The PACT.** The Partnership of Academicians and Communities for Translation (PACT) is a statewide collaborative of academic researchers, community-based organizations and individuals, and healthcare provider networks working together to provide a platform for innovation in community engagement, including sustainable programs. The PACT Council governs the PACT and meets bi-monthly.

**Community Research Liaisons.** Community Research Liaisons represent a new and innovative workforce for bidirectional research translation. Mixing elements of community health work, grass-roots community advocacy, public health, and research expertise, Community Research Liaisons have an innate ability to work and interact in both the community and academic environment. The CE&R Core currently provides funding and support for 11 Community Research Liaisons (4 FTE) working in diverse communities in urban and rural Colorado. Community Research Liaisons are responsible for cultivating relationships between academic researchers and individuals within a population so that they can identify community health priorities.
and design locally relevant studies that address real patient and provider needs. Community Liaison support in
the communities is integral in the success of our pilot grantees and CIT participants.

**Practice-based Research Networks.** Colorado Practice-based Research Networks (PBRNs) provide
ongoing commitment to network activities and an organizational structure that transcends a single research
project. They support clinicians and practices to work together with academic researchers to develop research
questions and design and conduct studies in pragmatic, real-life clinical practice settings. As the nationally
recognized leader in PBRN research, the Shared Network of Colorado Ambulatory Practices & Partners
(SNOCAP) provides an infrastructure for the study of naturally occurring phenomena in primary care, such
as unselected health problems and continuity of care, among many others. Additionally, PBRNs can take
into account issues like practice organization, patient population, and community factors that are critical to
enhance the generalizability of research findings. SNOCAP includes over 200 practices, 500 providers, over 1
million patients and community members, and statewide local public health agencies throughout Colorado.

**The Colorado Foundation for Public Health and the Environment (CFPHE).** While academic-
community partnerships new opportunities for generating and exchanging knowledge and performing research,
it also raises new social, ethical and administrative challenges. The CE&R Program has developed a unique
solution to these obstacles, involving an innovative partnership with the CFPHE. We have established
administrative systems that allow meaningful community representation and participation in the research
enterprise while eliminating the previously perceived “red tape” that often accompanies contractual
relationships in an institutional bureaucracy such as the University. CFPHE serves as an administrative liaison
between the University and Community to create efficiencies in the distribution of funding and other resources
to community-based partners and to improve responsiveness to community administrative needs.

**CE&R Core Implementation Team.** The CE&R Program Implementation Staff from CU-D provide
expertise to the PACT Council and academic investigators in community translational research methods,
cultural proficiency and health disparities, building and maintaining trust, community engagement and research
dissemination. This Team directs and plans PACT activities and events, monitors progress, tracks finances,
and prepares reports and documents.

c. **Approval process for use:** The PACT Council is the governing body of the PACT who work under the
Core Director, Dr. Westfall and PI/CCTS Director to guide the work and resources of the CE&R Core. The
PACT Executive Committee composed of 3 community members, 2 academic members, and CE Core staff,
meet regularly to guide the Core staff work. All decisions are approved through bi-monthly PACT Council
meetings. The PACT Council approves all pilot grants, and sets the work goals for Community Liaisons. The
PACT Council works closely with other CCTSI Programs and Cores and with investigators to integrate
community based research and the academic health center.

d. **Tracking of utilization and appropriate distribution of grant funds:** The CE&R Core works closely
with CCTSI Leadership and finance personnel to record and track all grant funds, and with pilot grantees to
assure appropriate community engagement, resource use, and alignment with CE goals. Grant funds are
tracked to assure equal distribution to the community. Grantees are queried to obtain information on use of
grant funds as well as outcomes of the pilot grants and new funding resulting from pilot awards.

e. **Cost recovery plan:** The CE&R Core is not anticipated to generate program income.

f. **Potential problems, alternative approaches.** Genuine community engagement requires long-term
commitment of time, energy, and resource. In addition to stable CCTSI support, the CE&R Core and the PACT
Council are exploring additional funding opportunities to assure and increase ongoing support. While currently
dependent on CCTSI support, the PACT is a significant community-academic research organization that is
eager to collaborate with all organizations and funders committed to translational research and patient-
centered outcomes.

g. **Metrics for Success.** The primary metrics to be tracked will be the outcomes of our Pilot Grant Awards,
Immersion programs and new Community Consult program. Secondary metrics will include new PACT Council
grants, new PACT partnerships and projects, and manuscripts describing the CE&R Core work.

2.C. **PRACTICAL TRIALS AND DISSEMINATION/IMPLEMENTATION RESEARCH (PT-D/I) UNIT -**
Elaine Morrato, DrPH, MPH Director

1. **Objectives and Significance:** The objective of the PT-D/I Unit is to catalyze and centrally support CCTSI
investigators in the development of practical clinical trials, comparative effectiveness research (CER) methods, and implementation science to achieve increased economies of scale and efficiencies.

The Institute of Medicine estimates that more than half of medical treatments delivered today lack clear evidence of effectiveness. (28) In response, policymakers have called for more broadly generalizable practical trials that provide results that are relevant to contemporary decision-makers, and the use of comparative effectiveness research methods to test/evaluate interventions against one another. (29) CER research is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care. The purpose of CER is to assist consumers, clinicians, purchasers, and policymakers to make informed decisions that will improve health care at both the individual and population levels. CER uses observational studies and practical trials in “real-world” settings and involves active stakeholder and community engagement (Fig. 24). Equally vital is effective dissemination and implementation of new evidence to facilitate its use by patients, clinicians, payers, and others. Without active intervention, an average of 17 years elapses before even a fraction of medical research is translated into practice. (30)

2. Innovation: The PT-D/I unit seeks to shift the current research paradigm in which researchers are “silied” based on academic disciplines. Instead we view PT-D/I as a continuous life cycle involving multiple disciplines (clinicians, social scientists, health services researchers, economists) and active engagement with stakeholders. Innovative PT-D/I approaches will arise through multidisciplinary collaboration in a trans-disciplinary environment.

2. Preliminary Data: Choice and Justification of Resource: Current PT-D/I efforts and expertise are fragmented across CCTSI-affiliated departments and institutions. The goal of this resource is to serve as a hub for advice on research design and methodologies, for resources to support grant development, and for training and networking among members with shared PT-D/I interests. The PT-D/I Unit will be housed within the Colorado Health Outcomes Program (COHO). COHO is a CU-D campus-wide program that conducts and evaluates interventions to improve population health and the quality of health care by measurement of patient-centered outcomes, evaluation of health communication technology, and assessment of the structure/function of healthcare delivery organizations. COHO is multi-disciplinary with faculty from the SOM, CSPH, and SOP and with active partnerships with community health care delivery organizations and public/private payers. The CCTSI and COHO have achieved national prominence as a Center for CER. By creating the PT-D/I Unit, we will provide resources for the CCTSI to meet the increased demand for PT-D/I research. Since CER and implementation research are critical to T3 and T4 translation, this new PT-D/I Unit was considered a high priority during evaluation of potential resources and services for the new CCTSI grant cycle.

3. Approach:
   a. Description of Resources. The PT-D/I Unit provides the following support services to facilitate and advance CER:

   **Support for Practical Trials.** The Unit staff will provide consultation with investigators on PT-D/I data resources and community-based partnerships (e.g., data dictionaries, strengths/limitations, appropriate research questions etc.). It will assist with development of practical trials, employment of CER methods in research, and will provide leadership in the development of advanced research methods and informatics that distinguish our institution and the CCTSI as innovators in PT-D/I research methods.

   **Education/learning community.** The Unit will a) serve as a conduit for actively disseminating NIH CER learning; (b) host annual CER workshops (content archived digitally) to disseminate state-of-the-art concepts/methods; (c) produce a library of CER use cases (grants, publications) and collaborations with large health systems and databases to provide effective role modeling; and (d) incorporate fellows/trainees into CER to increase research capabilities and to provide a pipeline of researchers. These activities will coordinate with ETCD programs, such as the Clinical Sciences Graduate Program.

   **Databases.** With the establishment of PT-D/I, we will seek additional internal matching funds to expand the set of databases and laboratories for practical trials and CER available to CCTSI members.

   **COHO Cores.** Additional resources within COHO available to CCTSI members are an advanced
dissemination and implementation center funded by AHRQ (CRISP), an advanced informatics core, a CER Core, and a Qualitative Methods Core; these core services may be needed to support individual studies.

b. **Organization and Governance:** The PT-D/I COHO will be led by Elaine Morrato, DrPH MPH, an Associate Professor in Health Systems, Management and Policy, Colorado School of Public Health who directs COHO's existing CER Core, is the Training/Education lead for CRISP, and who also serves as the CCTSI liaison to the NIH Key Functions Committee for Comparative Effectiveness Research. COHO houses governance structures that assure studies undertaken are of high priority and with proper oversight. A PT-D/I Unit Steering Committee of lead investigators at COHO will be set up to work with Dr. Morrato.

c. **Approval Process for Use:** Dr. Morrato and the Steering Committee will screen requests for PT-D/I resources. The Unit staff will work within the COHO structure to assist investigators to bring their ideas into viable research concepts and constructs. The PT-D/I will further assist investigators to seek and secure requisite regulatory approvals for their research, and will link researchers with the CER methods expertise, and the learning communities/networks needed to carry out practical trials in real world settings.

d. **Tracking of utilization and grant fund distribution:** PT-D/I Unit will track utilization of resources and services and be accountable to the leadership of the CCTSI for this activity.

e. **Proposed CTSA grant funds:** CCTSI funds will be used to support personnel involved in this program, with other sources of funding derived from the institution and federal grants.

f. **Cost recovery plan:** PT-D/I Unit will not have a traditional technical core pricing schedule for program income. Rather, individual departments, centers, or other entities will continue to fund the efforts to train, engage, and link faculty with research funding.

g. **Potential Problems, alternative approaches,** PT-D/I may encounter demand for its “services” beyond the ability of the institution to fund it adequately. Infrastructure funding, such as the SAFTINet and CRISP, continue to be sought to assure that the CCTSI will have access to resources necessary to conduct CER and practical trials, as well as to assure that the benefits of their findings are translated into improved care and care systems. Benchmarks of success are described in Table 14.

h. **Metrics for Success.** Metrics that will be tracked number of current and future investigators using services and mentorship of this program, number of grants developed, submitted, & awards, and publications.

**CLUSTER 3: STUDY DESIGN AND ANALYSIS**

Aim 4 is to provide a network of services to facilitate optimal study design and analysis of data that will assure the highest quality of research. CCTSI-supported services to address Aim 4 include the Biostatistics, Epidemiology, and Research Design (BERD) core, the Research Data Management and Integration Services, and the Research Support Centers (described below).

3.A. **BIOSTATISTICS, EPIDEMIOLOGY, AND RESEARCH DESIGN (BERD)** - John Kittelson, PhD, Director

1. **Objectives and Significance.** The BERD objective is to build, lead, collaborate with and support the full complement of translational sciences at CU-AMC and affiliated institutions of the CCTSI and to demonstrate the value of Team Science. The BERD program will build upon the excellence in biostatistics collaboration and consulting, excellence in research in the biostatistics methods and applications across the spectrum of translational science, and education to develop the next generation of biostatisticians and clinical scientists. The specific objectives of the BERD program are:

   **1. Collaboration and consultation:** Specific objectives are:

   Integrate the academic workforce for the design, implementation, oversight, and monitoring of clinical trials including multi-site NIH studies (e.g., improve coordination with CPC Clinical Research, a local Academic Research Organization (ARO) with capabilities to implement and support multi-center clinical trials)

   **Create innovative approaches and methods** for the design and monitoring of clinical trials

   Develop the biostatistics workforce for increased cross-discipline integration of advanced methods and ongoing improvements in the efficiency and quality of biomedical research

   Increase the efficiency, availability, and cost-effectiveness of biostatistics collaboration in the research enterprise of our academic partners and communities

   **2. Generate Reproducible Research:** Innovate new tools, processes, and methods to assure research reproducibility, integrity, and quality. Elements include development of new methods and approaches in collaboration with leadership of the National CTSA BERD consortium working groups on this subject. Specific systematic approaches are needed to assure preparation of pre-specified Statistical Analysis Plans; standards
to document and archive analyses so that all results are fully reproducible at any time.

3. Application and Methods Research: Develop the new biostatistics methods for translational science, including: 1) new biostatistics methods for important problems in diagnostics, methods for evaluating causal mechanisms; 2) new approaches to study recruitment to improve the speed, cost-effectiveness, and efficiency of clinical research; 3) new statistical methods, especially methodological developments stemming from biomedical collaborations (e.g., new methods for translational biomedicine)

2. Innovation. The CCTSI BERD program leads an innovative approach to collaborative, team science biostatistics across the CCTSI and CU-D. The ultimate objective is achieving excellence in the full spectrum of biomedical research in a cost-effective manner. Innovative BERD approaches include 1) our project intake, funding and management approaches described below; 2) our Research Consulting Lab (RCL), which is staffed by biostatistics graduate student research assistants who are supervised and mentored by an experienced PhD biostatistician. The RCL is an effective environment for training the next generation of biostatistician collaborators and provides excellent service for investigators with well-defined shorter-term projects; and c) our Biostatistics Methods Research program, which coordinates the MiTS (methods in translational science) groups as an effective mechanism for sharing expertise, developing new directions for biostatistics methods research, and guiding their implementation across the institute. There are MiTS groups in clinical trials, comparative effectiveness research, and psychosocial methods.

3. Preliminary Data, Choice and Justification of Resource: Expertise in biostatistics and research study design is a fundamental component of effective science and absolutely essential to the CCTSI. The cost of poor research design, inadequacies in the conduct of research, and bad practice in analysis and interpretation has been well documented in the biomedical literature and in the popular press. Strong biostatistics leadership and participation in all aspects of biomedical research is considered essential to the mission of the CCTSI. Since faculty biostatisticians provide substantial unreimbursed support to many groups and investigators, particularly in support of new grant applications, institutional and CCTSI BERD funds and a new business model are needed to sustain the ability of this central consulting resource to provide its essential services. Biostatisticians also provide educational opportunities ranging from formal didactic courses, informal short courses, seminars, and web-based materials.

Accomplishments: In biomedical research, successful biostatistics establishes effective collaboration between biostatisticians and investigators to yield high-impact Team Science, as demonstrated in the following example, one of many that have been fostered by the BERD program:

Case Study: Amanda Allshouse joined the BERD program shortly after its establishment and with experienced leadership from Dr Samantha MaWhinney (Department of Biostatistics and chair of BERD education program), developed long-term collaborations with Amy Meditz, a junior faculty member and her mentor, Dr. Elizabeth Connick, in the division of Infectious Diseases. Ultimately, their joint work resulted in a landmark paper on factors associated with treatment initiation in HIV-infection. The work received editorial recognition and was published in the annual compendium of the HIV Medical Association. Furthermore, this project has been extended by motivating additional biostatistics methods research related to R01-funded research by Dr MaWhinney (R01 DA030495).

A key objective for the BERD program is that biostatisticians eventually establish long-term collaborations with investigators and research groups that are self-supported. Currently such collaborations are in place with the College of Nursing, CUCCC, Center on Aging, Hemophilia and Thrombosis Center, Veterans Administration, Department of OB/GYN, Assistive Technology Partners, Cardiac and Renal Transplantation, Rehabilitation Medicine, Renal Division, Pediatric Endocrinology, and Division of Infectious Diseases. Evidence for the success of these collaborations includes high-impact joint publications, biostatistics methodology papers, and successful grant applications for biostatistics methods.

BERD activity has increased steadily since the establishment of the CCTSI. Over 1,100 investigators have sought biostatistics expertise. Currently, the BERD works with ~150 different individual investigators each month, and the number of investigators for each biostatistician FTE is remaining approximately constant. Investigator-initiated grants fund over 50% of this support with the remainder coming from institutional sources (~25% other institutional support, ~25% CCTSI). The BERD program has supported research in 83 of the 84 possible academic departments and programs at CU-D in addition to many affiliated programs and institutions.

4. Approach
   a. Description of Resource. The CCTSI BERD program is administered by the Department of Biostatistics and Informatics in the CSPH. In combination with the BERD, the department also administers and
manages the other key campus shared-resources for biostatistics collaboration; including specifically, the Children’s Hospital Research Institute biostatistics resource, the School of Medicine biostatistics shared resource, and the CUCCC biostatistics and bioinformatics shared resource. In total these shared resources comprise a consortium of 20 collaborative biostatisticians and 10 biostatistics graduate research assistants. The BERD program is the largest shared resource and provides the administrative and organizational nucleus for all of the other shared resources.

b. Organization and Governance: The BERD is led by a Director, Dr. Kittelson, and supported by committees that organize and direct specific programs. The director has primary responsibility for the ongoing operations, including supervision of faculty/staff, management of financial resources, and for the administrative organization and function of the key governance committees:

BERD Steering Committee: Overall advice and leadership for the BERD director and other BERD committees with particular attention to consistency across affiliate biostatistics groups. Membership includes chairs of all other committees, the BERD director, and directors for biostatistics at all partner hospital groups (NJH, DH, KP Colorado).

BERD Methods Committee: Directs the MiTS groups to assure the continued development of biostatistics methods in translational science.

BERD Committee on National Collaborations: Assure consistency with the national BERD KFC programs and developments and shares local BERD program advances and innovations with the CTSA consortium.

BERD Project Funding Committee: Determines the amount of central funding to allocate to specific collaboration award applications. Membership includes the director of the CCTSI, the director of the Children’s Hospital Research Institute, and a representative of the SOM.

c. Investigator Access: All investigators at CU-D and CCTSI-affiliated partner institutions have full access to the BERD biostatistics shared resources.

Office Hours: Biostatisticians will staff two centralized offices (at CU-D and CHCO) for drop-in questions, and to schedule separate meetings to develop a plan to support longer-term projects.

Project Registration System: Investigators can register their project in a simple online system in order to schedule a separate individual meeting to arrange appropriate biostatistics expertise and support.

d. Project funding and management system. Projects are funded and managed through 3 mechanisms:

First hour free: The initial consult (either through office hours or project registration) is funded with BERD resources. The initial consult may necessitate a longer-term arrangement in (b) or (c) below.

Biostatistics Collaboration and Consultation: Guided by a simple scope of work (developed in the initial free 1-hour meeting). These consultations are primarily fee-for-service or cost-shared using BERD funds.

Long-term collaboration agreement: Agreements that are arranged and funded by individual departments or research units/centers. Collaboration agreements provide salary on a %FTE basis to support an individual biostatistician’s collaborative work with investigators in that department, unit, or center.

e. Prioritization of projects: The project prioritization system is managed by the project funding committee (see 4.b) that develops the priorities that are used in the cost-sharing decisions. The use of BERD funds is prioritized toward supporting new researchers, trainees, pilot awardees, CCTSI-sponsored research, and the development of long-term independently funded research.

f. Tracking of utilization and distribution of grant funds to support BERD Core: The BERD has a robust project time-tracking system. All biostatisticians record their hours on a daily basis by project, fund source, investigator, and task. A complete reporting system provides summary tables of time and percent FTE by fund sources and projects to assure that funding agreements are satisfied.

g. Proposed CTSA grant funds supporting this resource: CTSA funds support the BERD education program, the methods research program (MiTS groups), the project management system and BERD governance. Most of the consultations will be funded by reduced fee-for-service subsidized by the CCTSI.

h. Program Income System: The BERD will continue to use its University–approved fee-for-service invoicing system as a service center. The use of this fee-for-service funding mechanisms will be expanded as part of the CCTSI Program Income System and it will be tracked within the Core Laboratory Tracking and Management System that will be purchased and implemented in 2013 by the CCTSI.

i. Potential Problems and Benchmarks for success: To date, core funding has supported most biostatistics consulting and short- to medium-term collaborative projects at no cost to investigators. With the reduction in the NIH CTSA grant award over the 5 years of this award cycle, the Program Income System will be implemented to recoup a portion of the resources that have in the past funded a major part of routine
consulting and short projects. It is anticipated that the combination of CCTSI and CHCO core funding and fee-for-service income will support the number of biostatisticians required to collaborate and consult with our investigators and trainees. This will be carefully tracked during the course of the grant award.

j. Metrics for Success. Benchmarks for success are described in Table 14. Additional metrics will be the hours of biostatistical consultation/collaboration, the number of grants submitted and awarded and publications arising from these consultations.

3.B. RESEARCH DATA MANAGEMENT AND INTEGRATION SERVICES - Michael Kahn, MD PhD, Director

1. Objectives and Significance. The Translational Informatics Pillar Program’s responsibilities are described in both Sections II and III off this application. Section II (page 544) describes creating a secure and compliant informatics environment and infrastructure to support research data access, delivery, storage, and sharing. In this section, we present existing and future biomedical informatics resources and services to be built upon the technical infrastructure described previously.

Our Data Management and Integration Services objectives are to:

- Collaborate with the CCTSI Enhanced Research Environment (Regulatory) Program and COMIRB to remove technical and regulatory barriers to creating compliant and secure research.
- Offer data integration services that merge data from electronic health records, data warehouses and biological data sources to create translational research databases for analyses.
- Implement data sharing policies, procedures, and technologies that encourage data sharing among local, regional, and national research collaborators.
- Enhance research data security and regulatory compliance by expanding existing Honest Broker services to ensure compliance with HIPAA regulations while promoting data sharing. This objective is described in detail in Section II.3, “Informatics Coordination and Research Data Security.”
- Promote the use of bioinformatics analytic consultative services, such as experimental design and data analysis for Next Generation Sequencing and Microarray technologies.

To these ends, the Translational Informatics Program will expand its consultative services to guide investigators to the most appropriate informatics tools and services from all CCTSI sites. Those services will include the CCTSI Regulatory Core, the BERD Core, genome and proteomic service centers, the CUCCC Informatics Core, the hospitals' information technology staff, institutional HIPAA and security officers, and regional and national data sharing programs. Technical components and institutional trust for collaborations were built during the first 5 years of the CCTSI.

2. Innovation. Our goal is to reduce barriers in the use of data with full regulatory compliance. We will make it easier for researchers to use better tools and approaches instead of ad hoc ones and drive this by an innovative expansion of services in three synergistic areas: 1) promoting the use of widely-used controlled terminologies, 2) promoting the use of a small number of widely-used data models, and 3) developing reusable data management components that provide added value to ensure adoption by translational investigators. Examples of added value components are: the ability to link with other data sources, such as the EMR; the ability to use an analytic tool without having to reformat or recode data; or the ability to auto-generate IRB-required annual reporting forms. We believe that these technical approaches, often desired but rarely achieved in translational research, are now possible based on experiences, partnerships and toolsets that we describe in detail in Section II.3 and in the Approach section below.

3. Preliminary Data: Choice and Justification of resources. The adoption of REDCap as the best-practice electronic data capture (EDC) system at CU-AMC and its affiliates has been a spectacular success (see Preliminary Data). Even so, data management was priority #3 in a needs assessment survey conducted by the Evaluation Core in 2009. The new systems described in Section II.3 bring EDC, study management, and data sharing capabilities that are not available through REDCap. The Informatics Core will use the CU Cancer Center deployment of OnCore (a CTMS) & CHCO’s selection of Remedy Informatics Registries & Biospecimen technologies to meet more translational informatics needs. We thus extend our existing strategy of technology partnership, providing investigators with a wide range of solutions not bounded by which organization “owns” the system. The Bioinformatics and Analysis Core provides experimental design and analysis consultations in high-throughput technologies, including microarray and Next Generation Sequencing. The core is a shared resource with the CCTSI Informatics Program and the CUCCC, partnering with this NIH-supported unit.

Table 17 shows the expansion of biomedical informatics services since the inception of the CCTSI. The
Translational Informatics Program released REDCap v2.1 in 2009 for use across CU-D and its affiliates. The CCTSI has fully underwritten REDCap technical, training and support costs to remove barriers to its use. Investigators from 56 institutions in Colorado and elsewhere, including faculty, trainees, and students, have used REDCap. In collaboration with COMIRB, pre-approved data management language is available for all REDCap users to include in IRB applications.

The CCTSI Informatics team is active in the national REDCap consortium. The Core hosted the annual REDCap Days in August 2011. CCTSI personnel lead the REDLoc standardized forms library and the FAQ committee, and are active in contributing to the REDCap community listserv. The CU-D REDCap team has become known in the consortium as a leader in user training and development of user resources, and for sharing its educational materials. CHCO has piloted data feeds from the Epic EMR into i2b2. An IRB protocol allows cohort counts from the i2b2 web client to be given to investigators for preliminary research studies. Our “facilitated self-service” model pairs an i2b2 technical analyst with the clinical investigator in side-by-side interactive sessions. This model has been popular and is being expanded to train “super-users” to provide the same technical consultation skills to specific user communities.

With CCTSI funding, the Bioinformatics Analytics Core (BAC) has provided pre-grant study design consultation. BAC also provides genomic analytic services on a fee-for-service basis. Between July and August 2012, BAC supported 74 investigators across 21 departments/divisions at AMC. Since January 2012, 19 grants have been submitted based on analytic consultations from the BAC; 2 have been awarded.

As an example of the creative ways the Translational Informatics Program has supported investigators, the Area Health Education Center (AHEC) has conducted health screenings at the National Western Stock Show for many years. However, 2011 was the first time they collected health data electronically, using REDCap on iPads, rather than recording test results on paper to give to participants. This change not only made the screening process more accurate and efficient, but enabled the investigators to conduct a follow-up study with participant volunteers to determine the effectiveness of the screening by contacting those with health issues several months after the screening to determine whether they had consulted with their primary care providers.

4. Approach

a. Description of resources. We will continue to offer REDCap services at no cost to the investigator. Linkage to UCH and CHCO Epic EMR data is our most frequent REDCap request. We will implement REDCap’s Data Transfer Service to import data from external sources, starting with the two EPIC installations. Other data integration use cases to be prioritized include bidirectional data sharing between REDCap and the CTMS, Remedy Informatics, i2b2 and VDW data sets. We currently are implementing REDCap’s application programming interfaces to export data to i2b2 and to automate IRB reporting.

The Translational Informatics Program currently provides limited data management consultation. We will develop a more comprehensive, structured approach to determining the data management requirements for investigator requests. We will develop a more comprehensive, structured approach to determining the data management requirements for investigator requests. We will establish tiered services using data management tools that meet a majority of investigator needs (e.g., REDCap without EMR linkages) while also using charge-back fees to provide services to increase investigator access to more sophisticated systems that require specialized informatics resources (e.g., REDCap with EMR linkage, CTMS, Remedy Informatics Registries, customized database development).

To support data integration and sharing, we will develop standardized research data collection vocabularies. We will expand the use of standard REDCap forms from the REDLoc library, and develop local forms for common data types (e.g., patient demographics and the most-often requested laboratory tests and clinical observations) that leverage common data element definitions from the NIH, CDC and CDISC. Through our consultation services, we will direct investigators to these forms and to other standard instruments. To encourage the use of standardized vocabularies, we will build tools that integrate EMR data, create annual IRB

<table>
<thead>
<tr>
<th>Table 17 Representative Utilization of Translational Informatics Services from 1 May 2008 to 1 Dec 2012</th>
<th>Pre-CCTSI</th>
<th>Current</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personnel fully or partially supported for research informatics</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>Servers supporting translational research administration or services</td>
<td>6</td>
<td>50+</td>
</tr>
<tr>
<td>Applications supported by Biomedical Informatics Core</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>REDCap research study databases and surveys</td>
<td>0</td>
<td>1435</td>
</tr>
<tr>
<td>REDCap users</td>
<td>0</td>
<td>2277</td>
</tr>
<tr>
<td>Attendees at bimonthly REDCap tutorials</td>
<td>0</td>
<td>796</td>
</tr>
<tr>
<td>Informatics-related educational materials</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td>Bioinformatics consults supported by CCTSI funds</td>
<td>0</td>
<td>112</td>
</tr>
<tr>
<td>Web hits to PROFILES.ucdenver.edu over past 30 days</td>
<td>0</td>
<td>3753</td>
</tr>
<tr>
<td>Research informatics-related grants, supplements</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>
reporting statistics, and other points of automation that are not available without using standardized terms.

The BAC will continue to provide consultation services, focusing on study design, data quality, and analysis accuracy. BAC will expand educational outreach focused on disseminating the latest information to be included in grant proposals that include funding for BAC.

b. Organization and Governance. Governance will be managed through the development of transparent program services and charge-back policies and procedures that will be available through the Program Income System, via the CCTSI web site, and with every initial interaction with investigators. Service needs that exceed the CCTSI capabilities or capacity will be referred to other technical resources, either on campus or by private parties, that could meet the investigator’s needs.

c. Approval process for use. The CCTSI Translational Informatics consultation services will be organized to accept “all comers” without regard to institutional affiliation and training status. Like all CCTSI services, we will require appropriate IRB approvals for CCTSI Informatics Services. We will continue to develop pre-approved IRB language for data management and data sharing plans to accelerate IRB approval.

d. Tracking of utilization and appropriate distribution of grant funds to support biomedical informatics services. The Core Laboratories Tracking and Management System will capture the key elements for all informatics consultations and be used to track Translational Informatics Program service utilization and invoicing. Use of basic REDCap will be tracked using the usage measures available in the current system. We will collaborate with the CUCCC and Children’s Hospital Research Informatics teams to collect utilization of the CTMS by CCTSI investigators.

e. Proposed CTSA grant funds to support this resource. CCTSI grant funds focus on providing consultative services to match investigator needs with available resources within the CCTSI or other campus service organizations. These resources are critical to providing translational investigators with a single source of comprehensive information regarding data management options, strengths, weaknesses, and costs across all CCTSI organizations. CTSA funds will also be used to develop standardized forms, to automate data extraction from the two Epic EMRs (UCH and CHCO) into standardized forms, and to create automation tools that encourage the use of standardized forms. CTSA funds will also be used for continued development of the campus-wide Honest Broker System and the BAC consultative services. CU-D Vice Chancellor of Research office will co-fund REDCap expenses with the CCTSI during the proposed 5-year grant cycle.

f. Cost recovery. Although the REDCap system will be fully subsidized, charge-backs will be imposed for services beyond the basic REDCap capabilities, such as:

- Data transfers from EMR systems into REDCap and the library of standardized forms that contain these data. EMR data transfers for variables not included in our pre-established library or from any other data source other than the EMR, such as the planned campus-wide Clinical & Research Data Warehouse, will be fully charged for both initial development and on-going maintenance during a study.
- Studies requiring access to the Remedy Informatics Registries or Biorepository tools will be charged the full cost for licensing, implementation and management.

g. Potential problems, alternative approaches. Successful programs for data extraction, integration, and sharing build on mutual trust more than technology. The CCTSI Informatics Core has a strong history of multi-institutional collaborations built upon personnel and technology sharing, joint-funded projects, and mutual strategic planning. Relationships with hospital IT leadership are strong, as evidenced by CCTSI leadership in the campus-wide data warehouse project. Should unforeseen technical issues arise with the use of REDCap's DTS technology, we will pursue alternative methods for providing access to EHR data, including sponsoring a hospital-based report writer dedicated to research data requests. We will also pursue alternative data sources including OnCore, Remedy Informatics and specialized registries if EHR data are not readily available. We will work with the HIPAA Privacy and Security Officers at all participating organizations to ensure regulatory “buy-in” to data sharing. If concerns arise from these discussions, we will support internal hosting of REDCap instances within institutional firewalls, which is a less desirable alternative to our current centralized model.

h. Metrics for Success. Benchmarks of program success are described in Table 14. Additional metrics to be tracked will be usage of REDCap, number of informatics consultations and requests for data integration and sharing. Program Income will also be carefully tracked and evaluated.

**CLUSTER 4: TECHNOLOGY & LABORATORY ANALYSES** - Mark Geraci, MD, Director

This component of the CCTSI R&S Program will address **Aim 5 which is to strengthen our integrated Network of Translational Technologies (NeTT) and laboratories that provide state-of-the-science...**
services for comprehensive clinical and translational research. The core laboratories that will receive CCTSI support will also contribute to accomplishing Aim 1, via integration with the tracking and charge-back systems described in section D.3.

4.A. **CTRC CORE LABORATORIES** – Lisa Maier, MD, and Frank Accurso, MD, Co-Directors

1. Objectives and Significance. The CTRC Core Laboratories include three bench labs and other specialized clinical phenotyping units affiliated with the UCH, CHCO, and NJH CTRC (clinical research) units. The primary objective of the CTRC Network Core Labs is to support investigators with a wide array of validated assays and services that are fundamental to a strong clinical and translational research program. The Core Labs also provide services for processing and storage of blood, body fluids and tissue samples, technical consultation regarding assay utilization, assay development and trouble shooting, and training for CTRC investigators, staff, visiting researchers and students. During the Year 1 of the new CTSA grant, these three labs will be integrated into a centrally administered network to streamline the delivery, tracking, and cost-effectiveness of services.

2. Innovation. The Core Laboratories meet the needs of multiple investigators by facilitating human physiological clinical phenotyping, performing biomarker and clinical assessment validations, collaborating in NIH- and industry-sponsored multi-site studies, and supporting primary care- and community-based research. Areas of current innovation include development and validation of: 1) multiplex assays for cytokines, growth factors and specific angiogenic factors in a variety of clinical matrices; 2) fat soluble vitamin and carotenoid assays; 3) assays for tissue injury; 4) assays for oxidative stress; 5) microbiomic descriptions of bacterial communities in human samples; and 6) processing of samples that require specialized handling (e.g., bronchoalveolar lavage cells from infectious individuals), and DNA extraction for microbiome and epigenetic analysis from skin and lung samples. Additional areas of innovation:

   a. *Efficiencies across participating institutions*: A high level of collaboration across the Core Labs minimizes avoids duplicative efforts and assay performance. Lab managers meet regularly to improve processes for providing services across labs on the same protocol or to integrate services for a protocol at a single lab. In the Year 1 of the new CTSA grant award, a single Core Laboratory Tracking and Management system will be adopted by all labs to improve the central management of Core Lab usage and charge backs for services.

   b. *Benefits of single review and approval of protocols*: All protocols requesting services from the Core Labs undergo review by SARC. The Core Lab manager and business administer review the protocol in advance of the SARC meeting to ensure that the requested services can be accommodated and that funds to cover the services are in place.

   c. *Expert personnel*: The Core Lab Managers have an exceptional level of combined experience (CHCO: Peggy Emmett, 39 yr; UCH: Pamila Allen, 28 yr, Kayla Carstens, 32 yr; NJH: Beth Canono, 36 yr). They are highly proficient in beta testing and validation of new assays and streamlining of laboratory procedures to optimize efficiencies.

   d. *Quality and human subject safety assurance*: All Core Lab personnel are trained in the conduct of Research involving Human Subjects and HIPAA. Close collaborations with our Translational Informatics Program provides assurance that samples and data are handled in a manner that is secure and compliant.

   e. *Training*: The CTRC Network Core Labs contribute to the training of students, postdoctoral fellows, junior investigators, and research assistants. Training includes lab safety, specimen collection and processing, instrumentation, assay validation, and College of American Pathologists (CAP) and Clinical Laboratory Information Act (CLIA) standards. Trainees learn to conduct assays relevant to their research interests.

3. Preliminary data: Choice and justification of resource. The CTRC Network Core Labs were selected for CTSA resource support because of their fundamental and necessary role in the support of high-quality clinical and translational research. The centralization of these services minimizes the need for investigators to duplicate equipment and personnel, thereby improving the cost-effectiveness of the CCTSI research enterprise. Moreover, the certifications of the Core Labs by CAP and CLIA ensure the high quality of data for investigators across a wide spectrum of disciplines.

The CTRC Network core labs maintain a high volume of activity and support a broad base of investigators. Table 18 depicts lab activity in grant Year 4. Fee structures for the Program Income System have been developed and will be adopted in Year 1 of the new award.

<table>
<thead>
<tr>
<th>Table 18. CTRC Network Core Lab Activity</th>
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<td>Core Lab</td>
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<td>CHCO</td>
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4. Approach

   a. *Description of resource*: The CTRC Network Core Labs have adjacency to CTRC clinics to facilitate

PHS 398/2590 (Rev. 06/09) Page 585

Continuation Format Page
through commercial labs or the hospital clinical laboratories, primarily by eliminating the profit margin. The labs support 196 different assays. The space and equipment for the CTRC Network Core Labs is included in the description of the CCTSI Environment.

b. Organization and governance. For the new award period, the Core Labs will be under the co-direction of Lisa Maier, MD, and Frank Accurso, MD. A centralized management approach for all the labs will help to avoid duplication of services across labs and will facilitate an organized strategy for expanding capabilities across labs. The cost recovery approach that has been in place for the Core Labs will be expanded through the adoption of a Core Laboratory Tracking and Management System to track requests, utilization, invoicing, and cost recovery. The workflow within each lab will be determined by the Lab directors in a manner that is sensitive to cost efficiencies and prioritization based on investigator needs.

c. Approval process for use. The CCTSI website provides a full description of all assays supported by the CTRC Network Core Labs, including the lab in which they are performed, the cost, and the characteristics (e.g., sensitivity, precision) of the assay. A tiered fee system facilitates profit for industry-sponsored trials, with profits directed toward new equipment and expanded services, or cost recovery for projects supported by federal or foundation sponsors. Requests for support at the highest fee tier (Industry supported) require only the approval of the Lab Director. All other requests are reviewed by SARC to ensure that the projects are of high scientific merit and that the requests for support are feasible. Assurance of funds to cover costs of assays will be required before the research protocol is approved.

d. Tracking of utilization and appropriate distribution of grant funds. The tracking of CTRC Network Core Lab services will be centralized during Year 1 of the new CTSA award. Annual reports on Core Lab productivity will be submitted to the R&S Management Committee, which will make recommendations to the CCTSI Director/PI and the Executive Committee for the distribution of grant funds.

e. Proposed CTSA grant funds supporting this resource. It is expected that services for research supported by federal or foundation funds will be cost neutral. Profits from services for industry-sponsored trials and CTSA grant funds will be used to expand services to ensure that the CTRC Network Core Labs remain on the leading edge of assay development. CTSA funds will be used to support services for which there is no cost recovery (e.g., training of postdoctoral fellows and junior investigators) through the Micro Grants program described in D.3 of this section of the grant application.

f. Cost recovery plan. A charge-back system is in place for the CTRC Network Core Labs; it will be modified in the new award period to accommodate the decline in NIH CTSA grant support over the 5 years. PIs are now instructed to request support for all costs for Core Lab services from the funding agency and, if this is not possible, to secure funds from other sources before CTRC protocol submission. Micro Grants will be available to support Core Lab costs for Junior Investigators on a competitive basis. The high level of activity of the CTRC Network Core Labs enables the provision of services at a lower cost than would be available through commercial labs or the hospital clinical laboratories, primarily by eliminating the profit margin.

g. Potential problems, alternative approaches. Over the past 4 years, the CTRC Network has been able to provide a small level of support for services, including Core Lab services, at no cost to investigators with limited funds, particularly junior investigators, or at reduced costs to other CCTSI members. With the impending changes in funding for the CCTSI from the CTSA grant and the push toward full cost recovery, the CTRC Network Core Labs may experience a reduction in service utilization. To avoid a drop in utilization, creative solutions will be required to improve cost efficiency by streamlining laboratory operations, with the goal of having a highly competitive cost structure that will incentivize investigators to use the Core Labs. CTRC Micro-grants will also be a source of funds to cover the costs of Core Lab services for Junior Investigators.

h. Metrics for Success. Metrics for success for the Core Labs will be to continue to diversify the studies and investigators being supported, maintain and grow the types and number of assays provided by the labs, and provide support for studies across the spectrum of basic to translational to clinical research. Additional important metrics will also be the ability to collect charges using the new core management system and to run the laboratory effectively with reduced CCTSI grant support.

4.B. NETWORK OF TRANSLATIONAL TECHNOLOGIES (NeTT) - Mark Geraci, MD, Director

1. Objectives and Significance. Translational technologies represent an ever-advancing discipline and their application to biomedical discovery and patient care is in rapid evolution. The CCTSI will establish an integrated network of translational technologies in Colorado along programmatic developmental missions. The
future of biomedical research depends upon creatively integrated translational technologies used in pursuit of better health care. Investigators must be aware of and educated about available technologies, including their utility, capability, and limitations. A compelling principle guiding transformation in medical care is the potential for current and future use of technologies to determine the best care for each individual person, as exemplified by personalized medicine.

2. Innovation. The innovation stems from the novel organization of the four NeTT Programs around a singular mission to catalyze the generation of innovative methods and technologies to enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. By integrating all the major technologies requisite for discovery and implementation into four highly related programs, the NeTT will further focus efforts of researchers toward scientific discovery and translation to human health.

3. Preliminary Data: Selection and Justification of Resources: The resources of the NeTT include technology services that were rated highly and showed increasing or continued utilization by CCTSI members during the first grant funding period. Furthermore, a SOM Research retreat in November of 2010 assessed research infrastructure and programmatic development. The results were that several CCTSI-aligned objectives were selected for programmatic emphasis and institutional support, including Genomics and Bioinformatics ($683,729), Advanced Microscopy ($130,000) and the Colorado Translational Research Imaging Center (C-TRIC; $2,717,783). Finally, the CCTSI Tracking & Evaluation Core conducted a Needs Assessment in 2011 for the 49 cores and shared resources identified in the CU-D system, which further confirmed the perceived need and scientific value of the resources selected for the NeTT.

Accomplishments. Over the past 4 years, the CCTSI was successful in establishing three new critical resources deemed as necessary for a comprehensive translational technologies program:

a. Biobank Consortium: The CCTSI supported the establishment of a robust Biobank consortium, accomplished by Scott Lucia, MD, Professor of Pathology. This biorepository forms the cornerstone of the utilization of patient samples for translational research and biomarker discovery and validation.

b. Clinical and Translational Research Imaging Center (C-TRIC): Prior to the institution of C-TRIC by Dr. Chip Dodd, the institution had an incomplete and fractionated effort in biomedical research imaging. C-TRIC has expanded capabilities in human imaging, novel radiochemistry, and advanced microscopy.

c. Translational Pharmacology Program: The School of Pharmacy, under Dr. David Ross, pioneered a comprehensive approach for novel therapeutic development through sophisticated computational modeling and chemistry. Expertise in High-Throughput Screening (HTS), High-Content Screening (HCS), and Medicinal Chemistry was established. Pharmacokinetic, pharmacodynamic, and pharmacogenomic approaches are used to foster drug development and improve the safety and effectiveness of medications.

The CCTSI T&E Core monitors the NeTT labs for user volumes and satisfaction. From March 2011 to February 2012, there were 262 investigators who utilized the NeTT, including investigators from two other CTSAs.

4. Approach

a. Description of Resource (Fig. 25): The NeTT is designed for optimal utility of translational research in four aligned programs. The programs align selected cores that share similar missions, and utilize lecture forums within each program to educate CCTSI members about technology updates, applications and the potential for cross-disciplinary research. The four Integrated Programs are:

1. Biomarker Development Program:
   - Biobank Consortium: A critical interface between basic researchers and translational researchers takes place with the application of defined investigative techniques that utilize human samples. Biorepositories are key for the discovery and validation of biomarkers as medicine moves toward personalizing diagnosis and treatment for individuals. The CCTSI established a Biobank consortium, which processes and stores human samples using the most up-to-date NIH guidelines. Acquisition of stored tissues and products by investigators will be facilitated by the establishment of an Honest Broker Service in Year 1 of the new CTSA Award.
   - Genomics: Technologies for high throughput sequencing, gene expression platforms, mutation detection, and platforms enabling whole genome assays for genetic variation are highly developed and mature within the NeTT. They have

Figure 25
been used to aid in the development of biomarkers, define new causes of genetic diseases, and potentially develop new therapeutic targets.

**Proteomics:** The Proteomics Core offers investigators access to analytical capabilities and the expertise to perform high-quality proteomic studies. It assists with the identification of therapeutic targets, the elaboration of underlying mechanisms, and the identification of markers of cancer and anti-cancer therapies. Methods for protein and peptide isolation, separations, quantification, identification and bioinformatics analysis, together with expert guidance in study design, are integrated into the service offered by the Core.

**Metabolomics:** This core supports technologies that enable investigators to perform high throughput analysis of metabolites to inform physiology and pathophysiologic processes. In cancer science, magnetic resonance (MR) is a proven technique for early diagnosis, for pre-clinical and clinical trials with new drugs, and to select or stratify patients. In this context MR measurements are biomarkers.

2. **Colorado Translational Research Imaging Center:** C-TRIC is a new comprehensive research imaging center that was established in 2010 with the support of institutional and CCTSI funds. The goal of C-TRIC is to create a research imaging environment that will facilitate collaborations of researchers from a broad array of disciplines with imaging scientists, and to provide the organizational structure and state-of-the art imaging facility that maximizes creative translational discovery.

**Human Imaging:** The expansion of human imaging capabilities has been remarkable. With institutional and CCTSI support, a new PET/CT scanner dedicated to research use was installed in 2012 in the same facility that houses a research MRI instrument. The institution has committed more than $2.5 million in infrastructure support for C-TRIC.

**Animal Imaging:** We have recently instituted a comprehensive Small Animal Imaging Program, under the direction of Dr. Natalie Serkova. The goal of this program is to develop a variety of imaging-based techniques in animal rodent models that provide reliable anatomic, physiologic, metabolic and molecular end. The animal imaging techniques (MRI, CT, PET, and bioluminescence) are highly complementary and provide both anatomic and mechanistic end points and can be translated into human medicine.

**Advanced Microscopy:** The Advanced Light Microscopy Core, under the direction of Mark Dell’Acqua, PhD, has a number of imaging instruments that deliver a range of important capabilities to users. On a functional level these include: Confocal Imaging, Label Free Imaging, Real Time Imaging, 3D Imaging, Spectral Imaging, Membrane Imaging, Diffusion and Binding Studies, Co-localization Analysis, Molecular Interaction Studies, Fluorescence Lifetime Imaging, and Molecular Photo-manipulation

**Radiochemistry:** Under the direction of Peter Smith-Jones, MSc, PhD, radiochemistry has been instituted with a comprehensive array of services and research, including: cGMP and GLP compliant synthesis facilities that are licensed for radioactive laboratory work; cell harvester – receptor binding studies; and radio HPLC – metabolite analysis.

3. **Translational Therapeutics and Modeling Program:** This program encompasses a comprehensive approach to molecular investigation and animal modeling.

**Vector Design:** Diego Restrepo, PhD, manages this service, which includes molecular technologies for vector design, cloning, and gene silencing and mutation.

**Murine Modeling:** Peter Koch, PhD, is the director of this facility, which specializes in transgenic and targeted disruption in mice. This has progressed to a point of conditional, organ-specific and inducible/repressible systems. These advancements support pre-clinical testing of potential drug targets.

**CSU Natural Animal Models:** The College of Veterinary Medicine and Biomedical Sciences at CSU will develop a Natural Animal Models/Clinical Trials core, directed by Susan Lana, DVM to develop therapies for human and animal diseases. CSU Veterinary Teaching Hospital and Clinical Sciences faculty are engaged in ongoing clinical trials for veterinary patients. We propose here to strengthen and coordinate this effort to result in a world class center for proof-of-concept therapeutics for veterinary medicine that are translatable into therapies for analogous human diseases. Although rodent models serve an important purpose in moving studies of disease and therapy forward, there is much to be realized by capitalizing on availability of naturally occurring disease in outbred species with greater genetic, phenotypic, dietary, and morphologic similarities to humans. Drawing on the strengths of a world-class clinical faculty, this center will provide opportunities to clinically evaluate drugs, surgical interventions, diagnostics and devices, in naturally occurring, well-characterized diseases of companion and domestic animal species that recapitulate human diseases.

4. **Translational Pharmacology Program:** The drug discovery pipeline is well established within pharmaceutical companies. The ability to perform comprehensive drug discovery on a smaller, more focused
scale in academic institutions is less prevalent. The Translational Pharmacology Program is under the
directions of Dr. David Ross, Professor and Chairman of the Department of Pharmaceutical Sciences.
Traditional biochemistry approaches are combined with genomic and proteomic analysis for target
identification. By the development of computational algorithms, virtual High Throughput screening can be
based on structural relationships for identified targets. Furthermore, the ability to access libraries of molecular
scaffolds enables investigators to identify scaffolds most appropriate for modification as molecular targets.

**Computational Modeling and Chemistry:** The Computational Chemistry and Biology Core Facility, under the
direction of Donald Backos, MPH PhD, provides a wide array of advanced tools and services for
computational-based simulations and modeling of chemical and biological systems.

**HTS and HCS:** Under the direction of Brian G. Reid, PhD, the HTS/HCS Core specializes in chemical
biology as it relates to drug discovery, biological probe discovery, and phenotypic characterization of small-
molecule effects on cellular systems. In addition to housing the instrumentation and robotics required for
traditional HTS, the Core houses a cutting-edge HCS image-based system for next-generation small-molecule
discovery research and analysis in fixed or live cells and cellular systems.

**Medicinal Chemistry:** The Medicinal Chemistry Core, directed by Michael Wempe, PhD, serves to validate
proof-of-principle target discovery and assist in preclinical evaluation of compounds by: 1) chemical synthesis;
2) assistance in lead compound identification and optimization; 3) structure-activity relationship analysis; and
4) improvement of chemical properties associated with ADME and/or toxicity issues.

**CSU PK/PD:** This CSU core is directed by Daniel Gustafson, PhD. It has a mature history of innovation and
service and has been co-supported by the CUCCC NIH Support Grant for 7 years. The objectives of the
PK/PD Core are to provide support to investigators for the planning and the analytical and mathematical
analysis of PK studies in both basic and clinical research settings. The services offered include: 1) consultation
on PK study design; 2) development, validation and implementation of appropriate analytical assays for drugs
in biological fluids and tissues; and 3) PK modeling and mathematical analysis of analytical data.

**b. Organization and Governance:** The NeTT will be led by a Director (Dr. Geraci) and co-directors from a
variety of schools and campuses. Our overall structure entails that technologies and resources with common
expertise are grouped within Programs. The **Internal Operations Committee** will be staffed by five individuals
chosen from senior membership of the CCTSI and elected to a two-year term. Their mission is to work with the
new CCTSI Operations Manager to optimize utilization of the resources, establish service centers for the newly
identified resources, and ensure that cost analysis is performed and equitable within the context of the CCTSI.
The **Local Advisory Committee** will consist of five senior members of the CCTSI, elected to three-year terms in
rotation. This advisory committee oversees the optimal content of the resources supported by the CTSA
mechanism. In the event that new resources require development, the Local Advisory Committee will work with
the CCTSI Director/PI and the Executive Committee to establish these new resources. In the event that any
grievances occur through utilization of any of the translational technologies or resources, adjudication of
grievances will occur through the Local Advisory Committee.

**c. Approval Process for Use:** The Programs and affiliated cores are open to use by all researchers. All
operate on a fee-for-service basis. Members of the CCTSI receive lower, subsidized rates.

**d. Tracking of utilization and appropriate distribution of grant funds to support the NeTT:** Tracking of
utilization will occur under the centralized mechanisms for the R&S component of the CCTSI. CTSA grant
funds will support each Core at the appropriate level based on utilization and need, to lower the cost of
services for CCTSI members.

**e. Proposed CTSA grant funds supporting this resource:** CTSA funds will be used to support the
infrastructure for the 4 major NeTT Programs. Each Core will receive a “module” of support to be used for
broad support of personnel, developmental projects and, if needed, equipment or maintenance.

**f. Cost recovery plan:** Each shared resource will be responsible for developing an annual cost-analysis
under the University guidelines. Cost analysis accounts for subsidized support through granting mechanisms and other sources and predicted expenditures of personnel, supplies and service contracts. The new Core Laboratory Tracking and Management system will be implemented in the Cores of this program.

**g. Potential Problems, Alternative Approaches:** We currently do not view any substantial barriers to the implementation of the NeTT Programs. The challenge may lie in the integration of purpose across cores within each program. One common solution for each of the Programs will be the establishment of a seminar series that serves several purposes, including education of the user base, interaction among all the members, and the potential for augmented collaborative research. The CO-Pilot program interfaces prominently with the NeTT, and partial consideration regarding funding of Pilot projects is the utilization of CCTSI resources.

**h. Metrics for Success** are described in Table 14. Metrics for evaluation of the NeTT include: review of oversight committee proceedings for documentation of expansion, development of consortiums, establishment of functional new resources, and integration with educational component; number of users of each resource; surveys of resource user satisfaction; timeliness of institutional charge-back system; and indicators of technology quality (publications/presentations, external funding, career advancement).

**E. INTEGRATION ACROSS CCTSI PROGRAMS**

Initiatives described in this section of the application will be integrated throughout the other major Pillar Programs of the CCTSI. Table 19 illustrates many of these programmatic integrations.

<table>
<thead>
<tr>
<th>CCTSI Program</th>
<th>Integration and interactions with Resources and Services</th>
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<tbody>
<tr>
<td>Translational Pilot Program</td>
<td>Implementation of CMH and CE pilot study programs</td>
</tr>
<tr>
<td>Research Environment</td>
<td>Pre-IRB review of protocols by Scientific Advisory and Review Committee (SARC) Controls of data access and security through Research Data Management and Integration Emphasis on research ethics and safety in CTRC Network Training and certification of clinical research coordinators and professional research assistants</td>
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<tr>
<td>Education, Training, Career Development</td>
<td>Educational opportunities in biostatistics and research design Structured engagement of undergraduate and graduate students in clinical and translational research Nutrition internship program Baby Blanket Educating and Mentoring program Education in community-based participatory research Training in comparative effectiveness and practical trials research</td>
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<tr>
<td>Translational Informatics</td>
<td>Research data management and integration</td>
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<tr>
<td>Quality &amp; Process Improvement</td>
<td>Process improvement for implementation of clinical research</td>
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<tr>
<td>Tracking Assessment and Evaluation</td>
<td>Development of metrics of success for CTR Resources and Services</td>
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**F. MILESTONES AND IMPLEMENTATION TIMELINE**

Table 20 describes milestones and a timeline for their achievement during the 5-year grant cycle.

<table>
<thead>
<tr>
<th>Milestone and Implementation Timeline</th>
<th>Active Development</th>
<th>Ongoing Activity</th>
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<tbody>
<tr>
<td><strong>Specific Aim 1: Program Income System</strong></td>
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<td>Adopt and integrate CTMS and core laboratory management systems</td>
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<td>Establish fee structures and develop charge-back process</td>
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<td><strong>Specific Aim 2: Study Implementation</strong></td>
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<td>Develop the micro-grant program</td>
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<td>Streamline the CTRC Network to meet budget reductions and UCH expansion</td>
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<td><strong>Specific Aim 3: Population-based Translational Research Programs</strong></td>
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<td>Implement charge backs for access to Perinatal Database and Biorepository specimens</td>
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<td>Implement Community Consults for CTRC studies</td>
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<td>PT-D/I Consultation Service has yielded new grant applications</td>
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<td><strong>Specific Aim 4: Study Design and Data Analyses</strong></td>
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<td>Implement charge-back system for consultative services</td>
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<td>Integrate protocol approval process across the CCRO and CRSC</td>
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<td><strong>Specific Aim 5: Technology and Laboratory Analyses</strong></td>
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<td>Task</td>
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<tr>
<td>Integrate CSU core laboratories into the NeTT</td>
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<tr>
<td>Bring core laboratories online in management system</td>
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Research Plan

IV. Education, Training and Career Development Section

Specific Aims
1 page

Education Overview
12 pages

Mentored Career Development Program (KL2)
12 pages

Predoctoral and Postdoctoral Research Training Program (TL1)
12 pages
IV. EDUCATION, TRAINING AND CAREER DEVELOPMENT

NOTE: Commonly used abbreviations in this section are defined on page 516 of this application.

A. SPECIFIC AIMS:

Prior to the creation of the Colorado Clinical and Translational Sciences Institute (CCTSI), the University of Colorado Denver (CU-D) had three successful educational programs for clinical and translational researchers: a clinical sciences Ph.D. program established in 1998, the Clinical Faculty Scholars program to support junior health outcomes researchers, and a regulatory knowledge and compliance curriculum. While these programs achieved remarkable success and often served as models for similar courses nationally, further institutional transformation was necessary to achieve the full potential of the educational mission that we embrace.

The CCTSI Education, Training, and Career Development (ETCD) program has expanded and fortified the CU-D clinical and translational research educational portfolio, and ensured its alignment with the 14 NIH core educational competencies. By more than tripling the number of ETCD programs over the last four years, we have increased the number and quality of committed clinical and translational researchers and positively impacted the success and trajectory of their careers. In essence, we have built a clinical and translational “educational pipeline” that spans the continuum from high school students to our university leadership (Fig. 26). The black beams in this figure represent our ETCD initiatives that support the various stages in the career development pipeline. This flourishing educational system trains mentors to create a culture of team-oriented science, provides vital protected time and essential resources to junior investigators, and teaches fundamental research and regulatory skills. As a result, we have transformed the educational landscape across the University of Colorado system.

Through an improvement over the previous model of academic silos, systematic deficiencies remain in the current educational pipeline model. While traversing the academic ladder, difficult transition points can diminish productivity and delay the development of even the most talented researchers. Building and sustaining a high-impact translational workforce is essential for a successful and vibrant research enterprise. These challenges are national in scope, thus our three innovative aims are designed to address local and national needs.

Aim #1: To enrich the PhD and Masters Clinical Science program and augment the content and outreach of our clinical research education and responsible conduct of research programs.

Aim #2: To improve the impact and effectiveness of our KL2 and career development programs.

Aim #3: To enhance our pre-doctoral TL1 training and pipeline programs and ultimately build a diverse clinical and translational workforce throughout the Rocky Mountain region.

The current success of our ETCD program is founded on seven overarching themes (Table 21). The vision of our new proposal is to identify and “strengthen the seams” of our academic pipeline. Integration of each trainee into the academic and social realms of the university fosters academic persistence, strengthens commitment to the university, and increases the likelihood of them remaining in an academic environment. In order to build and retain a high-caliber translational workforce, we will expand the breadth of our programs, and further incorporate the conduct of team science into the academic fabric while strategically targeting high-risk career transitions. We will also cultivate collaborations with existing programs to improve the visibility and synergy of our educational programs and to continue to attract the most promising students and junior faculty to careers in clinical and translational science. Furthermore, we will enhance programs that promote and maintain excellence in regulatory knowledge and compliance. With the support of our Tracking & Evaluation Core (T&E), we will continuously assess our successes and identify new challenges in establishing a flexible, responsive infrastructure. As a result, our programs will be able to nimbly adapt to the changing needs of the future clinical and translational research workforce.

Table 21: Over-arching Education, Training, and Career Development Themes

| 1. Expand the current culture of team science |
| 2. Build the workforce for the future |
| 3. Enhance efficiency of our programs |
| 4. Forge local and regional collaborations |
| 5. Enrich mentorship for trainees |
| 6. Improve recruitment and retention |
| 7. Inspire academic persistence |
B. OVERVIEW OF ETCD STRUCTURE AND FUNCTION

The portfolio of ETCD programs is outlined in Table 22. Each individual program is intertwined and supported by the entire ETCD structure in conjunction with the University educational system. Our PhD and Master’s Program in Clinical Sciences (CLSC), the Clinical Research Educational Program, and our Responsible Conduct of Research Training Series all provide didactic and experiential learning for students from a variety of programs including most of the CU-D T32 training programs. The Clinical Faculty Scholars Program, the CCTSI KL2 and seven additional K12 programs are enriched by ETCD-sponsored career development programs in mentoring, team science, and grant reviewing that were created during the last four years. The underrepresented minority high school and college students enrolled in CCTSI supported pipeline partnership programs will ultimately enhance the applicant pool for our TL1 pre-doctoral program and other CU-D programs focused on clinical and translational research, and become an integral part of the clinical translational workforce of the future.

<table>
<thead>
<tr>
<th>Table 22: Current ETCD Programs</th>
<th>Description of Program</th>
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</thead>
<tbody>
<tr>
<td>1. Clinical Sciences Program (CLSC) #</td>
<td>Primary degree granting program for advanced training in clinical translational research</td>
</tr>
<tr>
<td>2. Clinical Research Educational Program (CREP) #</td>
<td>Curriculum to improve regulatory knowledge and compliance for junior investigators and research coordinators</td>
</tr>
<tr>
<td>3. Responsible Conduct of Research Training (RCR)#</td>
<td>Required regulatory courses available in a variety of forums</td>
</tr>
<tr>
<td>4. Thematic Seminar and Lecture Series*</td>
<td>Programs and lecture series focused on clinical and translation research related topics</td>
</tr>
<tr>
<td>5. Clinical Faculty Scholars Program (CFSP) #</td>
<td>Two year fellowship for junior faculty with an interest in health outcomes research</td>
</tr>
<tr>
<td>6. KL2 program*</td>
<td>Three year comprehensive training program for junior investigators</td>
</tr>
<tr>
<td>7. Colorado Mentoring Training Program (CO-mentor)*</td>
<td>Formal mentoring program focused on training mentor-mentee dyads.</td>
</tr>
<tr>
<td>8. Leadership in Innovative Team Science Program (LiTeS)*</td>
<td>Comprehensive eight day program to enhance effective leadership and build productive research teams</td>
</tr>
<tr>
<td>9. K to R Mock Study Section and Grant Review Program (KTR) *</td>
<td>Provides written and verbal reviews prior to NIH grant submissions</td>
</tr>
<tr>
<td>10. TL1 program*</td>
<td>Certificate granting program for PhD candidates to foster development of a clinical and translational research focus.</td>
</tr>
<tr>
<td>11. Pipeline programs (American Indian and Alaska Native College Partnership, SUMMiT, Regis Externship, and STaRS)*</td>
<td>Clinical/translational research programs for underrepresented minority high school and undergraduate students</td>
</tr>
</tbody>
</table>

* = Created by CCTSI, # = Pre-existing program that has been enhanced by the CCTSI

ETCD Leadership Council and Staffing: Drs. Marc Moss and Jane Reusch are respectively the Director and Co-Director of the ETCD program, and form the ETCD Leadership Council with the individual ETCD program directors (Fig. 27). This Council provides complementary and integrated areas of expertise and leadership skills for the ETCD program. (Please see Section A of their Biosketches for a more complete description of the qualifications of individual program directors). The leadership council meets on a monthly basis to manage the components of the program, to review and allocate the program budget, and to ensure alignment with the 14 NIH CTSA Core Educational Competencies. Dr. Moss (a CCTSI Associate Director) and Dr. Reusch will continue to be members of the CCTSI Executive Committee.

National involvement: The ETCD leadership has played major roles in national CTSA initiatives including the planning of TL1 and KL2 meetings, collaboration on research initiatives, and serving on national boards:
- Dr. Ellen Burnham chaired the poster committee for the 2012 Translational Sciences meeting, is on the writing committee for the Wisconsin mentoring trial, is first author on
two mentoring articles in *Clinical Translational Science* (39, 40) and a co-author on a recent article on mentoring published in *JAMA* (60).

- Dr. Lisa Cicutto was a member of the Association for Clinical Research Training (ACRT) Educator Subcommittee, Planning Annual Conference Committee, 2008-2010.
- Dr. Madeleine Kane was an invited speaker at the TL1 national meeting.
- Dr. Spero Manson chaired a meeting of six CTSAs to plan collaborative outreach and capacity-building efforts with American Indian and/or Alaska Native communities.
- Dr. Marc Moss has been an invited speaker at the TL1 and Translational Sciences national meetings. He also was an invited chair for an educational session at the Translational Sciences meeting in 2012.
- Dr. Jane Reusch serves on the board of directors of the ACRT. As the mentoring committee chair, she will lead the mentoring sessions at the 2013 Translational Sciences meeting.
- Dr. Celia Sladek is on the planning committee for the National Predoctoral CTSA meeting.
- Drs. Maggie Wierman and Marc Moss were site facilitators on the Wisconsin CTSA Mentoring Trial.

In the following, each of the three major components (Sections) of the ETCD program will be described. In each section we outline the distinctions in the current program followed by the future directions we will pursue under the current CTSA application.

**SECTION I. EDUCATION COMPONENT OF ETCD**

**A. SPECIFIC AIM:** To enrich the PhD and Masters programs in Clinical Science and augment the content and outreach of our clinical research education & responsible conduct of research programs.

**B. OBJECTIVES AND SIGNIFICANCE.** With the support of the CCTSI and CU-D, each of our ETCD programs have been transformed and grown considerably since 2008. In combination, our educational portfolio addresses each of the CTSA recommended core competencies for investigators at any stage in their clinical translational research career. To identify the most imperative areas of need and difficult transition points for future clinical translational investigators, the ETCD leadership turned to the results of CTSA sponsored national surveys, and our own CCTSI questionnaires and focus groups for guidance. The 2011 WESTAT national survey of 553 CTSA sponsored trainees and 665 of their mentors praised the current structure of the CTSA educational programs. However, five areas of need were identified that could improve the effectiveness of existing education programs (Items 1-5 in Table 23). Our T&E core also conducted local surveys and identified two additional areas of potential improvement (Items 6-7 in Table 23). The Future of Biomedical Research Workforce Report also provided recommendations for CTSA supported education programs. Based on comments from over 200 respondents, this report advocated to broadly train researchers in a branching career pathway and to address existing bottlenecks in career development. The report also reiterated the need for career development and mentoring and the expansion of diversity in the workforce. We embrace these future needs and will address them as part of the overarching themes in our educational programs (Table 24).

**C. INNOVATION.** To help build a sustainable workforce, we will use a conceptual model of academic persistence as our theoretical framework. Dr. Spero Manson (one of our ETCD core directors) developed this integrated model based on Tinto’s theory of academic persistence (34, 35). The major tenet is that integration into the academic and social realms of the university strengthens commitment to the institution and the likelihood of academic or scholarly persistence. Participants in many clinical translational science programs are initially attracted to a research career due to the thrill of discovery, naïve assumptions about autonomy and control over their professional lives, and a desire to make a difference (34). Without a formalized plan to develop and sustain a research career, their enthusiasm can wane over time. Though characteristics of the trainee are important, integration into the academic and social university fabric strengthens commitment and increases the likelihood of the trainee remaining in an academic environment. Institutional characteristics most relevant to achieving academic persistence include academic support; facilitating peer networks; advising/counseling resources; formal training programs; and research infrastructure. Innovative aspects of our educational programs include the interdisciplinary and team science emphasis in our didactic and experiential learning programs coupled with the provision of a solid foundation in

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<table>
<thead>
<tr>
<th>Table 23: Future Needs of ETCD programs</th>
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<tbody>
<tr>
<td>1. Expansion of Training in Team Science</td>
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<tr>
<td>2. Growth of Career Development Resources</td>
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<tr>
<td>3. Development of an Ethnically Diverse Workforce</td>
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<tr>
<td>4. Increased Multi-disciplinary Training</td>
</tr>
<tr>
<td>5. Increase knowledge of technology transfer issues</td>
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<tr>
<td>6. Increased opportunities for RCR training</td>
</tr>
<tr>
<td>7. Increase awareness of ETCD sponsored programs</td>
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</tbody>
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clinical and translational science. Our programs also allow the flexibility to identify personal learning goals and individualize formalized learning experiences. All students in the Clinical Science Graduate Program (CLSC) have mentoring teams that integrate the trainee into the academic network. This structure has facilitated the involvement of students into new programs such as our Community Engagement Immersion Programs. In addition, the collaborative efforts of the academic community maximize interdisciplinary training of fellows, faculty, and affiliate/community partners across the spectrum of clinical and translational research. In summary, we maintain an interdisciplinary team science community of learning.

The CCTSI leadership will strive to create a culture of team science throughout the University system. At present the School of Medicine (SOM) promotion criteria specifically includes recognition for collaboration in inter-disciplinary and team science. We will work with the other School and College promotion committees at the three CCTSI University partners to stress the importance of recognizing the participation in team science as a research criterion for promotion.

### D. APPROACH:

In this section, we will initially describe the existing structure of our current educational programs. Subsequently, we will discuss the future plans for the next five years for each educational program. The designs for these programs capitalize on the foundation of our previous achievements, are aligned with our seven overarching themes (Table 24), and will be made possible by receipt of continued CTSA funding.

#### D1. THE CLINICAL SCIENCE GRADUATE PROGRAM (CLSC)

CLSC is the primary degree-granting program for advanced training in clinical-translational research, and will maintain this role within the CCTSI. One of the first clinical science training programs in the United States, the CLSC was initially funded by an NIH K30 award from 1999 until the start of the CCTSI in 2008. Originally the program offered a PhD degree (*Clinical Investigation*) and a certificate in Clinical Science. In 2005, with support from the SOM through a Strategic Initiative Grant (approximately $250,000), the CLSC Program expanded to include two additional PhD tracks (*Health Services Research* and *Health Information Technology*) and, most recently developed a Masters in Clinical Science. All of these training programs are multi-disciplinary in nature and include core courses on biostatistics, clinical epidemiology, clinical studies design, critical appraisal, ethics and responsible conduct of research, team science and grant writing. In addition, formal mentoring from interdisciplinary clinical and translational faculty is an inherent component of the CLSC program.

**Accomplishments:** The CCTSI has fostered dramatic advances in collaboration and coordinated efforts between the CLSC and the CU-D Graduate School, Colorado School of Public Health (CSPH), College of Nursing (CON), SOM, and the CCTSI Community Engagement and Research Core. Following are several examples of new integrated efforts that catalyze team science, reduce duplicative efforts, and enhance training efficiency.

1. The Health Services Research PhD program became a collaborative effort between the CLSC and the Health Systems Management and Policy Department in the CSPH. As a result, three new courses were developed: Health Systems and Management, Health Services Research Methods II, and Special Topics: Foundations in Health Services Research. The program is administratively run through the CLSC Program with meetings held every 4-8 weeks with the chair and faculty of Health Systems Management and Policy Department. The Health Services Research thesis committee structure requires that faculty from both the CLSC and Health Systems Management and Policy Department are represented. In addition, the admissions committees of CLSC and Health Systems Management and Policy Department review and discuss applicants prior to providing a letter of offer for admission. The existence and success of this degree program was crucial for the CSPH to receive their accreditation as a School of Public Health in 2010. In addition to our clinical-
based students, the Health Services Research track attracts non-clinician students trained in public health, which inherently promotes the training of interdisciplinary students.

2. A common interest of the College of Nursing and the CLSC is Health Information Technology. As a result, three new courses are taught collaboratively between programs. The College of Nursing recently developed and offers a certificate program in health information technology. CLSC faculty members teach within this program and serve as advisors. Graduates of the certificate program that are interested in extending their learning experience have applied to the CLSC for a more advanced degree.

3. The CLSC program collaborated with the Physical Therapy Program to develop a PhD Rehabilitation Sciences training program. This PhD curriculum includes two CLSC courses as required courses and recommends several CLSC courses as electives. This program currently has six PhD students who are actively engaged in CLSC courses and faculty mentorship. This year, two of their students were successful in attaining training awards after developing their proposals in the CLSC Grant Writing class.

4. The CLSC program has also established a partnership with the Medical Science Training Program (MSTP). Currently, two PhD students, prepared in basic sciences from Oxford and Cambridge, are simultaneously completing their MD and CLSC Masters degrees.

**Impact of the CLSC program:** Prior to the CCTSI, there were 36 students in the CLSC program of which two were Masters students. In our 2008 CTSA proposal, we planned to reach a target enrollment of 60 students by the fifth year of the CCTSI. Remarkably, this goal was exceeded during the second year of the CCTSI. Currently, the CLSC has 85 students (41 Masters of Science in Clinical Sciences (MSCS) students and 44 PhD students), and has become the largest non-professional degree granting program in the CU-D Graduate School (Fig. 28). The MSCS program has experienced an 11-fold expansion since the CCTSI was funded. *The 85 current students hold 46 grants and have published over 250 peer-review manuscripts.* Over the past 4 years, the CLSC program graduated 27 PhD students and 19 MSCS students. Prior to CTSA funding, the program had awarded 15 PhDs over a nine-year period. Entry and exit surveys with our students demonstrate that they are very well trained and confident in their ability to conduct clinical and translational research. On a ten-point scale (10 being perfect), 95% of the students rated the program higher than a score of 8. Students also reported more than a doubling in their confidence scores to perform core competencies including; advanced statistical tests, the ability to acquire resources to conduct a clinical study, and the ability to prepare, write, and submit a grant application. Most CLSC graduates (70%) remain in academia following graduation and an additional 20% work in industry or non-government organizations. *Currently, over 70% of CLSC alumni hold grant support of which 45% is NIH funding. Our 61 alumni hold over 197 grants and have published over 1,000 peer-review manuscripts in high impact journals such as JAMA, Circulation, Pediatrics and Cancer.* We view the CLSC program as a distinct institutional asset and look forward to infusing our experience into the CTSA Consortium.

**Figure 28: 3: Growth of the CLSC Program (# of students)**

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**CLSC Case Study:** “As a junior faculty, I found myself in the position of being expected to develop a clinical research program in the field of human genetics. In the absence of a Human Genetics Clinical Division or other faculty active in this particular area, the charge was substantial and I felt ill equipped to meet it. During the last year of my medical genetics training I had heard of the Clinical Science Program (CLSC) and had taken a few classes that grabbed my interest. I quickly saw the value in the CLSC’s approach to preparing clinician scientists. In my first six months as a faculty member, I applied for a NIH K23 award and used the CLSC as the central training vehicle for the career development portion of the K23 proposal. I firmly believe that the inclusion of the CLSC program as a formal part of my K23 application was the key factor in the grant being awarded. Now, as an Associate Professor, I remain closed tied to CLSC faculty as well as to my colleagues who I met along my journey as fellow students in the program.” Dr. Matthew Taylor, Former CLSC student and present CLSC faculty

**Additional Course Expansion:** In the 2008 CTSA application, five new course offerings were proposed. However, in response to identified needs from key informant interviews and surveys, eight new courses were developed and are now offered: Seminars in Community Engagement and Research, Immersion in Community Engaged Research, Research Seminars in Clinical Science, Clinical Trials for Investigators, Critical Appraisal...
Seminars in Clinical Science, and the three Health Services Research courses mentioned above. CLSC students also take elective courses from several other programs (including Bioinformatics, Computational Bioscience, School of Pharmacy, and College of Nursing) to achieve the individualized knowledge and skills necessary for their specific research. For example, if a student requires informatics training, there are now over 15 complementary courses available (nine bioinformatics in the Computational Bioscience program, four through Nursing, two through Business Management, and two CLSC).

**CLSC Credit Hour Requirements:** The Clinical Science MSCS Program requires a minimum 30 credit hours of which 4-6 credit hours are thesis/publishable paper research hours. The CLSC PhD requires at least 30 thesis credit hours and depending on the specialty track requires 30-34 course credit hours. There are several central and core courses for all CLSC degrees including Critical Appraisal of Clinical Studies, Ethics and Responsible Conduct of Research, Clinical Outcomes, Biostatistics, Epidemiology, and Grant Writing.

**Description of CLSC Program:** Lisa Cicutto RN, MSc, ACNP (cert), PhD has directed the CLSC program since 2008. Core CLSC faculty include four specific track directors (Allan Prochazka, MD, MSc, Matthew Taylor, MD, PhD, Heather Haugen, RD, PhD and Catherine Battaglia, RN, PhD) and one full time administrative coordinator. Together this core forms the CLSC Executive Committee that meets monthly to integrate all aspects of the CLSC program, review each student’s progress, the program's progress and activities, and plan future activities. These leaders also serve on the CLSC Admissions Committee and Curriculum Committee along with additional program faculty. The Admissions Committee establishes entrance requirements and selects new students for the MSCS and PhD programs. The Curriculum Committee oversees the development of new courses, reviews syllabi and course evaluations, and provides direction to improve courses as needed. With the more than doubling in the number of students in the CLSC program, the number of faculty has also expanded. At the time of our original CTSA submission there were 40 CLSC faculty members. Presently, there are more than 110 faculty to support the training and mentoring of our students.

At the time of enrollment into the program, students meet with their Academic Advisor to formulate and complete an Academic Plan that outlines the requirements and milestones of the degree as well as a tentative timeline for completion. **Each student has an Academic Advisor, one or more Research Mentors, and a research project/ thesis committee that meets regularly to provide expertise, career guidance, networking opportunities and mentorship.** We have identified 30 investigators who are representative of the strong and experienced community of established investigators that can serve as potential mentors for our CLSC program. A list of these experienced investigator/mentors is included in Table 38 (see TL1 section). Core CLSC Faculty (Director or Track Directors) serve as Academic Advisors for all students and, for PhD students, serve as Chairs of Comprehensive Examination and Thesis Committees to achieve consistency in guidance and expectations for successful degree completion.

**Pool of potential participants and selection of successful applicants:** Highly qualified students with a bachelors or graduate degree in a clinical or related field are eligible to apply to the CLSC program. Applicants to the doctoral program are required to hold a professional doctorate degree and/or a master’s degree, such as a Master of Science. Exceptions are made for non-clinicians who are highly qualified and have prior clinical research experience. Criteria that guide the applicant selection process includes: overall grade point average from previous degrees, MCAT or GRE scores, letters of recommendation, previous experience in research, and essay explaining reasons for seeking admission. The CLSC offers rolling enrollment for the MSCS degree with three applicant deadlines (Feb.1, May 1, and Oct. 1) and one applicant deadline (Feb. 1) for the PhD.

Program. Applications are reviewed and discussed by all members of the Admissions Committee. Applicants to the PhD program meet with CLSC faculty, typically the Director and Track Director, prior to admission decisions. During the review process, if the committee is uncertain as to whether admission should be offered, a formal interview with the applicant is held. Typical reasons for the request for an interview include the application lacks a specific area of research focus, the applicant has limited experience in research, or borderline undergraduate degree grades. Our applicant acceptance rates range from 65% to 90% with the PhD program being more selective. Our students are truly interdisciplinary, highly motivated and represent both clinicians and non-clinicians. For the MSCS program, approximately 80% are physicians. The profile for PhD students is approximately 10% physicians, 30% non-MD clinicians and 60% non-clinicians. Examples of non-clinicians include bioengineers, statisticians, software programmers, research associates, clinical immunologists, molecular biologists, public health professionals, and health administrators. The program is now also attracting out-of-state (15%) and international (37%) students.
Future Directions and Expansion for Proposed Grant Cycle: The proposed growth of the CLSC is aligned with the National CTSA Strategic Goals-1: Building Clinical and Translational Research Capability, 2: Providing Training and Improve the Career Development of Clinical and Translational Scientists, and 3: Advancing T1 Translational Research. Specifically, we will expand the CLSC program (described in detail below) by offering a collaborative Masters of Science in Health Services Research, two collaborative dual degree programs (MSCS-MD and PharmD-MSCS), and five additional courses. These new programs will build a unique workforce of investigators who are trained at the intersection between currently distinct disciplines such as clinical and translational research and pharmaceutical sciences. In light of the new CTSA grant budget reductions, the CLSC and CCTSI leadership have developed several strategies to prevent any deleterious effects to the current program or its proposed growth. Specifically, we have obtained substantial institutional support from the University leadership and developed a tuition reimbursement system with the Graduate School. Please see the letter of support from Dr. Barry Shur, Dean of the Graduate School. By developing new courses and programs in collaboration with other schools and colleges on campus, we have also leveraged resources, reduced redundancy, and improved the efficiency of the CLSC program. The new programs are described in the following:

1. A new collaborative Masters of Science in Health Services Research will be developed and offered by the CLSC program and the Health Systems Management and Policy Department of the CSPH. Three CLSC courses will be required courses for the degree (Clinical Science Research Seminars, Clinical Outcomes Assessment, and Ethics and Responsible Conduct of Research). It is anticipated that five students will be admitted to the collaborative program each year. Faculty from the CLSC and the Health Systems Management and Policy Department (CSPH) will serve on the student research project committees and will be involved in the admissions process. The program has been approved by the University of Colorado Board of Regents, and the first cohort of students is set to begin in the Fall 2013.

2. Dual PharmD-MSCS: The dual PharmD-MSCS degree program will be an interdisciplinary collaborative program between the CLSC and the Skaggs School of Pharmacy (SOP). It is anticipated that 2-5 students would be admitted to the program each year. Targeted students would include those indicating an interest in the Honors stream of the PharmD program. The Honors stream requires students to complete a research project that integrates with the expectations of the CLSC program and to complete an original research manuscript for peer-reviewed publication. Students will begin with introductory CLSC courses during the summer term before starting their PharmD coursework. Subsequently, they will complete advanced CLSC coursework within the Pharm D four-year program. During the spring term of their first year, students will identify pharmacy faculty to work with throughout the degree to complete their research project. During the subsequent summer term, students will work with faculty to write and present their research proposal, defend their proposal to their Research Project Committee, and initiate project work. It is expected that much of their research will be completed during the summer terms of their second and third years, as Pharm D courses are not required during this time. Student MSCS Research Project committees will consist of both CLSC and SOP faculty members, although it is anticipated that most research mentors will be SOP faculty.

3. Dual MD-MSCS: The dual MD-MSCS degree program will be a collaborative program between the School of Medicine and the CLSC. After completing the third year of medical school, dual degree students will take three terms off from medical school to focus on completion of MSCS coursework and to conduct and write their research project as a publishable paper. The SOM currently has two collaborative dual degree programs, a MD-MBA program and a MD-MPH program, which follow the same basic structure of time off from medical school studies between the third and fourth years. Dean Richard Krugman, Dean of the SOM, is very supportive of this new endeavor and expansion.

4. New courses: We will develop five new courses, all of which will stress the skills needed for team science, in response to student survey results, the ACRT/CTSA core competencies for clinical translational research, the NIH-sponsored Future of Biomedical Research Workforce Report, and our focus on cultivating a culture of team science. Two courses will address several of the competencies identified for academia-industry drug development and medical device, and technology transfer. The intent of the courses is to build the necessary skill set so that rigorous research can be conducted in an accelerated manner to bring new effective therapeutics to our patients more quickly.

The first course, “Seminars in Responsible Conduct of Clinical Research related to Device and Therapeutics Agents I,” will be a one credit hour seminar series that capitalizes on pre-existing seminars organized and offered as part of the clinical research educational (CREP) and responsible conduct of research.
Clinical research education. Experienced investigators and research coordinators can also benefit from additional training and continuing education. Many new investigators and research coordinators lack training in clinical research methods.

A. Clinical Research Educational Program (CREP).

D.2. REGULATORY AND COMPLIANCE TRAINING: Clinical Research Educational Program (CREP) and Responsible Conduct of Research (RCR) Program

A. Clinical Research Educational Program (CREP). The performance of clinical and translational research requires a multidisciplinary team including but not limited to investigators, study coordinators, research nurses, and pharmacists. Many new investigators and research coordinators lack training in clinical research methods. Experienced investigators and research coordinators can also benefit from additional training and continuing clinical research education. In conjunction with our CCTSI Regulatory program (Enhanced Research Environment - Section II of this application), the ETCD program has developed a 24 hour curriculum for clinical research professionals called the Clinical Research Educational Program (CREP). The goals of the CREP are to span the continuum of clinical and translational research. The course will cover the main theories and principles for the translation and uptake of evidence by scientists, clinicians, policy makers and community. Topics will include differences between dissemination research and implementation research; designing for dissemination and implementation studies, tools for dissemination and implementation, multi-level interventions; measurement; and community engagement. An AHRQ Center of Excellence in Implementation Science exists at UCD and multiple faculty from this center will participate and lead the course.

The fourth course "Knowledge Translation, Dissemination and Implementation Sciences," will be developed to span the continuum of clinical and translational research. The course will cover the main theories and principles for the translation and uptake of evidence by scientists, clinicians, policy makers and community. Topics will include differences between dissemination research and implementation research; designing for dissemination and implementation studies, tools for dissemination and implementation, multi-level interventions; measurement; and community engagement. An AHRQ Center of Excellence in Implementation Science exists at UCD and multiple faculty from this center will participate and lead the course.

The fifth course "Introduction to Team Science" will be developed to address the shift in science from an individual-based model of scientific advance to a teamwork model, in order to educate junior investigators regarding the importance of teams in the discovery of high impact science. The course will focus on learning how to build productive and effective teams, and to understand the value of team building. Specific concepts that will be discussed include emotional intelligence, leadership qualities, communication skills, and understanding the importance of diversity of skills in highly functioning teams. Students will attend didactic sessions, and work in groups on specific team building projects. The faculty for this course will include instructors for our formalized Leadership in Innovative Team Science (LITeS) curriculum. This new course will likely become a future requirement for all Masters and PhD students enrolled into CLSC graduate program.

**Case Study - Clinical Sciences Program:** "As part of my clinical cardiology fellowship, I obtained a PhD in Clinical Sciences (CLSC) which provided me the foundation for my current work in cardiovascular outcomes research. I am currently leading 2 multi-site interventions, and serve on several national committees including the American College of Cardiology (ACC)’s ACTION Registry Research and Publications and Quality Improvement subcommittee. I am also the Clinical Coordinator for the VA’s Ischemic Heart Disease Quality Enhancement Research Initiative (IHD QUERI) program. This is 1 of only 10 disease specific VA national quality improvement programs, which utilizes a six-step process to diagnose gaps in performance and to identify and implement interventions. I direct the Cardiovascular Outcomes Research Fellowship Program with the goal of training the next generation of cardiovascular health services researchers. Because of the important contributions from the CLSC program to my academic career, I require my mentees to complete at least the MSCS program."  

Dr. Michael Ho, Associate Professor of Medicine
to improve the regulatory knowledge and compliance of clinical and translational research and to improve job satisfaction and job longevity among our research coordinators. While the curriculum is aimed at both novice and experienced investigators and coordinators, it is especially recommended for investigators who are experiencing problems with COMIRB review, writing consent forms, protocol violations, or patient safety issues. Each of the lectures in this program meets the requirements for Society of Clinical Research Professionals continuing education credits for interested research coordinators. This program will be continued and expanded during the proposed new grant funding cycle.

While various educational platforms including web based classes and on-line videotaped sessions have been used in CREP, the most popular format remains interactive face-to-face training. Attendance at these lectures has exceeded expectations. In our funded CTSA application from 2007, it was estimated that 40-50 individuals would be trained each year. As demonstrated in Table 25, attendance is four times more than anticipated. Based on feedback from prior attendees, the frequency that courses are offered has changed from intensive sessions conducted three times per year to offering 1-3 seminars every week that are repeated throughout the calendar year, and that cover the variety of required topics.

Created in 2010, the Clinical Research Forum (CRF) is a monthly gathering of clinical research professionals (including investigators, coordinators, regulatory affairs coordinators, data managers and administrators) that gather to network with peers, exchange pertinent knowledge and improve standardized practice across our research community. This program offers 20 seminars in clinical research that span from introduction to clinical research, informed consent process and submitting to the IRB to building budgets and preparing for FDA audits. In addition we offer a Clinical Research Professional Lecture series. This is a one-hour lecture held monthly and presented by experts in a variety of fields. The topics provide clinical research professionals with an opportunity to learn about various treatment and research programs.

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<th>Year</th>
<th>Curriculum Courses</th>
<th>Clinical Research Forum</th>
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<tr>
<td></td>
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<td>2011</td>
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**Future Directions and Expansion for Proposed Grant Cycle:** The CREP has identified four areas of growth that will improve the conduct of clinical translational research across the Rocky Mountain region.

1. In collaboration with the University of Colorado Hospital and Children’s Hospital Colorado, the CREP is establishing a Basic Training Course for Research Coordinators. This course integrates key elements of human subject research and regulatory science with basic patient care skills such as properly obtaining vital signs, EKG, phlebotomy, and starting IVs. To date two classes have been offered with approximately 40 participants in each class. The class will be offered monthly over the next year to enable all coordinators access to training. Subsequently, the hospitals will mandate completion of this course as part of the hospital credentialing process in order to certify all coordinators engaged in human subject research.

2. We are also developing a new program that will standardize a career ladder for research coordinators. This program will initially have three levels: basic, intermediate, and advanced. By standardizing the career trajectory for research coordinators, their crucial role will be acknowledged and formalized as a member of the research team. This program will improve the retention of research coordinators. The requirements for each level are currently being determined by members of the ETCD and Regulatory programs.

3. The CREP will also develop an intranet accessible tool box or resource kit to help new investigators. This intranet resource will be a centralized repository with template forms and best practice guidelines.

4. To make training accessible to investigators and coordinators from outside of the Denver metro area (such as from Ft. Collins and Colorado Springs, sites of UC Health System expansion), we plan to offer intensive weekend courses based on our successful CREP curriculum. To determine the appropriate content and timing for these courses, we will first conduct a needs assessment of research coordinators that work with our Cancer Center-affiliated hospitals. Once established, these courses will then be provided at sites throughout the state of Colorado and would be structured as a source of revenue generation for the CCTSI.
B. Responsible Conduct of Research (RCR) Training Program. The ethical conduct of research is an essential component of research training, and is integrated into all aspects of our educational activities. All trainees, both in the Career Development (KL2 scholars) and the Institutional Training programs (TL1 scholars), and all trainees supported by the CCTSI, are required to participate in didactic courses covering the concepts of ethical conduct of research, issues of scientific integrity, and ethical theories and principles. These courses are specifically designed and designated by CU-D to meet all requirements of the NIH guidelines.

There are two CLSC courses that meet the NIH requirements for RCR, one a required course for CLSC students (CLSC 7150) and the second, a course available to the broader university community (CLSC 7151). Both courses are offered during the Spring, Summer, and Fall terms. The difference between these two courses is that the required course has students attend and participate in reviews of at least two Institutional Review Board meetings. In addition, the Graduate School offers Ethics in Research (BIOS/PHCL 7605) that covers the concepts of ethical conduct of research. Instruction in all of these courses involves in class face-to-face discussions, and the course content follows the NIH recommended curricular requirements (NOT-OD-10-019). Topics covered include: ethics and regulation of human subject protection, preparation of a consent form, human embryonic stem cell research, industry-sponsored research, confidentiality, respect, identifying legal and regulatory constraints, scientific integrity, ethical theories and principles,live vertebrate animal subjects in research, federal and institutional guidelines for research pertaining to human and animal models, safe laboratory practices, mentor/mentee responsibilities and relationships, collaborative research including collaborations with industry, peer review, and responsible authorship and publication. All UCU-D Faculty/staff are able to take any of these courses at no cost through their University tuition reimbursement program.

Future Directions and Expansion for Proposed Grant Cycle. In collaboration with the CCTSI Research Ethics program and Enhanced Research Environment Program, and the CU-D Graduate School, the ETCD has recently piloted a new interactive and innovative campus-wide RCR Curriculum. The goal of this program is to make RCR training more easily accessible to all clinical and translational investigators. The curriculum was initiated in September 2012 and consists of nine one hour sessions, given once per month. These sessions are open to all faculty, students and trainees across the spectrum of research and are free to all participants. Using videos, mock grant review committees, and interactive discussions, these classes are designed to provide the basic framework and tools to maintain exemplary responsible conduct of research. The response has been remarkable: there have been over 100 attendees at each of the first four sessions. Thus, the program will be continued into the next CCTSI grant cycle. These sessions will be taught by a rotating group of faculty involved in the various training programs on campus. A certificate will be awarded to participants who complete the nine classes within 4 years. The goals of each session are to stimulate on-going discussions and problem solving within labs and research groups and to facilitate subsequent small group discussions. In the future, this curriculum will also be offered as a one-day (8 hour) seminar and will be made available two times per year. A RCR website is also being developed which will include the key components of this curriculum as a resource for other faculty who prefer to develop their own RCR course using this framework as a starting point.

D.3. CROSS-CUTTING EDUCATIONAL PROGRAMS: A variety of CCTSI programs and cores have developed educational seminars and lecture series open to all CCTSI members. The goals of these sessions are to expose investigators and trainees to a wide spectrum of concepts and techniques that are critical for clinical and translational research. Over the last four years, these seminars have been well attended and well received. In this section, we include a brief description of each of these seminars and lecture series.

Biostatistics: The BERD program currently sponsors a heavily subscribed education program that ranges from a seminar series (“Biostatistics for Non-biostatisticians”) and short courses for non-statistician investigators to special-topic short courses for the continuing education of practicing biostatisticians.

Translational Informatics: A new educational video formatted series was created in which the audience learns 5 things about a clinical translational topic in 5 minutes (5X5 series). A monthly Bioinformatics Seminar Series was also created. All of the sessions are videotaped and available on the CCTSI website.

Community Engagement & Research: The Colorado Immersion Training in Community Engagement is a unique community-campus partnership that aims to introduce researchers to community-based participatory research and community engagement. The program takes place on the AMC campus and in six community settings: urban African American, urban Asian and Refugee, urban Latino, urban American Indian/Alaska Native, rural northeast Colorado, and rural Latino-San Luis Valley. Components include a four-week directed
CE&R Core will also develop a comprehensive training program for our Community Research Liaisons, that into research groups, increase trust, and expand the concept of team science to include key stakeholders. The eventually assist prioritized certain research initiatives. This program will help incorporate community members formally meet with investigators that are investigating disorders of specific interest, tour research facilities, and participation in the research process. Community members will be also brought to our academic campuses to increase understanding about how research and clinical trials are conducted and promote community trust and to individuals and communities of participating in research and clinical trials. The goal of this program will be to program to be delivered for community members by Community Research Liaisons about the potential benefits transfer and clinical trials. These videos will be made public and shared with all the other CTSAs.

Future Directions and Expansion for Proposed Grant Cycle. All of the current lecture series will be enhanced based on evaluations and surveys.

1. Biostatistics: will provide additional educational and training opportunities for investigators, biostatistics graduates students, and practicing biostatisticians. Specifically, we will 1) extend our workshops and short courses for biomedical researchers to include new research groups and new topics such as statistical literacy program, 2) expand biostatistical faculty involvement in supervising biostatistics graduate student theses and dissertations, 3) develop research topics that are motivated by collaborations with biomedical investigators, and 4) expand the specialized short-courses and seminar series for practicing biostatisticians

2. Translational Informatics will continue to generate additional 5X5s videos focusing on technology transfer and clinical trials. These videos will be made public and shared with all the other CTSAs.

3. Community Engagement and Research program is currently expanding our Academic Immersion program to be delivered for community members by Community Research Liaisons about the potential benefits to individuals and communities of participating in research and clinical trials. The goal of this program will be to increase understanding about how research and clinical trials are conducted and promote community trust and participation in the research process. Community members will be also brought to our academic campuses to formally meet with investigators that are investigating disorders of specific interest, tour research facilities, and eventually assist prioritized certain research initiatives. This program will help incorporate community members into research groups, increase trust, and expand the concept of team science to include key stakeholders. The CE&R Core will also develop a comprehensive training program for our Community Research Liaisons, that
includes courses on clinical trials participation, research ethics in community engaged research and qualitative research methods. These courses will be intended to provide Liaisons with the skills and information necessary to educate their constituents about the benefits of research and to participate in research themselves.

4. Child Maternal Health Research Program: A child and maternal research coordinator curriculum will be developed to improve operational knowledge and expertise in child and maternal research issues. Content will be delivered in a variety of forums including CREP and during Perinatal and Pediatric CTRC nursing meetings.

5. The Nutritional Internship program will expand to train 14-15 students per year over the next 2-3 years.

D.4. DISSEMINATION OF INFORMATION AND INCREASING AWARENESS OF OUR PROGRAMS: Local surveys conducted by our T&E core identified the need to increase awareness of our educational programs. In response, we developed and enhanced several venues to advertise our CCTSI educational programs.

1. The Nuts and Bolts Lecture Series: educates the greater campus about the offerings of the different CCTSI programs and how their resources can be leveraged to accelerate research. This series provides faculty, students, and staff a better understanding of the entire CCTSI and our ETCD specific programs well as disseminating information about available opportunities and resources.

2. Educational Pamphlets: With the help of our marketing department, we developed a pocket size pamphlet describing our ETCD programs. These pamphlets include important contact information for the ETCD program manager, and are distributed at all CCTSI events.

3. Website: We have developed an active ETCD website. From June 1, 2012 through August 28, 2012 (3 months) there were a total of 3,838 unique visits to the ETCD portion of the CCTSI website (average of 43 visits per day). The website contains a variety of resources including templates for mentored letters of support, contact information of investigators who are willing to share their funded grant proposals for a variety of career development awards, links to clinical translational research opportunities for high school and undergraduate students, and summaries of all the ETCD programs that have been formatted for NIH grant proposals.

E. ETCD EVALUATION PROCESS OVERVIEW

NOTE: The following section discusses the general overview of our Tracking & Evaluation system. An additional description of the KL2 and TL1 specific Tracking & Evaluation processes are included in those sections of the proposal.

These four questions (and their associated Themes from Table 21) frame our evaluation and tracking process:

1. Do the ETCD programs effectively recruit and support the retention of a diverse workforce? (Recruitment and retention, and inspire academic persistence)
2. Will the ETCD develop the properly trained workforce to meet the clinical and translational research needs of diverse investigative communities, locally and nationally? (Build future workforce, forge collaborations)
3. Are our trainees and scholars adequately prepared for productive and collaborative careers in clinical translational research? (Expand the current concept of team science and enhance efficiency)
4. What is the evidence that we are promoting a culture of effective mentorship? (Mentorship)

Improve recruitment and retention while inspiring academic persistence: Evaluators will work in concert with ETCD leadership to develop metrics to guide an examination of the impact of its robust pipeline programs (see TL1 section) and establish a database to longitudinally follow past and current program participants. We will include participants who have initiated their involvement in an ETCD pipeline program as many as five years ago. Telephone or electronic surveys, that can be completed using an i-phone, will explore former participants’ continued participation in any pipeline program, major in school, interest in and self-efficacy with science, technology, engineering, and mathematics (STEM) subjects, and future academic and career goals. Respondents will also be asked demographic questions and whether they would be willing to participate in a focus group. Focus groups will be conducted (in person or using Skype, when necessary) both with individuals who did and did not maintain an academic career in clinical and translational research. Both groups will be asked what factors contributed to their initial participation in a pipeline program and how individuals like them could be recruited and better supported in pursuing careers in science (research, in particular) and medicine, and what has or would have made a critical difference in terms of their own engagement and aspirations in this regard. This information will be used to make recommendations regarding ways that ETCD pipeline programs can enhance the support available to diverse student populations at various stages of their academic careers. External evaluators of the CCTSI T&E Core will draw on the expertise of CU-D faculty colleagues who are content experts in STEM education among urban and diverse student populations.
Core competency development and workforce readiness: The revised, 88-item Clinical Research Appraisal Inventory – a validated instrument applicable to clinical and translational scholars – will be used to measure self-efficacy across a comprehensive range of research competencies, including conceptualizing, designing and managing a study; collaborating; protecting research subjects and engaging in RCR; collecting and analyzing data; and, disseminating results (36). Repeated measures will be established across time, as the assessment will be administered at the beginning of program participation and annually through program completion. In addition, an institute-wide Needs Assessment Survey will be expanded to explore local workforce development needs, diversity and gaps. Results will be compared with trends nationally as a way to gauge the effectiveness of the ETCD program and CCTSI research environment in preparing a robust workforce that has the capacity and resources to meet the demands of a clinical translational research career.

Research Productivity and Career Success: KL2 scholars will be surveyed annually during the course of program participation and every-other-year thereafter to document the achievement of critical career milestones (such as the K to R transition), faculty rank (promotion and tenure), job satisfaction, work-life balance and support. At the time of the survey, respondents will be asked to share an up-to-date copy of their CV. Evaluators will extract information regarding research productivity – grants awarded, publications, patents, presentations, membership in professional organizations, courses taught, honors/awards. Evaluators will adapt an existing database to longitudinally track the outcomes of pilot awards, to store and process this information for analysis. For those grants, publications and presentations cited, evaluators will analyze the number of co-authors and the composition of the research team in terms of disciplines and institutions represented. Bibliometric analysis will be conducted annually to collect metrics regarding the impact of published research produced by current and past trainees/scholars. Finally, an annual analysis will be conducted comparing research productivity of scholars to the group of applicants who, although not funded, received the next best scores.

Assessing Quality: Alumni at various stages in their careers will be asked to reflect on their experience in using the knowledge, skills, and professional networks gained or enhanced through the ETCD training, into career success pathways and persistence. These insights will be gathered in a formal review process, structured as a focus group-like session. Importantly, engaging program graduates in a meaningful way may have an added benefit of aiding the process of maintaining accurate contact information that will facilitate efforts to follow trainees and scholars longitudinally.

Reporting: Formative and summative reports will be provided to ETCD leaders quarterly to support ongoing quality improvement and to assess the degree to which programmatic objectives are being met. The T&E personnel will provide interpretation of all data and develop recommendations to ETCD leadership.

F. MILESTONES AND IMPLEMENTATION TIMELINE. Specific milestones and a timeline for the development of new programs have been developed in coordination with our T&E program (Table 26).

G. ETCD INTEGRATION WITH OTHER CCTSI PROGRAMS. The full integration of all of our education and career development programs with the other CCTSI programs is demonstrated in the matrix below (Table 27).
SECTION II. KL2 COMPONENT OF ETCD

A. SPECIFIC AIMS: To improve the impact and effectiveness of our KL2 and career development programs.

B. OBJECTIVES AND SIGNIFICANCE. The goal of our KL2 Scholar program is to increase the quantity and quality of high-caliber clinical-translational researchers throughout the CU system and the State of Colorado. Prior to the funding of the CCTSI in 2008, CU-D did not have a KL2 program. Consequently, the CTSA grant award in 2008 included funding for only four KL2 positions. Despite this setback, the CCTSI leadership immediately obtained additional institutional resources to increase the total number of KL2 scholars to seven positions. Our KL2 program provides scholars with guaranteed protected time, an outstanding research environment, and a comprehensive educational, mentoring and career development plan (Fig. 29) to prepare them for a successful academic research career. KL2 scholars receive up to 3 years of CCTSI funding.

Collaborative oversight between the scholars’ research co-mentors and the KL2 leadership provides each scholar with an individualized training program designed to address their specific interests and needs. During our first CTSA funding cycle, the ETCD leadership developed three programs to provide complementary training for the KL2 scholars and their mentors. The Colorado Mentoring Training Program (CO-Mentor) is a formalized mentoring program designed to enhance the mentor-mentee relationship. The Leadership in Innovative Team Science (LITeS) program enhances training in effective leadership and team science. Most recently, we developed the KTR Mock Study Section to help K awardees improve the quality and competitiveness of their first independent grant proposals. These three programs focus on improving mentoring and career development, and developing the proper skills to work collaboratively in a team science environment. In addition, these programs help to build a community of clinical and translational researchers that can attain academic persistence. Though conceptually developed for KL2 trainees and their mentors, these three programs are available to all of the members of our clinical and translational research community. The ETCD program also assists our pre-K two-year Clinical Faculty Scholars program (CFSP) fellowship. This partnership supports outstanding junior faculty members who need additional assistance and mentoring before they are ready to apply for a K award such as our KL2 program.

These KL2 and KL2-affiliated programs are aligned with our overarching ETCD themes outlined on Table 21 of this section of the proposal. Each of these programs will foster specific aspects of our overarching themes during the next five years (Table 28).

| Table 28: Alignment of our KL2 and KL2 affiliated programs with our overarching themes |
|---|---|---|---|---|---|---|---|
| | Expand the ETCD portfolio | Build the future workforce | Enhance efficiency | Forge local/regional collaborations | Enriching mentorship | Recruitment and retention | Inspire academic persistence |
|KL2 program | X | X | X | X | X | X | X |
|CFSP | X | X | X | X | X | X | X |
|CO-mentor | X | X | X | X | X | X | X |
|LITeS | X | X | X | X | X | X | X |
|KTR | X | X | X | X | X | X | X |

C. INNOVATION: Our KL2 scholars have demonstrated the success of our integrated approach to education, mentoring and career development. The CO-Mentor program provides a unique, shared experience for mentor-mentee pairs. Based upon similar business career programs, we designed this program to promote development of foundational skills for career success including communication skills, career development planning, and goal setting, all of which are applicable to both mentors and mentees. Furthermore, the interactive group-oriented format of the sessions allows mentees to gain valuable feedback from a variety of different senior mentors. Mentees also develop mentoring skills as a result of the interactive format, allowing them to be better mentors in the near future. Our LITeS program develops the skills for effective collaborations...
and introduces our academic leadership to the assets of team science. This innovative program will continue to change the research culture to embrace interdisciplinary team science. All of these career development programs have strong representation of clinical, community, basic and behavioral scientists. The KTR grant review program has vastly improved funding rates for first independent awards, and will be a model for implementation of an institution-wide grant pre-review process. Investigators from our three partner Universities and affiliate hospitals across the Rocky Mountain region are invited to participate in the KTR program.

D. APPROACH:
In this section, we will first describe the foundational structure of our current KL2 and career development programs. We will then propose the five year plans collectively for these programs. The future directions for programs take into account the newest recommendations derived from local and national surveys, and integrate with our seven overarching educational themes (Table 28).

D.1. KL2 SCHOLAR PROGRAM

1. KL2 Scholar Performance. Current and former CCTSI KL2 scholars broadly represent the field of clinical and translational research from diverse disciplines and settings, including but not limited to physical therapy, emergency medicine, and biostatistics. Twenty-nine percent of our KL2 scholars have primary appointments at one of the CCTSI partner hospitals such as NJH. The success of the KL2 program is best reflected by the accomplishments of our scholars including their grant funding, improvement in core competencies, and publication record.

1. Grant funding: The first cohort of seven KL2 scholars began in September of 2008. Six of these scholars received independent NIH funding before the completion of their three years of KL2 funding (Table 29). The one non-funded scholar developed a life-threatening medical condition that required a leave of absence. We are glad to report that she is medically doing well and received an excellent score on the first submission of her R01 grant. After a formal review by our KTR grant program, she re-submitted her grant proposal last October.  

<table>
<thead>
<tr>
<th>Scholar &amp; Affiliation</th>
<th>Department</th>
<th>Duration of support</th>
<th>Title of KL2 research project</th>
<th>NIH Grant obtained (direct costs)</th>
<th>Current position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adit Ginde, MD (CU-D &amp; UCH)</td>
<td>Department of Emergency Medicine</td>
<td>10/1/08-9/30/11</td>
<td>Vitamin D in Respiratory tract infection and asthma</td>
<td>NIA Beeson K23 $202,091</td>
<td>Assistant Professor</td>
</tr>
<tr>
<td>Katina Maluf, Ph.D. (CU-D &amp; UCH)</td>
<td>Physical Medicine &amp; Rehabilitation</td>
<td>10/1/08-7/31/10</td>
<td>Mechanisms and treatment of stress-evoked muscle activity</td>
<td>R01 grant $955,682</td>
<td>Associate Professor</td>
</tr>
<tr>
<td>Nicole Carlson, Ph.D. (CU-D)</td>
<td>Department of Biostatistics and Informatics</td>
<td>10/1/08-9/30/11</td>
<td>Statistical methods for understanding endocrine physiology</td>
<td>R21 grant $200,576</td>
<td>Associate Professor</td>
</tr>
<tr>
<td>Wei Tan, Ph.D. (CU-D, CU-B, &amp; CHCO)</td>
<td>Department of Pediatrics and the Center for Bioengineering</td>
<td>10/1/08-8/31/10</td>
<td>Pulmonary Arterial Stiffening in Pulmonary Hypertension:</td>
<td>K25 grant $291,600</td>
<td>Assistant Professor</td>
</tr>
<tr>
<td>Karin Hoth, Ph.D. (NJH)</td>
<td>Medicine, Division of Psychosocial Medicine</td>
<td>10/1/08-4/30/11</td>
<td>Cardiopulmonary Function and Cognition in COPD</td>
<td>K23 grant $449,976</td>
<td>Assistant Professor</td>
</tr>
<tr>
<td>Shama Ahmed, Ph.D. (NJH, UC-D, &amp; CHCO)</td>
<td>Department of Pediatrics, Pediatric Airway Research Center</td>
<td>10/1/08-9/30/11</td>
<td>Airway epithelial cell response to oxidative stress in CF: Role of calcium signaling</td>
<td>R01 grant under review at NIEHS $489,598 of grant support</td>
<td>Assistant Professor</td>
</tr>
<tr>
<td>Tim Bernard, M.D. (CU-D &amp; CHCO)</td>
<td>Department of Pediatrics, Section of Pediatric Neurology</td>
<td>1/1/09-8/31/12</td>
<td>Markers of Inflammatory Coagulopathy as Predictors of Childhood Stroke</td>
<td>K23 grant $477,900</td>
<td>Assistant Professor</td>
</tr>
</tbody>
</table>

To determine the impact of acceptance into the KL2 program, we compared the success of our first cohort of KL2 scholars (n=7) against those applicants that applied but were not funded in our first KL2 cohort, yet received the next best scores (n=7). The KL2 scholars were more likely to submit grants when compared to their unfunded colleagues (Table 30). Over the period of 2009 – 2011, KL2 awardees from the initial 2008 Cohort received $1,302,291 of grant support. During the same period, the comparison group received only $489,598 of grant support. Therefore, investigators who applied for and were awarded a KL2 award in 2008
garnered over 2.6 times as much grant support as the next highest scoring applicants who were not funded. These data reveal that KL2 scholars received independent funding more quickly when compared to unfunded KL2 applicants, supporting the notion that the KL2 program accelerates the academic course of its scholars. It should be pointed out that unfunded applicants were successful in receiving grant support (but not as quickly as KL2 awardees), indicating a larger pool of qualified applicants that could have benefited from KL2 support.

| Table 30: Comparison of Numbers of Submitted Grants by Funded & Unfunded KL2 Applicants |
|------------------------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| Scholars                           | 2009 total       | 2009 per person  | 2010 total       | 2010 per person  | 2011 total       | 2011 per person  |
| Funded KL2 scholar (n=7)           | 9                | 1.3              | 11               | 1.6              | 8                | 1.1              |
| Unfunded KL2 applicants (n=7)      | 5                | 0.7              | 2                | 0.3              | 1                | 0.1              |

2. Improvement in Core Competencies: Our KL2 scholars were asked to report their level of confidence for 19 core competencies (including the 14 NIH Core Competencies) using a scale of 1-10. During their final year in the KL2 program, our scholars had an average competency rating of at least 9 for all 19 competencies. KL2 scholar’s average reported level of confidence was rated as a ten on 47% (9/19) of the competencies while an additional 42% (8/19) of the competencies were rated at an average of 9.5. The competencies that demonstrated the largest gains between the first and third year of participation in the program were:
1. Design a process utilizing special considerations for obtaining consent from vulnerable subjects (+4.20)
2. Develop appropriate methods to recruit and retain clinical subjects (+ 3.70)
3. Perform more advanced statistical tests and use in their research, such as power calculations, sample size calculations, multiple logistic analysis, survival analysis, or time series analysis (+ 2.40)

3. Publication record: The seven trainees that comprised our first cohort of KL2 scholars published a remarkable total of 183 articles from the beginning of their award in 2008 until July, 2012, or an average of 26 articles per scholar. Each of these manuscripts has been cited an average of 15 times, and the average total number of citations per scholar is 399. The impact of their publications is demonstrated by the fact that the top cited paper for each scholar ranked in the top 20% of cited papers when matched by journal and year.

4. Achievements of our second cohort of KL2 scholars: Our second cohort of KL2 scholars has been a part of our program for 1-2 years. They have already been extremely productive, publishing 25 original research manuscripts since receiving their KL2 funding. Several scholars have already received additional grant support. Dr. Magda Gorska received a two year NIEHS Children’s Environmental Health Center award with total direct cost of $100,000. Dr. Amy Huebschmann was awarded a CTSI Community Engagement ($25,000) Pilot Grant, and a CU Center for Women’s Health Research Junior Investigator award ($25,000). Finally, Dr. Dave Nichols received a NJH Translational Research Award.

2. The Clinical Faculty Scholars Program (CFSP) is an outstanding CTSI supported mentoring program that has also been an excellent source of highly qualified applicants for the KL2 program. Created in 2004, the CFSP is a two-year fellowship that develops research-oriented junior faculty with an interest in health outcomes and health services research (T3 and T4 translation). Participants must also have the support of their home department/division, and at least 50% protected research time is required during the duration of the two-year program. CFSP provides guided research project development, educational seminars, and grant writing classes. Each trainee receives regular individual mentorship from four experienced senior researchers in clinical epidemiology, health services research, biostatistics, and health economics. The CFSP accepts 4-5 new junior faculty trainees each year. These trainees represent many disciplines of medicine (e.g. internal medicine, pediatrics, neurology, rheumatology, emergency medicine, and surgery), and other health related disciplines (e.g. epidemiology, law, decision sciences, nursing, and medical anthropology). The target population has recently expanded to include researchers with interests in biomarkers of disease, dissemination and implementation, drug policy, financial and structural incentives, and comparative effectiveness research.

The success of the CFSP program based on publication record is exceptional. Since 2006, the CFSP trainees (n=27) have published a total of 564 articles, or an average of 21 articles per trainee. Each of these manuscripts has been cited an average of 20 times, and the average total number of citations per scholar is 421. The single most highly cited paper for the majority of these trainees were ranked in the top 20% of all cited papers when matched by journal and year. To date, 29% of our KL2 scholars were formerly trained in the CFSP program. The CTSI supports the CFSP by providing salary support for some of their faculty and leadership. In addition, CFSP trainees and their mentors benefit from participation in CTSI supported career...
development programs. The CCTSI also supports the stipend for one scholar from a non-SOM program such as the College of Nursing and for one underrepresented minority (URM) scholar through semi-annual tuition match scholarships.

Case Study: an alumnus of the CFSP and KL2 programs: “Coming from a primarily clinical department (Emergency Medicine) with few research-oriented resources or experience, the CCTSI has been particularly instrumental in my development as a successful clinician-investigator. From 2008-2010, I participated in the CCTSI Clinical Faculty Scholars Program (CFSP), which very quickly sharpened my grant writing skills, ability to collaborate across disciplines, and strategize about funding opportunities. Perhaps more importantly, the CFSP provided a robust network of senior and peer mentors that I continue to utilize for guidance and support. Concurrent with the CFSP, I was fortunate to be selected in the first cohort of CCTSI KL2 awardees from 2008-2011. The funding markedly accelerated my research career trajectory by providing the protected time, mentorship, and resources for career development and research activities. Indeed, I was able to leverage these KL2 support and resources to an advanced, external K23 award through the NIA Beeson Career Development Scholars Award (2011-2014)”  Adit Ginde, M.D.

3. Pool of KL2 Applicants. CU-D has 27 active postdoctoral T32 training programs, in which many of the applicants for the KL2 program trained initially. Our T32 programs are among the best in the nation, with seven of these programs (Behavioral Pharmacogenetics of Drug and Alcohol Abuse; Gastrointestinal Diseases; Developmental Psychopathology, Psychobiology and Behavior; Pulmonary Disease; Respiration and Circulation during Hypoxia; Renal and Electrolyte Disease and Hypertension; and Perinatal Biology and Medicine) having been funded for more than 30 consecutive years. Many other KL2 applicants are newly recruited junior faculty from top-tier academic institutions. Another measure of the number of qualified trainees is the number of submitted proposals for the KL2 program. In our first cycle of applications conducted in 2008, we received 31 proposals for the 7 positions (funding rate of 23%). In our second round of applications conducted in 2010, we received 37 proposals for the 7 positions (funding rate of 19%). We believe the large number of applications that we have received, the success of all of our previous KL2 scholars, the institutional commitment to the KL2 program, and the relative success of some of the non-funded applicants, all justify the size of our KL2 program. By providing CCTSI financial support for URM investigators to participate in the CFSP, we anticipate increasing the number of URM KL2 scholars. We will also continue to work with the American Indian and Alaska Native Programs to solicit KL2 applications from their junior investigators.

4. Pool of Potential KL2 Mentors. We have identified 30 investigators who are representative of the strong and experienced community of established investigators that can serve as potential mentors for our KL2 scholar program. A list of these investigators is included in Table 38. In addition to these investigators, there are numerous other faculty members across the University and our partner institutions with similar mentoring and funding credentials. For example, many of the CCTSI leadership are presently serving as mentors or would be stellar mentors for our trainees. However, to avoid redundancy, they were not included in the table of representative mentors.

5. Eligibility, recruitment, and selection of KL2 scholars. All candidates for the K12 program must have a research or health-professional doctoral degree, have a faculty appointment and be actively engaged in or planning to conduct clinical-translational research. Every 24-36 months, requests for applications are distributed by email to the entire academic community at least six weeks before the application deadline. We solicit applications from all of our affiliate hospitals and from CU-B. Applicants are required to identify two co-mentors who are physically located at a CCTSI affiliated institution. Expansion of the KL2 program to include CSU is currently being discussed by the administration of both universities.

We have included two common co-mentoring models. However, other models may be acceptable. 1. Clinical/Methodological Mentors: Scholars may require co-mentors with different research skills and areas of expertise. For example, a translational project may require one epidemiological mentor who is adept in study design while the second mentor has expertise in the processing and analysis of samples obtained from human subjects. This model encourages and has resulted in new collaborations between the senior mentors. 2. Senior/Junior Mentors: In this model, one mentor provides extensive experience in the scholar’s research area of interest while the second, junior mentor, is a mid-level investigator with independent funding yet less research experience. The junior investigator provides for the hands on mentoring and the senior mentor provides advice on the broader research goals and career development issues. This system fosters an actual mentoring experience for the junior mentor, and will continue to build the number of potential mentors.

Application process. We have implemented an electronic on-line submission process for the KL2 proposals through a CCTSI website link. Instructions to assist with the completion of the application are posted
on our website. All of the KL2 program directors and our ETCD program manager are also available to answer questions. Applicants submit a 10 page proposal with the following sections: prior research experience, career development plan, and a research plan including study design, statistical methods and feasibility sections. Preliminary data are not required. A combined letter of support from their research co-mentors is required describing their commitment to the applicant and their specific mentorship plan. The division chief or department chair also provides a letter of support stating that at least 75% (9 calendar months) of the full-professional effort of the applicant will be protected for research career activities and an additional $25,000 per year will be provided to help support research costs for the duration of the award.

**Review process.** Our review process has two stages. The first stage mirrors an NIH study section. Members of the study section are chosen to represent a broad sector across the University. All reviewers electronically receive assigned proposals with our review criteria and definitions of conflict of interest. Each proposal is read by at least two reviewers. Using the 9 point NIH scale, the reviewer assigns an overall score and individual component scores in five areas: candidate, career development plan, research plan, mentors and mentoring plan, and environment and institutional commitment. Only those grants with an average overall initial score in the top 50% are formally discussed at the study section meeting. Both reviewers present their evaluation of the proposal and then the grant is discussed by the entire group. Subsequently, each committee member submits an overall score for all of the discussed proposals. All applicants receive the written review of their KL2 application. In the second stage, applicants who received a composite score in the top 25% are interviewed by the three KL2 program directors. Each applicant is asked the same five questions about their future research plans, and the co-directors rate the responses using a Likert scale. Based on a combination of the reviews from both stages, the KL2 scholars are selected. To provide comprehensive feedback to the unfunded applicants, Dr. Moss also individually meets with those applicants whose proposals were unfunded yet scored in the top 50%. During the meeting, he identifies methods to improve their science and presentation for future grant proposals.

**Case study: one of the KL2 scholars:** “Prior to the starting the KL2, I had my original K23 application triaged. I knew that my grant would have to improve considerably. I am proud to report that with the direction and support of the KL2 program, I received a fundable score of 20 on my second application. In the span of less than 2 years – and under the guidance of the KL2 directors – I transformed my K23 application. Since attaining my K23, I have been able to finalize my Master’s coursework, attain multiple other grants, and continue to produce an average of 5-6 publications per year in the pediatric stroke literature. Without the assistance of the KL2 and the active mentorship of its directors, I do not think I would have been able to attain these successes.”  

**Tim Bernard, M.D.**

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**6. KL2 Program Leadership:** Marc Moss, M.D. will continue to serve as the Director of the KL2 program. Drs. Jane Reusch and Ellen Burnham will continue in their roles as co-Directors. These three investigators have expertise in basic (Reusch), translational (Burnham), and clinical research (Moss). All three directors attend the monthly meetings with the KL2 scholars and provide oversight to the program.

**Marc Moss, MD** is the Roger S. Mitchell Professor of Medicine and Head of Critical Care at CU-D. Dr. Moss has received NIH funding as a PI for over 12 consecutive years. He was the first author on the landmark *JAMA* study identifying alcohol abuse as the first comorbid condition associated with increased susceptibility to develop ARDS (37). He was also the senior author on the *New England Journal of Medicine* article reporting disparities in the incidence of sepsis (38). Presently, Dr. Moss is the PI on an NINR funded R0-1 grant examining weakness in critically ill patients and a NHLBI K24 award to mentor to junior investigators. Dr. Moss also serves on the NHLBI K23, K24, and K25 review panel. His experience in regulatory issues is demonstrated by his appointment at the NHLBI as Chair of the DSMB for their Pediatric Insulin Titration Trial.

**Jane Reusch, MD** is Professor of Medicine in the Division of Endocrinology, Metabolism and Diabetes. She has been elected to the ASCI and AAP, and is past-president of the American Federation for Medical Research. Dr. Reusch currently serves on the board of directors of the Association for Clinical Research Training and has participated in the development of the Federated Association for Clinical and Translational Science where she will chair the Mentoring committee. Dr. Reusch co-directs a translational research team focused on diabetes, and she has served as the primary mentor to multiple postdoctoral fellows who are now independently funded at the Associate Professor level.

**Ellen Burnham, MD, MS** is an Associate Professor of Medicine in the Division of Pulmonary Sciences and Critical Care Medicine at CU-D. She is the PI on a NIAAA-funded R24 grant to build a biorepository and conduct multi-site investigations relating to alcoholism and pulmonary disorders. Dr. Burnham served as the site PI for the Wisconsin mentoring trial, and due to her active participation she will be included as one of the...
primary authors on the primary publication. She is the first author on two articles on mentoring published in Clinical Translational Sciences (39, 40). She is also a co-author on a recent perspective on mentoring in JAMA (60).

7. Description of KL2 Program. The KL2 program is aligned with the five components of our comprehensive training program (Fig. 29). All KL2 scholars are prepared and encouraged to apply for either an individually mentored K award (e.g. K08 or K23), or an independent research grant (e.g. R01 or equivalent award) prior to the end of their 2nd KL2 year.

1. Individual Research Project. All KL2 scholars enter the program with an established individual research project. In fact, the strength of this research is one of the criteria used for selection as a KL2 scholar. In general, the KL2 leadership defers oversight of the research project to the primary co-mentors. However, they discuss any scientific related issues with the scholar and their mentors when indicated.

2. Research Project Supervision. The core of the KL2 program is the monthly 90-minute seminars that are held on the second Friday of each month. At these meetings, two KL2 scholars present an update on their research and career development to the entire group, each for approximately 45 minutes. The discussions are guided by the three directors of the KL2 program. Because of the diversity of the research background of our scholars, most of the discussions focus on general research issues and challenges. Peer mentoring is encouraged. Like traditional dyadic mentoring, relationships among peers are a valuable source of positive feedback and constructive criticism, advice on balancing personal and professional responsibilities, and collective expertise for skill development (41-43). In addition, because of shared generational values, peers provide emotional support, encouragement, feedback, a sense of acceptance, and build academic persistence. Throughout the year, outside speakers from various departments and services across the CU system meet with the KL2 scholars. These one-hour sessions are designed to teach trainees important skills necessary to advance their career. Some of the sessions are focused on career development skills including time management, how to hire personnel, and understanding the promotion process. Based on the results of the national WESTAT CTSA survey, we have already incorporated lectures by our Technology Transfer Office on the commercialization of scientific and clinical research into this series.

The three KL2 Program Directors provide additional support for the KL2 scholars. They will continue to review the KL2’s grant applications or manuscripts, facilitate career development, help improve the relationship between the KL2 scholar and their mentoring team, assist with networking both at the University and national levels, and provide support when negotiating for new positions. When necessary, the KL2 directors meet with the KL2 scholars and co-mentors to handle any concerns with the progress or career trajectory of the trainee.

Case Study: one of the KL2 scholars: “My KL2 mentorship team provided invaluable career support by providing research training and professional networking opportunities, reviewing manuscript and grant submissions, and writing letters of support for two successful grant awards including an R0-1 grant. I have also developed lasting scientific and personal relationships with these mentors, who continued to provide career guidance. I also gained valuable networking opportunities with other junior investigators resulting in a new interdisciplinary research collaboration that was recently submitted for Department of Defense funding. Finally, I had the fortunate opportunity to serve as a reviewer for the second round of KL2 grant applications as an alumnus of the program. The CCTSI KL2 review panel was structured according to the NIH format, and allowed me to gain valuable experience with the grant review process prior to serving as an ad hoc reviewer for three NIH study sections in the last year.” Katrina Maluf, PhD

3. Training in Clinical and Translational Research Methodology: To meet the needs of each scholar, the KL2 program allows flexibility with his/her didactic educational training. Dr. Lisa Cicutto, Director of the CLSC program, assists each scholar to develop an individualized course schedule. KL2 scholars without previous training in clinical research methodology are expected to enroll in either the CLSC PhD or Masters Program. Tuition support for trainees has been included in the KL2 budget. KL2 scholars who have already completed formal research training often complete advanced coursework appropriate to their career goals. A complete description of the RCR training for KL2 scholars is included in the Education section (p. 9-10) of this proposal.

4. Participation on National Research Conferences: All KL2 scholars present their research at one of the Clinical Research Training/Society for Clinical and Translational Science (ACRT/SCTS) meetings. At these conferences, trainees are exposed to important research concepts and have an opportunity to practice their oral presentation skills. KL2 scholars are encouraged to present at other specialty focused national meetings.
5. Mentoring and Career Development Programs: KL2 scholars and their mentors are integrated into the valuable CCTSI career development programs. The KL2 scholars and their mentors now participate as a dyad in our formalized CO-Mentoring program. The mentors participate in our Leadership in Innovative Team Science (LITeS) program. KL2 scholars also submit their first independent proposal to our KTR Study Section.

D.2. COLORADO MENTORING TRAINING PROGRAM (CO-Mentor). Proper mentorship is absolutely essential for successful career development as it positively influences academic productivity, feelings of self-efficacy, job satisfaction, and builds academic persistence (44-47). Mentees with influential and sustained research mentoring are more likely to devote additional time to research, publish more papers, become principal investigators on grants, and mentor others trainees in the future (48). One barrier to effective mentoring is a generalized lack of training on how to be an effective mentor (49, 50). Recent studies have demonstrated that mentors and mentees can benefit from a formal, structured training program to cement the mentor-mentee relationship (49, 51). Successful mentoring requires commitment and certain interpersonal skills of both the mentor and the mentee, and also a facilitating environment. To maximize the mentoring capabilities of our investigators, a new cutting-edge mentor training program was initiated during the second year of CCTSI funding. The aims of the CO-mentoring program are to: 1) develop skills and behaviors for effective mentoring relationships; 2) enhance the particular mentor-mentee relationship; and 3) build a network of trained mentors and mentees who will model these practices for others, and result in a sustainable culture of mentoring. Greg Austin, MD will continue to lead the CO-mentoring program.

Initially, junior investigators funded through a K mechanism (including our KL2 scholars) and their mentors were our primary target group for the CO-mentoring program. However, due to the success and subsequent demand for the program, we have expanded our selection criteria to include mentor-mentee pairs in which the mentee is supported by any career development award, including an institutional T32 training grant, an individual NRSA grant or a foundation-supported award. Participants must commit to attend all sessions and must enroll as a mentor-mentee pair. Enrollment is capped at 48 participants (24 mentor-mentee pairs). If a mentee has co-mentors, they choose one mentor who will attend all of the sessions. In the two years of the CO-mentoring program, a total of 45 mentor-mentee pairs have participated.

**Program Description.** The program consists of four five-hour sessions (discussed below) distributed throughout the academic year, starting in October and ending in April. This spacing of the sessions provides the best balance between maintaining momentum from the previous session and allowing sufficient time for participants to apply their newly learned skills. An active learning component utilizes the time between sessions to connect with other peers in the program. Mentees meet with another mentee to discuss an element of the program, while mentors meet with another mentor. At the beginning of each session, time is devoted to debrief the prior meetings, discussing reflections and experiences. Each participant also develops a personal development plan that focuses on concrete skills or behaviors that they can improve, specifying measures for evaluation and monitoring of progress. This plan becomes a living document for their own use, and provides a model for personal gap analysis and structured methods to approach personal development. The success of the CO-mentoring program is revealed in the exit surveys of the 2011 cohort of mentors and mentees (Table 31). The mean scores are based on a Likert 1-5 scale.

**Table 31: Results of CO-Mentoring Exit Survey**

| Establishment of professional relationships | 3.71 | 4.00 |
| Sense of connection to the University | 3.14 | 4.00 |
| Career satisfaction | 3.23 | 3.53 |
| Relationship with mentor/mentee | 4.14 | 3.67 |
| I can have a successful academic medicine career | 3.07 | 3.40 |
| I can assist others in achieving a successful career | 3.71 | 3.60 |

Session 1 focuses on setting goals, career mapping skills, and interpersonal communication skills. The CVs of mentors and mentees are reviewed to highlight whether an individual’s career goals are appropriately reflected. These interactive self-knowledge and communication skill-building activities are the foundation for enhancing mentoring outcomes. Before the next session, the mentor-mentee pairs reflect on their communication with each other and identify at least one new way to communicate. Also, participants craft a brief personal narrative that elaborates on the rationale, values, and passion for their career path.

Session 2 is directed to improve written and verbal communication skills and incorporate coaching techniques, such as goal setting and active listening, as a way to enhance mentoring skills. In small groups, the personal narrative section of their Biosketch is reviewed, and participants share what they learn about the effectiveness of the written communication. Additionally, interactive presentation occurs on writing effective...
letters of support. Before the next session, mentees revise the personal narrative with their mentor, and mentors write or improve a mentor letter of support.

Session 3 addresses improving goal setting skills using individual values and effectively involving peers and mentors to design, implement, and track achievements and goals. The second half of Session 3 is the only time mentors and mentees are separated. During an interactive discussion on “Managing Up,” mentees focus on how they can optimize the relationship by knowing their needs and communicating expectations to the mentor. Separately, mentors discuss techniques to give and receive feedback from mentees. Before Session 4, mentees craft a personal mission statement and delineate short-term and long-term goals to review with their mentor. Mentees also map their mentoring network and review it with their mentor to identify gaps.

Session 4 is conducted in a way for participants to discuss a conceptual framework for making personal work choices that promote academic growth and persistence. Time management strategies are also reviewed in the context of achieving work goals, and an interactive network exercise is used to reinforce networking skills that are important in building professional relationships.

D.3. LEADERSHIP IN INNOVATIVE TEAM SCIENCE (LITeS): Higher education has been slow to adopt training for leadership. As a result, faculty and academic administrators rarely assume their roles with adequate management and leadership skills (52-54). Interdisciplinary and collaborative research creates additional challenges that require even more sophisticated leadership skills (55-57). LITeS provides a unique environment for exploring individual strengths and development needs (including standardized assessments), for understanding and practicing critical team building skills, and for building support networks to sustain intentionality and development of more effective leadership behaviors. The aim of the LITeS Program is to enhance effective leadership for team science by: 1) providing training in exemplary leadership skills for emerging leaders; 2) providing focused opportunities to practice and reflect on those skills most critical for team science; and 3) creating communities of clinical translational researchers who will foster innovation and mutually support effective leadership. The need for this program is suggested by results of a WESTAT national survey of CTSA-supported trainees and their mentors that identified the need for more training in team-based science as the primary deficiency in most CTSA programs. LITeS seizes upon this unmet need.

LITeS accepted its first cohort in 2008. The program is structured in four two-day blocks scheduled quarterly over the academic calendar. To date, three cohorts and a total of 80 individuals have participated. In 2011-12, two one-day “booster” sessions were provided for LITeS alumni. Based on survey results, these booster sessions were well received and will be continued. Senior faculty leaders who direct collaborative research centers, programs, or projects were identified as the target audience for LITeS, and the first cohort included the senior leadership of the CCTSI. Subsequently, program directors of externally funded training programs (T32 and K12 directors, and K24 recipients), and the mentors for the KL2 scholars were asked to participate, along with graduate program chairs, department chairs, and deans. By 2011, all of the six deans on the Anschutz Medical Campus had participated. By reaching broadly into the pool of clinical & translational research talent, LITeS impacts the quality of the next generation of clinical translational leaders, as well as the leadership currently in place.

Case Studies: LITeS Alumni: “The LITeS program has been surprisingly effective for me. Both my research lab and the NIH-funded Ph.D. training program that I administer have benefited from the many useful lessons offered. I also very much appreciate the time spent getting to know the other faculty leaders on campus.” Lawrence Hunter, Professor Pharmacology & Computer Science, Director: Computational Bioscience

“The LITeS program provided me with the basic skills, tools, and insights into my own personality needed to transition from functioning as a manager to being a leader.” Doug Fish, Professor & Chair, Clinical Pharmacy

Program Description. Judith Albino, PhD, Professor CSPH, assumed directorship of LITeS in 2012. She is the President Emerita of the University of Colorado, and is formally trained in executive coaching and experienced in leadership coaching for higher education. The agenda over the four 2-day sessions varied somewhat from year to year, based on feedback from participants and trials of new approaches. The program reflected three major domains of learning: Leadership, Teamwork, and Innovation. Topics/Activities include Personality/Work Style, Leadership Models and Leadership Practices, Effective Meetings, Emotional Intelligence, Conflict Management, Giving and Getting Feedback, Generational Differences, Stress Management, Respectful Workplace, High Performing Teams, and the Meaning of Work. Learning activities used five types of training experiences: (1) didactic training in an interactive workshop format with small group exercises; (2) quantitative, validated assessments to aid self-reflection, (3) Q&A sessions with notable local...
leaders from outside the university; (4) personal leadership development planning with behavioral objectives and assessment; and (5) homework exercises focused on trying new skills from the trainings and peer coaching (after training) involving participants from different research areas and schools. Both external experts and CCTSI faculty who are experienced coaches and/or leadership trainers deliver the program content. As the program has matured, LITeS alumni have been asked to contribute to programs for subsequent cohorts. Both approaches have contributed to high program credibility.

LITeS participants included roughly equal numbers by gender and by training degree - PhDs (53%) and MDs (47%) and approximately half were translational and half clinical researchers. Most were full professors (75%). School of Medicine faculty comprised 40% of participants, with 22% from Public Health, 17% from Pharmacy, and 17% from Nursing. Although participants from Dentistry have been missing, the dean of that school participated in the last cohort, and we have five applicants from Dentistry this year. The T&E Core formally evaluated the LITeS program. Table 32 displays participant self-reports of knowledge gains for session topics that addressed team science concepts. Quantitative ratings of programs were high, using a 1-5 Likert scale. Participants reported implementing newly learned skills immediately and an eagerness to share concrete strategies to improve teamwork and meeting efficiency. Participants reported plans to use leadership and teamwork skills in their academic environment, and 83% reported using their new skills in leading their research teams. Moreover, 100% of participants indicated that LITeS increased their connection to the University, and all of the participants valued the interactions with investigators from multiple schools and disciplines. Over the one-year course, a remarkable 30% developed new collaborations from their participation in LITeS. This connectivity is vital to achieving a pervasive culture of academic persistence.

D.4. K-to-R (KTR) MOCK STUDY SECTION AND GRANT REVIEW: Approximately 25-30% of K awardees do not apply for an R01 grant (58) and as low as 9% of female K23 awardees who apply for an R01 grant are actually funded (59). Recent changes in the overall length of proposals, the reduction in the number of submission from three to two, and the decrease in funding levels have also increased the importance of the quality of the initial grant submission. Although their grant proposals are likely reviewed by their primary mentors, K awardees could benefit from additional expert review of their research proposals. Therefore we created the KTR Program in 2011 to improve the success of investigators transitioning from a K to an R grant. This program is an internal NIH-style mock grant review panel of R01 or equivalent proposals for clinical-translational K awardees. The goals of the KTR Program are to 1) improve the quality and competitiveness of first time R01s or equivalents from our K (or equivalent career development) awardees, 2) allow K awardees to learn about the grant review process including the importance of clarity, the organization of their proposal, and the interactive exchange of ideas and opinions among study section panelists, 3) provide mentoring to K awardees regarding grantmanship from senior faculty with study section panel expertise, and 4) offer an opportunity for junior faculty to participate in a mock study section and prepare them to review grants on a national level.

**Program Description.** The KTR Grant Review is scheduled three times per year prior to each major NIH deadline. Investigators submit their R-proposals approximately 6-8 weeks before the deadline to provide sufficient time to incorporate ideas from the study section reviews into their proposals. Reviewer assignments are made by the Program Director (Dr. Margaret Wierman) to members of a core review team and other content experts in the specific area of research from across the CU and CSU system. Proposals and reviews are uploaded to the electronic system created by the CCTSI Translational Informatics Core. *The applicants and their mentors are required to attend the Study Section session.* The KTR panel is organized similar to a NIH study section with the unique opportunity for the applicants to attend the meeting and see how the formal review process occurs, including scoring and discussion about strengths and weaknesses of each application. During each review session, the Director of the KTR program provides a handout to applicants on the grant review process. The reviewers use individual proposals to exemplify areas of strength or weakness to aid all

<table>
<thead>
<tr>
<th>Table 32: Team Science Knowledge</th>
<th>Before</th>
<th>After</th>
<th>Change *</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Std. Dev.</td>
<td>Mean</td>
</tr>
<tr>
<td>Effective Feedback</td>
<td>2.75</td>
<td>1.18</td>
<td>4.13</td>
</tr>
<tr>
<td>Emotional Intelligence</td>
<td>2.46</td>
<td>1.14</td>
<td>3.71</td>
</tr>
<tr>
<td>Building Respective Workplaces</td>
<td>2.90</td>
<td>0.77</td>
<td>4.05</td>
</tr>
<tr>
<td>Effective Meeting Strategies</td>
<td>3.07</td>
<td>0.78</td>
<td>4.00</td>
</tr>
<tr>
<td>High performing Teams</td>
<td>2.81</td>
<td>0.91</td>
<td>3.68</td>
</tr>
<tr>
<td>Conflict Management</td>
<td>2.77</td>
<td>0.86</td>
<td>3.46</td>
</tr>
</tbody>
</table>

* All differences in mean significant at the p < 0.01 level
applicants in style, language, and approach. After the Study section, all reviewers are available for additional in depth discussion with the applicants to further improve the application. On average, the KTR program reviews 7 applications per cycle. A total of 35 investigators have participated in the program to date, and 32 have submitted their R01 applications. To date 8/33 (24%) of the proposals have already received their funding. Based on the recommendations of the KTR committee, 27 of the 35 participants also submitted 48 additional non-NIH grants. A total of 16 (33%) of these submissions have been funded, and an additional 31% are pending review. Therefore, the KTR program is also educating applicants to persevere and seek additional sources of funding. In summary, 24 grants have been funded to 35 investigators participating in this program.

D.5. FUTURE DIRECTIONS AND EXPANSION FOR PROPOSED GRANT CYCLE

1. Enhance the KL2 program by improving synergy with other clinical translational programs.

The excellence in clinical and translational research at CU-D is no better illustrated than by the high number of K-awardees, including 82 individuals with NIH early career development awards (23 K08, 29 K23, and 30 K01 awardees [10 at CSU and 5 at CU-B]) and 7 K12 programs (supporting 29 scholars) in addition to the CCTS KL2 program, complemented by eight K24 awardees (Table 33). Despite this high rate of K-award success, the training of these awardees is often fragmented and duplicative between programs, without any coordination between programs. The ETCD leadership will prioritize the development of a more efficient work flow for training K-awardees in an integrated and more cost-effective manner. ETCD leadership will work with the K12 directors and the 82 individual K-awardees to integrate the CCTS educational opportunities into their career development, and reduce duplicative efforts. In addition, we will coordinate our career development programs with the eight K24 awardees on campus and integrate their trainees into CCTS sponsored activities in mentoring and career development. Finally we will invite the 82 current individual K awardees (and their mentors) to participate in the KL2 educational and career development programs, thus leveraging the considerable effort that has already been put into developing the KL2 program. By bringing together all of these trainees and synergizing efforts, the CCTS will have a positive impact on over 100 K-funded trainees and reduce duplication of efforts (and cost) for training programs.

For the K-12 and individual K-scholars, the CCTS will enhance their educational and career development in three specific ways: 1) All of these scholars will be invited to participate in our C-CO-mentoring program with one of their primary mentors. 2) The scholars will be invited to submit their first independent proposal to be reviewed by our KTR program. 3) We will sponsor a lecture series addressing topics that are relevant to all investigators with a career development award. For example, in conjunction with the Graduate School and the SOM, the CCTS ETCD will be sponsoring a professional writing consultant (Dr. George Gopen from Duke University) as a visiting professor for three days in March of 2013. Dr. Gopen will give several plenary sessions on scientific writing, and then meet individually with the KL2 and other K-awardees to help improve their scientific writing.

Efforts will also be initiated to use existing CCTS resources to enhance mentorship of the K-awardees. The mentors of the individual K-awardees and of the K12 scholars will be invited to participate in our LITeS program and in the CO-Mentor program, as already stated. We will also invite these mentors to participate as reviewers of grant proposals for our KTR program. Finally, we will assemble our K24 awardees as external career development advisors for the trainees with individual K23 awards. To help align expectations between

<table>
<thead>
<tr>
<th>Table 33: CU-D K12 Training Grants</th>
<th>Program Director (Department)</th>
<th>Postdoctoral Trainees Supported per Year</th>
<th>Total Number of Faculty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child Health Research Career Development Award</td>
<td>Stephen Daniels (Pediatrics)</td>
<td>4</td>
<td>39</td>
</tr>
<tr>
<td>Colorado Career Development Program in the Genetics and Genomics of Lung Diseases</td>
<td>Mark Geraci (Internal Medicine)</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Paul Calabresi Award in Clinical Oncology Research</td>
<td>Madeleine Kane (Medical Oncology)</td>
<td>6</td>
<td>52</td>
</tr>
<tr>
<td>Developing Pediatric Diabetes Investigators for the Future</td>
<td>GeorgeAnne Klingensmith (Pediatrics)</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Colorado Comparative Effectiveness Research and Safety Scholars Program:</td>
<td>Anne Libby (Clinical Pharmacology)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Colorado’s Building Interdisciplinary Research Careers in Women’s Health Program</td>
<td>Judith Regensteiner (Internal Medicine)</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>Colorado Women’s Reproductive Health Research Career Development Center</td>
<td>Nanette Santoro (Ob-Gyn)</td>
<td>3</td>
<td>33</td>
</tr>
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</table>
K-awardee trainees and their mentors, we will encourage use of the written mentoring compact between trainee and mentor (that we will make available on our website along with examples of effective compacts), which was originally developed by the Association of American Medical Colleges. K awardees and their mentors will be instructed to complete a series of questions together covering issues such as ground rules for discussions, and conflict resolution.

2. **Enrich and expand our Mentoring and Career Development Programs.**
   
   **Junior Mentor Development Program (JuMP).** Data from the CO-Mentoring program confirms that earlier in their career, our junior faculty members are beginning to mentor trainees. Therefore we will create an additional JuMP for junior faculty members who are faced with the unique challenge of serving as a mentor while still developing their own path to independence. The JuMP program will provide a foundation for mentoring skills and will serve as a pipeline for faculty members to participate in the CO-Mentor program as their mentoring role expands. Investigators at the assistant professor level who have or will soon mentor in some capacity (such as a summer research student, or a resident with a 1-2 month research elective) will be eligible for participation. We will target previous mentees in the CO-Mentor program, Clinical Faculty Scholars, and trainees with career development awards. We are proposing two separate two-hour interactive JuMP workshops during the academic year. Specific issues that we will address include: 1) Communication skills; 2) Determining whether the mentee is appropriate to mentor based on the mentee’s research skills and goals and the faculty member’s own expertise; 3) Setting expectations about the time dedicated to research and deadlines for abstract and manuscript submission; 4) When to say no and redirect the mentee to another mentor; 5) Developing a mentored research project in the context of whether the research is “independent” or a project that is integral to the faculty member’s own research career.

**LITes.** The participants in the LITeS program will be expanded to include midcareer faculty who demonstrate outstanding leadership and mentoring potential. We will ensure the recruitment of all K-award related mentors. To provide more intensive training in team science we will incorporate team projects for interdisciplinary groups of 7-9 participants within the cohort. Projects will engage the teams in meaningful tasks that will have real impact on the conduct of clinical-translational research across the CCTSI. For example, one of this year’s teams is developing a tool box to help facilitate team science. Senior administrators will serve as mentoring resources for the teams. Time will be allocated during sessions for teamwork and feedback from trainers, but teams will continue work over the course of the year. Our LITeS faculty will also assist other campus groups to develop specialized spin-off leadership programs, including the Center for Women's Health Research that is designing a program specifically for women faculty. Since the creation of our LITeS program, additional leadership programs with overlapping content have also been developed on campus. In order to improve the efficiency and cost-effectiveness of leadership training across of system, we will work in conjunction to hold combined plenary sessions on mutually relevant topics. In year 4-5 of the proposed grant, we will begin to charge a nominal tuition to participate in the LITeS program in order to cover the costs of this program as our NIH CTSA grant budget reductions take hold.

**KTR program.** Because of the current success of the KTR program, we will expand the program in three ways. 1) We will make the KTR program available to investigators from the Rocky Mountain region, including our new partner Colorado State University and other universities from neighboring Institutional Development Award (Idea) States. This NIH sponsored program broadens the geographic distribution of NIH funding for biomedical and behavioral research, fosters health-related research, and enhances the competitiveness of investigators at institutions located in states in which the aggregate success rate for NIH proposals has historically been low. Therefore, we will open the KTR program to institutions from Wyoming, Montana, and North and South Dakota. Applicants will participate in the actual mock study sections by videoconferencing. 2) To introduce newly funded investigators to the process of reviewing grants, we increase the number of junior investigators on the KTR study section. Recently funded R01 investigators will be invited to review KTR proposals to develop their grant reviewing skills. 3) The transition from fellowship to a mentored Career Development Program such as the NIH K23 award is another time point that investigators require additional support. Borrowing from the success of the KTR program, we will create a second mock study section for K or other career development proposals. The reviewers will specifically focus on the development of effective career development plans, mentoring letters, and personnel statements. The Directors and faculty mentors of the KL2 and K12 programs, and our NIH K24 awardees, will serve as reviewers for the Pre-K programs. Rolling review will be available for foundation grants and other CDAs. We anticipate that this program will increase the competitiveness of applications for local and national career development awards.
E. EVALUATION OF THE KL2 PROGRAM. Program evaluation will center around following the progress of KL2 and CFSP scholars throughout their training and for at least five years after program completion to assess the impacts of program participation on the following metrics: core competency development (repeated measures will be collected using the Clinical Research Appraisal Inventory described previously); research productivity, including engagement in team science and the impact of research (examined primarily through bibliometric analysis adjusted for self-citation); the effectiveness of mentorship support provided and how the inherent resources of this/these relationship(s) are leveraged by both the mentor and mentee; and, career success, including the achievement of critical career milestones. During the course of program participation, annual key informant interviews will be conducted to explore and document the following types of information: Program milestone: indicators of progress toward timely program completion and maturation as a CTR scientist, including submission and acceptance of abstracts and manuscripts, grants submitted and awarded, disclosures filed. Scholars will be asked to describe the evolution of their research and research orientation – specifically, clinical significance, research endeavors on the T05-T4 continuum; and career aspirations. Mentorship: including perceived insightfulness of content and/or methodological guidance and responsiveness of administrative and career development support, and frequency of contact. General satisfaction with and feedback on the program: specifically perceived strengths or elements that have been particularly impactful and ways to improve. Institutional assets: opportunities – resources and services that have catalyzed their research program and career (that they feel they would not have had access to at any other institution)

Portfolios, started in Year 1, will provide another source of information about goals, career development needs, grants, publications and the trajectory of research plans. Any publications and grants cited will be reviewed and rated in terms of their translational scope and significance and the degree to which they represent team science endeavors. The Team Science Rubric – i.e., a series of anchored rating scales developed by evaluation partners and refined in response to national expert reviews – will be used to classify research products in relation to these outcomes. Comparisons will be made between the research productivity of program participants and KL2 program applicants who had the next highest scores but were not selected. Alumni will be tracked and contacted annually to submit an updated CV that will be reviewed for evidence of research productivity (grants, publications), career success (e.g., faculty appointment and rank, professional honors, etc.), and the degree to which the investigator is engaging in multi-disciplinary translational research (vis-à-vis co-authorship networks and study team composition). They will also be asked, by phone or survey, about metrics such as career satisfaction, research and mentor support, and career goals/aspirations. Evaluative studies of impact will examine differences and changes over time in key metrics between program alumni and a group of demographically similar investigators.

Associated evaluation activities will assess the impact of the programs on mentor-mentee pairs (specifically in terms of creating and supporting a productive and mutually-beneficial relationship) and the environment for mentorship. Increases in knowledge and skills (related to giving and receiving feedback, managing up), and evidence that participants have applied the knowledge and skills obtained during their training will be assessed for all participants. Pre and post assessments, key informant interviews, and case studies (comparing highly effective and less effective pairs) will be used to collect data regarding mentor-mentee relationships, mentoring aptitudes, and future plans for leveraging mentor-mentee relationships and the associated, inherent resources to achieve CTR and career goals. These data will be examined in relation to factors such as professional preparedness, career aspirations and persistence. One of the objectives of the ETCD program is to further integrate the KL2 program with other career development programs, leading to increased collaboration and cost effectiveness as resources are expanded, redundancies removed, and economies of scale achieved. The degree to which this integration is achieved will be evaluated against milestones established in collaboration with ETCD leadership, the QPIP program and evaluation partners.

F. MILESTONES AND IMPLEMENTATION TIMELINE. Milestones and the Timeline for implementation of these initiatives are presented in Table 34.

<table>
<thead>
<tr>
<th>Table 34: Timeline for KL2-related Programs</th>
<th>Yr1</th>
<th>Yr2</th>
<th>Yr3</th>
<th>Yr4</th>
<th>Yr5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Improve synergy of the KL2 program</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Development introductory mentoring program</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Expand the LITeS program</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Forge collaborations for the KTR program</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SECTION III. TL1 TRAINING PROGRAM AND OUR UNDERREPRESENTED MINORITY PIPELINE PROGRAMS

A. SPECIFIC AIM: To enhance the pre-doctoral TL1 training, expand our pipeline programs, and ultimately build a diverse clinical and translational workforce through the Rocky Mountain region.

B. OBJECTIVES AND SIGNIFICANCE: In 2008, the CCTSI established the Clinical Translational Science TL1 Certificate Program for students enrolled in our basic, population, and behavioral science PhD programs. The goal of this program is to train a cadre of PhDs who will understand disease processes in the context of human physiology and who can apply their research training to clinical-translational science. The program was originally awarded four one-year positions. Over the last four years, the TL1 program has inherently transformed the CU-D pre-doctoral training program model. Based on the overwhelmingly positive feedback from the first cohort of trainees, and the impact on multiple graduate school programs, the CCTSI increased the size of the TL1 program to eight positions per year. Our current TL1 training program can conceptually be divided into five components (Fig. 30).

The Advisory Committee to the NIH Director Working Group on Diversity in the Biomedical Research Workforce identified definite racial and ethnic disparities in the number of individuals receiving PhDs, particularly in the biological sciences, chemistry and physics. This shortfall in PhD awards to underrepresented minority groups (URM) has also been documented by the 2011 National Science Foundation Women, Minorities, and Persons with Disabilities Report. The NIH is committed to increasing the number of URM principal investigators. Although there are many causes of the small pool of URM s applying for NIH funding as a principal investigator, one fundamental etiology is the shortage of URM students initially pursuing a career in clinical and translational research. The CCTSI has made this a priority focus of our training programs.

The CCTSI is committed to increasing the diversity of the clinical and translational workforce. The ETCD Pillar Program has focused on increasing the number and developing the quality of URM students who will be applying for careers in clinical translational sciences. In this regard, we have partnered with the CU-D Office of Diversity & Inclusion (ODI) to expand educational opportunities for URM high school and undergraduate students and strengthen the pipeline into our TL1 program. The primary goal of these pipeline programs is to expose promising students to the excitement of careers in clinical and translational research and strengthen this vital “seam” of the pipeline into our TL1 and other graduate school programs. Consistent with Manson’s conceptual theory model, these pipeline programs integrate students into the academic and social realms of our university and thereby strengthen their academic persistence, commitment to graduation, and their allegiance to CU1. Programs that provide academic enrichment, personal support and research experiences can substantially improve the retention of URM students in clinical and translational science careers. A key component of the pipeline programs has been the development of a network of scientific experts to serve as advisors, mentors, and role models to pipeline program participants. Over the last three years, the ETCD (in conjunction with the CCTSI Community Engagement & Research program and community partners) has developed partnerships with existing programs to advance the quality of their educational programs while increasing the number of participating students. As a result of these efforts, the ETCD now offers five integrated pipeline programs for either high school or undergraduate URM students:

1. The Native American Collegiate Partnership
2. The Summer Undergraduate Minority Mentoring in Translational Science (SUMMiT)
3. The CREATE Health Scholars (CHS) Program
4. Regis University Masters of Science in Biomedical Sciences Research Externship
5. Denver Student Training in Research Science (Denver STaRS) for high school students

Our TL1 and pipeline programs completely align with our overarching educational themes set forth for the next five years (Table 35). For example, both programs inspire academic persistence and thereby enrich the recruitment and retention of the finest junior investigators. We also will expand our undergraduate pipeline programs by building new collaborations with universities throughout the Rocky Mountain region.
C. **INNOVATION:** Our TL1 program focuses on providing *traditionally non-clinical PhD students* with the opportunity to learn about translational aspects of basic research complemented by a research-focused clinical experience. By pairing basic and clinical mentoring, the program has fostered new cross-disciplinary collaboration involving mentors and students. An important byproduct of these interactions is the development of academic persistence within the scholars as they become an integral part of a larger team of investigators. Our commitment to increasing the diversity of our PhD graduate students and the CTR workforce led us to focus efforts on students at earlier stages in their education. Prior to the creation of the CCTSI, several successful summer programs had been established for high school and undergraduate students on the CU-AMC campus. Over the past 4 years, we have collaborated with these programs to increase the number of students they can train each year, and to augment and enrich the quality of their curricula. Our CCTSI summer seminar series allows students from all of these different programs to meet inspirational scientists and learn about careers in clinical and translational science. These programs attract individuals from all underrepresented racial and ethnic groups, with disabilities and from disadvantaged backgrounds. However, due to the unique racial and ethnic diversity in the Rocky Mountain region, the CCTSI has been the most successful in attracting Hispanic American and Native American students to these programs. For example, we have established unique, strong and productive collaborations with a Native American college (Dine College) in our region. CCTSI efforts to enhance pipeline programs have prompted a CU-D wide initiative to establish a single portal for all pipeline programs. This centralized website will provide information to prospective students, increase the efficient placement of students into labs, improve the ability to track outcomes and evaluate programs, ensure safety training, and provide essential information for renewal and future grant applications.

D. **APPROACH (for the TL1 and Pipeline Programs)**

*In this section, we initially describe the structure and accomplishments of our current TL1 program and then discuss plans to enhance the experience for these pre-doctoral students. In the final portion of this section, we describe our current URM high school and college Pipeline Programs and plans for the future.*

D.1. **TL1 PRE-DOCTORAL SCHOLAR PROGRAM**

1. **Accomplishments of Prior Trainees in the TL1 program.** To date, the TL1 program has trained 41 scholars representing 16 different PhD-granting programs. Most trainees enrolled in the program near the end of their 2nd or 3rd year of graduate school. *In total, the TL1 pre-doctoral trainees have published 60 original peer reviewed manuscripts.* Ten trainees have completed the TL1 program and received their PhD certificate (Table 36). All of the graduates of the TL1 program have incorporated a clinical or translational research component into their careers. Several of them are currently in postdoctoral fellowships that include a translational or clinical component of their research.

| Table 35: TL1 and Underrepresented Minority Pipeline Program alignment with Overarching Themes |
|---------------------------------|---------------------------------|--------------------------------|-----------------------------|
| Expand the ETCD portfolio       | Build the future workforce      | Enhance efficiency            | Forge local/regional         |
| Forge local/regional            | Enriching mentorship            | Recruitment and retention     | Inspire academic             |
|                                 |                                 |                               | persistence                  |
| TL1 program                     | X                               | X                             | X                           |
| College pipeline programs       | X                               | X                             | X                           |
| High school pipeline programs   | X                               | X                             | X                           |

<table>
<thead>
<tr>
<th>Table 36: TL1 GRADUATES</th>
<th>PHD PROGRAM</th>
<th>CURRENT POSITION</th>
<th>TRANSLATIONAL RESEARCH PROJECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angela Rachubinski</td>
<td>Neurosci (2011)</td>
<td>Post Doc, CU-D</td>
<td>Autism in individuals with Down syndrome</td>
</tr>
</tbody>
</table>
2. Pool of TL1 Applicants. The pool of applicants for the TL1 program will be derived from the graduate programs at CU-D and CU-B. As shown in Table 37, there are multiple eligible PhD programs with over 1100 current PhD trainees. Last year, these programs plus the two ‘entry’ graduate programs, the umbrella Basic Biomedical Sciences Program and MSTP, received a total of 884 applications. The availability of the TL1 program for PhD students has attracted applicants interested in translational research to many of these University graduate programs listed and has positively impacted their recruitment. Expansion of the TL1 program to include pre-doctoral students from CSU is currently being discussed by the administration of both universities. Travel times for CSU students may be addressed through videoconferencing.

Table 37  TL1 Applicant Pool: Programs participating and number of trainees receiving NIH T32 funding

<table>
<thead>
<tr>
<th>Programs participating and number of trainees</th>
<th># Trainees (URM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic Sciences Doctoral Programs at CU-D AMC: Biochemistry &amp; Molecular Genetics*, Biomolecular Structure*, Cancer Biology*, Cell Biology, Stem Cell, &amp; Development, Human Medical Genetics*, Immunology †, Microbiology†, Molecular Biology†, Neuroscience†, Reproductive Sciences*, Pharmacology †, Physiology &amp; Biophysics</td>
<td>330 (14)</td>
</tr>
<tr>
<td>Analytical Health Sciences Graduate Programs at Colorado School of Public Health: Biostatistics; Epidemiology; Computational Bioscience*</td>
<td>39 (3)</td>
</tr>
<tr>
<td>Doctoral Programs at Downtown CU-D campus; Bioengineering; Health and Behavioral Science Program; Clinical Health Psychology</td>
<td>80 (16)</td>
</tr>
<tr>
<td>Nursing PhD Program</td>
<td>43 (5)</td>
</tr>
<tr>
<td>Pharmaceutical Sciences Graduate Programs: Pharmaceutical Sciences; Pharmaceutical Outcomes Research; Molecular Toxicology*</td>
<td>56 (9)</td>
</tr>
<tr>
<td>CU-B Graduate Programs relevant to CT research: Chemistry † <em>(159) 125/11, Biochemistry†</em> (77) 67/8, Integrative Physiology† * (28) 27/1, Cognitive Science* (33) 33/4, MCD Biology†* (70) 57/4, Neuroscience† (67) 66/2, Psychology (27) 26/4, Chemical and Biological Engineering* (98) 81/9</td>
<td>559 (43)</td>
</tr>
</tbody>
</table>

3. Eligibility and Recruitment. Students will be recruited for the TL1 program from all of the graduate programs outlined in Table 37. To date, we have received a total of 116 applications from students for our four application cycles. Because there are more qualified applicants interested in the TL1 program than we can support, we have invited students to join the program without funding. In the first four TL1 cohorts, 13 students participated despite no additional funding their first year, however 9 received a funded position in subsequent years. CCTSI non-funded positions also have been filled by trainees with individual NRSA fellowship support, other independent fellowship support, or support from their research mentor. This strategy has multiplied the impact of our TL1 program on numerous PhD training programs. In the current year (2012-13), there are seven unfunded TL1 students. Our TL1 scholars are a diverse group of students with 74% women and 10% URMs. We anticipate a higher percentage of URMs in future years as our Pipeline Programs mature in attracting exemplary URM students to clinical and translational science.

4. TL1 Selection Process. All TL1 applicants will have received a baccalaureate degree, be trained at a post-baccalaureate level and enrolled in a clinical research-related doctoral degree (PhD) program. Prior to applying, each student will identify a research mentor from their PhD program. The research mentor is required to be 1) an Assistant Professor or above, a member of the Graduate Faculty, and actively associated with an existing PhD training program; 2) a principal investigator engaged in research with a history of RO1 or equivalent external funding and the ability to offer a research environment relevant to human health and disease; and 3) be able to demonstrate commitment to graduate education by teaching, serving on exam committees, and/or directly mentoring graduate students and fellows. Each student (with the assistance of the Clinical Integration Committee) will also identify a clinician mentor who is: 1) Assistant Professor or above with a primary appointment in a clinical department; 2) actively engaged in clinical practice and research congruent with the interest of the student; and 3) is eligible for a full or adjunct appointment to the Graduate Faculty. We have implemented an electronic on-line submission process for these proposals through a CCTSI website link. Instructions to assist with the completion of the application are posted on our website, and both of the TL1 Program Co-directors and the ETCD program manager are also available to answer questions from prospective applicants. The application includes the applicant’s CV, their current graduate school transcript, a description of their proposed PhD research and clinical experience, a statement of career goals including their commitment to clinical-translational research in humans, letters of reference from both mentors and the Director of their PhD-granting program, and NIHbiosketches for the mentors. These materials are reviewed by the TL1 Steering/Admissions committee with 50% of the weight allotted to the planned research project, clinical
experience, and career goals; 25% to the applicant's credentials; and 25% to the letters of reference. In ranking the applicants, a key consideration is whether TL1 participation will significantly enhance their PhD experience. The committee evaluates whether the applicant will obtain an essential skill or experience that they would not have accomplished in the absence of participation in the TL1 program. We also consider the diversity of the trainee group in terms of gender, minority and disadvantaged status, and broad representation of PhD granting programs. We anticipate with the expansion of our pipeline programs, that the number of URM applicants to the TL1 program will begin to dramatically increase over the next few years.

**Case Study: URM TL1 scholar:** Sarah Brannon joined the CCTSI TL1 Program in 2008 with a research interest on the relationship between diabetes, the metabolic syndrome, and cognitive impairment. A portion of her thesis work utilized data from a randomized clinical trial on dietary restriction regimens on cognitive performance. Her clinical mentor is an Endocrinologist with clinical trials experience. Sarah has shadowed her mentor at a Weight Management Clinic and observed neuropsychological testing and assessment. Sarah was selected to give an oral presentation at the National CTSA Predoctoral Meeting and received the Outstanding Research and Creative Activity Award. Her clinical experience provided her with direct patient interactions, and increased her understanding of the feasibility and power of a team approach to solving health problems. This is evidenced in her future plan to establish an interdisciplinary team of faculty from the School of Medicine, and CU-Boulder, CU-Colorado Springs, and CU- campuses to address use of behavioral modifications to promote healthy cognitive aging.

5. **TL1 Program Leadership and Committees.** Celia Sladek, PhD, Professor of Physiology and Biophysics, and Madeleine Kane, MD, PhD, Professor of Medicine, Division of Medical Oncology, will continue to serve as Co-Directors. Dr. Sladek has extensive experience in graduate education, having served as primary thesis advisor for 10 PhD students (including 4 MD/PhD students) and as a thesis committee member for 23 students. She has trained 10 postdoctoral fellows, all of whom are employed in academia or the biotech industry. Her research has integrated cellular and molecular approaches with whole animal physiology. While Professor of Neurology at the University of Rochester, she collaborated with clinician scientists in human studies evaluating alterations in vasopressin secretion following stroke, meningitis, brain trauma, and in animal models of hypertension and congestive heart failure. Dr. Sladek chairs the Steering and Admissions Committees for the TL1 program. She monitors the progress of all students in the program and coordinates the 'T-Club' activities. She has actively participated in planning and routinely attends the annual National CTSA Predoctoral Meeting. Dr. Kane has extensive experience in training and research. She has been Co-Director of the Hematology Oncology Fellowship Program, has mentored 11 MD postdoctoral fellows, of whom 5 remain in academic settings, and has served as Program Leader for the K12 Clinical Oncology Research Training Program. As Medical Director of our Cancer Center Clinical Investigations she managed approximately 400 cancer clinical trials. Her laboratory-based research focused on growth factor receptor expression and regulation in human cancer cells as potential targets for cancer therapy. Dr. Kane also regularly attends the National TL1 meeting and led a career development workshop at the 2010 meeting entitled 'Finding Funding and Diverse Career Paths'.

**Program committees.** A Steering/Admissions Committee develops and monitors program strategies and selects applicants for funding and admission into the program. The membership includes senior basic scientists and active clinician scientists. The Curriculum Committee, chaired by Joan Hooper, PhD, Associate Professor of Cellular/Developmental Biology, implements the new integrative course, Tissue Biology and Disease, and developed the list of approved Systems/Disease level courses. The Clinical Integration Committee, chaired by Dr. Kane, establishes guidelines for the Clinical Experience (described below) and helps prospective students identify clinical mentors and formulate their clinical experience plan.

6. **Pool of Potential Mentors (TL1, Clinical Sciences Graduate Program, and KL2, programs).** Representative faculty members who will serve as mentors for the TL1 (and our other CCTSI training programs) are listed in **Table 38.** They are all accomplished investigators in clinical and translational research and have a track record of success in training new investigators and fostering their transition to independence. All of these mentors have sufficient funding to cover costs of their trainee’s research. These investigators demonstrate the diversity in our mentoring pool in regard to areas of research interest, types of clinical and translational research, and primary location. Four of these mentors are primarily located at CU-Boulder, and three from our new partner institution, CSU. Overall, 30% of these mentors are women. As a demonstration of the broad spectrum of mentoring opportunities for junior investigators, we did not include mentors from the CCTSI leadership in this table.
Table 38. Representative Mentors for TL1, KL2 and Clinical Sciences Graduate Program

<table>
<thead>
<tr>
<th>Mentor</th>
<th>Institution</th>
<th>Department or Training Program</th>
<th>Area of Research Expertise</th>
<th>Funding</th>
<th>Pre/post docs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Steve Abman, MD</td>
<td>CU-D SOM</td>
<td>Pediatrics</td>
<td>Pulmonary Hypertension</td>
<td>R01x2, T32, T35</td>
<td>1/39</td>
</tr>
<tr>
<td>2. Natalie Ahn, PhD</td>
<td>CU-B</td>
<td>Chemistry Biochem</td>
<td>Signal transduction in cancer</td>
<td>R01, T32, HHMI</td>
<td>21/24</td>
</tr>
<tr>
<td>3. Steve Anderson, PhD</td>
<td>CU-D SOM</td>
<td>Cancer &amp; Pathology</td>
<td>Breast Cancer</td>
<td>R01, P01</td>
<td>11/10</td>
</tr>
<tr>
<td>5. Kurt Beam, PhD</td>
<td>CU-D SOM</td>
<td>Neuroscience/Physiology</td>
<td>Ion channels/neuromuscular disease</td>
<td>R01, P01, Natl. Acad</td>
<td>10/24</td>
</tr>
<tr>
<td>6. Susan Boackle, MD</td>
<td>CU-D SOM</td>
<td>Immunology/Rheumatology</td>
<td>Pathogenesis of Lupus</td>
<td>K24, R01</td>
<td>6/5</td>
</tr>
<tr>
<td>7. Amy Brooks-Kayal MD</td>
<td>CU-D SOM</td>
<td>Neuroscience/Ped. Neurol</td>
<td>Epilepsy</td>
<td>R01</td>
<td>9/0</td>
</tr>
<tr>
<td>8. John Cambier, PhD</td>
<td>CU-D, NJH</td>
<td>Immunology</td>
<td>B &amp; T Cells; Autoantigens; Diabetes</td>
<td>P01x2, R01x2, T32, R21</td>
<td>49/18</td>
</tr>
<tr>
<td>9. Sean Colgan PhD</td>
<td>CU-D SOM</td>
<td>Immunology/Medicine GI</td>
<td>Inflammatory Bowel Disease</td>
<td>R01x2 (MERIT), R37</td>
<td>3/38</td>
</tr>
<tr>
<td>10. Dana Dabelea MD</td>
<td>CSU</td>
<td>Epidemiology</td>
<td>Diabetes and Obesity</td>
<td>R01x3, U18</td>
<td>6/8</td>
</tr>
<tr>
<td>11. Frank Dinennon, PhD</td>
<td>CSU</td>
<td>Health Exercise Science</td>
<td>Vascular Phys &amp; Aging</td>
<td>R01, R21 (NCE)</td>
<td>0/7</td>
</tr>
<tr>
<td>12. Holger Eltzschig, MD</td>
<td>CU-D</td>
<td>Immunology/Anesthesiology</td>
<td>Mucosal Inflammation</td>
<td>R01x3, K08</td>
<td>9/14</td>
</tr>
<tr>
<td>13. Larry Hunter, PhD</td>
<td>UC SOM</td>
<td>Bioinform/Pharmacology</td>
<td>Bioinformatics</td>
<td>R01x3, T15</td>
<td>18/13</td>
</tr>
<tr>
<td>14. Nancy Krebs, MD</td>
<td>CSPH</td>
<td>Community Behav Health</td>
<td>Nutrition</td>
<td>T32, K24</td>
<td>30/30</td>
</tr>
<tr>
<td>15. Leslie Leinwand, PhD</td>
<td>CU-B</td>
<td>Mol Cell Biol</td>
<td>Cardiomyopathy</td>
<td>R01, MDA, CCF, CUTTO, BDEG</td>
<td>33/37</td>
</tr>
<tr>
<td>16. Philippa Marrack, PhD</td>
<td>CU-D, NJH</td>
<td>Immunology</td>
<td>T cell receptors/autoimmunity</td>
<td>R56, P01, HHMI, IOM</td>
<td>12/28</td>
</tr>
<tr>
<td>17. Raf Nemenoff, PhD</td>
<td>CU-D SOM</td>
<td>Canc Biol; Pharm/ Medicine</td>
<td>Lung cancer metastases</td>
<td>R01, P50</td>
<td>7/27</td>
</tr>
<tr>
<td>18. Huntington Potter PhD</td>
<td>CU-D SOM</td>
<td>Neurosci/Neurology</td>
<td>Down’s Syndrome; Alzheimer’s</td>
<td>R01x2</td>
<td>9/21</td>
</tr>
<tr>
<td>19. Dennis Roop, PhD</td>
<td>CU-D SOM</td>
<td>CDSB; Dermatol. Regen Med</td>
<td>Stem cell biology</td>
<td>R01x2</td>
<td>10/17</td>
</tr>
<tr>
<td>20. Hugo Rosen, MD</td>
<td>CU-D SOM</td>
<td>Immunol/ Medicine GI</td>
<td>Hepatitis B</td>
<td>U01, K24, R01</td>
<td>3/11</td>
</tr>
<tr>
<td>21. Nanette Santoro, MD</td>
<td>CU-D SOM</td>
<td>Repro Sci/Ob Gyn</td>
<td>Ovarian Failure; Menopause</td>
<td>U54, K24, K12</td>
<td>4/32</td>
</tr>
<tr>
<td>22. Doug Seals, PhD</td>
<td>CU-B</td>
<td>Integr Physiol</td>
<td>Exercise Physiology Vascular Aging</td>
<td>R01x3, R37 (Merit), R21</td>
<td>24/27</td>
</tr>
<tr>
<td>23. David Schwartz, MD</td>
<td>CU-D SOM</td>
<td>Immunology/ Medicine</td>
<td>Epigenetics of asthma</td>
<td>P01, R01x3</td>
<td>5/19</td>
</tr>
<tr>
<td>25. Robin Shandas, PhD</td>
<td>CU-D/ CU-B</td>
<td>Bioengineering</td>
<td>Medical ultrasonics</td>
<td>R21x2, R01x2, NSF, T32</td>
<td>15/15</td>
</tr>
<tr>
<td>26. Kurt Stenmark, MD</td>
<td>CU-D SOM</td>
<td>Pediatrics</td>
<td>Pulm HTN/ Vascular Biology</td>
<td>P01, P50, R01, T32</td>
<td>4/14</td>
</tr>
<tr>
<td>27. Michael Tamkun PhD</td>
<td>CSU</td>
<td>Biomed Sci</td>
<td>Ion Channels in Cardiovasc Disease</td>
<td>R01x2, NSF</td>
<td>9/14</td>
</tr>
<tr>
<td>28. Stuart Tobet, PhD</td>
<td>CSU</td>
<td>Biomed Sci; Neuroendocrine/Biomed. Engineering</td>
<td>R01; P50; NSF</td>
<td>5/10</td>
<td></td>
</tr>
<tr>
<td>29. Kenneth Tyler, MD</td>
<td>CU-D SOM</td>
<td>Mico; Neurosci/Neurology</td>
<td>Neurovirology</td>
<td>R01x2, R21</td>
<td>11/8</td>
</tr>
<tr>
<td>30. Carl W. White, MD</td>
<td>CU-D, NJH</td>
<td>Pediatrics Pulmonary Crit Care</td>
<td>Immunology Pulmonary Injury</td>
<td>U54, P50</td>
<td>5/16</td>
</tr>
</tbody>
</table>

7. Description of TL1 Scholars program. Prior to entering the program, all TL1 students will have completed the basic course requirements, laboratory rotations, and passed their preliminary exam in their degree-granting program. Funded students will receive 1 year of stipend support, and commit to completing the remaining requirements for their degree granting program and the required courses for the TL1 program. However, students will continue to attend their Clinical Experience and ‘T-Club’ activities for the remainder of their graduate studies. Students who successfully complete these requirements will receive a Clinical Translational Science Ph.D. Certificate that is officially recorded on their transcript.

The Clinical Experience: The clinical mentor will work with the student to develop a clinical experience relevant to the student’s thesis project and is a member of the student’s thesis committee. Requirements for the Clinical Experience include: 1) attending the clinical experience orientation, 2) shadowing their mentor in a patient care environment and discussing the medical problems of patients relevant to their research, and 3) preparing and submitting reports on patients seen (“clinical diaries”) on each clinic attendance. The frequency of clinic attendance will be tailored to each individual project and the specific disease process they are studying. Some students develop a short intensive experience that is best suited to their individual needs while other students follow a cohort of patients over a longer duration of time. The shorter more intensive model is more suited for patients with acute medical disorders (for example: myocardial infarctions and acute lung injury), and the longer expanded model is more effective for patients with chronic diseases (for example: rheumatoid arthritis and diabetes). On average, students will attend clinic with their clinical mentor 1-5 times per month for up to 20 months. Students report on their clinical experience at thesis committee meetings, and include a clinical experience report in their thesis.

The following are three examples of clinical experiences and their impact of TL1 trainee outcomes:

1) Lisa Wilson, a neuroscience PhD student whose research involved assessment of phonological processing skills in first degree relatives of people with autism spectrum disorders, learned and became certified in diagnosing and categorizing autism spectrum patients. She participated in recruiting subjects for her brain imaging work as well as designing the tasks and analyzing the data. She defended her PhD in March, 2012, and has eight publications related to this work.
2) Richard Sullivan, an immunology PhD graduate who worked on development of new flu vaccines, wrote the IRB application and helped to conduct a clinical trial that was an integral part of his thesis.

3) Kristen Rumer, an MD/PhD student in the Reproductive Sciences PhD Program, utilized both cultured cell lines and primary placental tissue for her thesis work on leptin and its receptor, Siglec-6, expression in normal and pathologic human placentation. In addition to shadowing her clinical mentor in the High Risk Obstetrics Clinic, she participated in recruiting patients from that clinic for the Placental Origins of Preeclampsia study from which the human placenta and maternal blood samples used in her thesis work were derived.

**Didactic Requirements:** All TL1 trainees must complete three didactic requirements:

- **Human disease and systems course requirements:** Students complete two disease/systems oriented courses. One is the “Tissue Biology and Disease Mechanisms” course that was developed during the first CCTSI funding cycle. This course considers cellular and molecular pathways in the context of the organ and organism, and helps trainees to understand complex, multi-organ diseases. The second is an existing systems-level course in their specialty (e.g. Overview of Immunology, Fundamentals of Neuroscience, Cancer Biology), or an appropriate course from the medical school curriculum when approved by the TL1 Director.

- **Translational didactic requirements:** All students are required to complete courses in Biostatistics, Epidemiology, and Design of Clinical Trials/Experiments. Depending on the PhD degree granting program, some or all of these requirements may overlap with existing requirements or can be met by the more rigorous requirements of the degree granting program (e.g. Epidemiology and Biostatistics students may complete more rigorous statistical coursework). All TL1 students have access to the resources in the CCTSI Biostatistics core.

- **Responsible Conduct of Research:** All students complete HIPAA training and certification, the Good Clinical Practice online course (CITI) through the COMIRB website, and a course on Responsible Conduct of Research (as described in the educational section of this proposal).

**T-Club Activities:** The T-Club is a monthly meeting that will be attended by all TL1 program participants. The goal of these sessions is to develop skills that promote a successful and sustained translational research career. T-Club will focus on training skills aligned with the NIH core competencies in clinical research that are not covered in the trainee’s degree-granting programs, and provides opportunities for networking and career development. The ‘Disease of the Month Club’ is a format for discussing examples of clinical/translational research. The goal is to familiarize students with the challenges inherent is translating research from the bench to the clinic. This will be accomplished by group attendance at selected seminars, reading background materials, and discussing the presentation, problems, and successes. The presentations represent work that spans animal/bench and human/clinical research. For these meetings, we will take advantage of the high profile scientists featured in the Dean’s Distinguished Lecture Series or Medical Grand Rounds. These forums provide the opportunity for trainees to discuss the study design and feasibility issues with other students and identify the impact of clinical translational research in different research areas. Other sessions will be devoted to fundamental skills that are necessary to perform clinical and translational research. We have had sessions devoted to grant writing and others that have highlighted the efforts to bring translational work to the rural communities in Colorado presented by the CCTSI Community Engagement & Research program. Dr. Kane and colleagues from the CU Comprehensive Cancer Center also will discuss opportunities and challenges of funding and performing large clinical trials. We will conduct a T-Club ‘Book Club’ that has included readings and discussion such as examples of self-experimentation from ‘Who Goes First’ a book documenting historical examples of self-experimentation. We also will continue our sessions on Diversity/Cultural Competency presented by Leslie Wright from Kaiser Permanente using Leslie’s presentations on other URM groups. As a result, the T-club will continue to foster the connection of students with the larger university community.

**Participation in the National CTSA Research Conference:** A major career development focus of the TL1 program will continue to be preparing the trainees for the National CTSA Predoctoral Annual Meeting. All of our TL1 trainees will be supported to attend the National Meeting and are strongly encouraged to attend as many times as possible during their participation in the TL1 program. In general, we sponsor meeting attendance for 8-15 trainees each year. All of trainees have presented their research and two to three of our students have been selected each year for oral presentations. In preparation for these presentations, we will conduct a session on Best Practices in Abstract, Oral, and Poster Presentation of Research and will hold a practice session for all trainees prior to attending the National CTSA Predoctoral Meeting. These activities have received excellent trainee feedback, and will continue in the future. In addition, the National CTSA Predoctoral Annual Meeting serves as an excellent networking opportunity outside of the CU system for our trainees.
Joint basic and clinical mentorship: All of the TL1 trainees will have dual basic and clinical mentors. This model not only results in a unique mentoring skill set for the trainee but also encourages collaborative efforts between the co-mentors. The role of the clinical mentor is to 1) participate as a member of the Ph.D. thesis committee, 2) serve as preceptor for the clinical experience, 3) provide the trainee with at least one peer-reviewed clinical research paper to read for each monthly session, 4) review and discuss clinical protocols, 5) discuss translational ideas for research based on patient problems observed in clinic, and 6) review the clinical diaries from their trainees. The basic science and clinical mentors will meet together with the trainee at least quarterly to discuss how their clinical experience will enhance the thesis project.

8. Future Directions of the KL1 program and Expansion for Proposed Grant Cycle. The many successful aspects of the TL1 program described above will continue during the next funding period, in order to expand our capacity to train and build interdisciplinary teams of scientists to tackle major health issues. To expand its reach to clinical scientist students, the TL1 program has begun to offer an additional track, the Research Methodology Enrichment Track, designed for students in clinically oriented PhD programs such as Nursing, Physical Therapy, and Clinical Health Psychology. This track will provide the opportunity for a bench Research Experience. The goal of this track is not to train clinicians to be bench scientists, but rather to provide experience with techniques that are used to assess the cellular, molecular or genetic mechanisms underlying diseases that are the focus of their clinical research. Students in the Research Methodology Enrichment Track will identify an appropriate research methodology mentor and design a bench research experience in the mentor’s laboratory that is appropriate to the student’s research. The rationale for developing this track is to enhance the translational training for students who are in a clinically based PhD program such as Clinical Health Psychology or students who have extensive clinical experience such as those in the Nursing or Clinical Science PhD programs. The training will be individualized to the needs of the student and ultimately enhance their research opportunities and knowledge. The trainee will spend time learning techniques and performing bench research that will become incorporated into their thesis work. Instead of one of the disease/systems courses, trainees in this track will take “Practical Application of Molecular and Cell Biology Techniques for the Clinical Investigator”. This course is designed to teach clinical investigators “hands-on” approaches to basic molecular and cellular biology techniques. Weekly lectures will also cover cutting edge technologies and their clinical application. For example, Shannon Madore, a current Clinical Health Psychology PhD student and TL1 scholar will learn to perform plasma extractions and oxytocin radioimmunoassay in order to measure plasma oxytocin in her study on ‘Biomedical Markers of Stress and Psychosocial Factors in Informal Caregivers of Hospice Patients’.

In addition, we will build two new programs for all TL1 students. Based on feedback from the TL1 trainees, students will attend several of the Clinical Research Educational Program (CREP) sessions. The goal of this collaboration is to enhance the knowledge and awareness of feasibility and logistical regulatory research related to clinical and translational research. With the assistance of our LITeS faculty, we will also develop a seminar series on Team Science including sessions on team building, career development in the context of team work, and readings on the ‘pros and cons’ of Team Sciences. We will also invite outside speakers to lecture on how to build a highly functional multidisciplinary research teams and enhance collaboration.

D.2. CCTSI PIPELINE PROGRAMS: ENHANCING DIVERSITY IN CLINICAL AND TRANSLATIONAL RESEARCH

1. General Recruitment and Retention Plan to Enhance Diversity across the Anschutz Campus. CU-D established the Office of Diversity and Inclusion (ODI) to strengthen its recruitment of URM, as well as other groups to broaden the diversity of its faculty, housestaff and students. ODI mission is to “instill diversity into the institutional consciousness; reinforcing equity and inclusion through policies, practices and programs that prepare all faculty, students and staff for a multicultural world”. In addition, CU-D developed a comprehensive plan to enhance diversity in 2007. The plan seeks to: 1) Promote the academic advancement and success of URMs, 2) Enhance cultural, bilingual and diversity instruction throughout the curriculum, 3) Encourage an institutional climate of inclusiveness, respect and understanding, 4) Promote innovative research and scholarship related to cultural and racial disparities in health and health care, and 5) Improve access to quality health care for URM. As a result of these efforts, there has been a sustained doubling of URM enrollment in the SOM Residency and Fellowship Programs from 3% in 2002-03 to consistently 6% over the past 5 years. The SOM continues to prioritize increasing the diversity of its medical student body through increased
community outreach, pipeline programs and financial support from the public and the university, and the results have been nothing but striking. Of the 160 medical students in each of the next three classes: 13 students in the Class of 2013 are URMs; 33 in the Class of 2014, and 52 in the class of 2015 (17 Hispanic/Latino/Latina; 13 Mexican/Mexican American/Chicano/Chicana; 9 African American, and 4 American Indian or Alaska Native.) Half of these students received scholarship money from a fund created by the President of CU. Specific efforts are also being made across the University system to recruit trainees and investigators who are URM or women. All advertisements for academic positions specifically solicit applications from URM and women. Individuals with disabilities or disadvantaged backgrounds are also encouraged to apply.

2. The CCTSI Pipeline Programs. Prior to the CCTSI, several programs providing a meaningful summer experience for URM high school and undergraduate students were conducted across the University system. Though many of these programs were very successful, they were fragmented and duplicated resources. Some of these programs also required assistance with tracking and evaluation, and many lacked sufficient funding to accept the majority of their most highly qualified applicants. Starting in 2010, the CCTSI ETCD program made a strategic decision to expand and augment these programs to reach a larger group of needy students. We developed partnerships with those existing programs that had successful training records, and individualized our assistance to fit the needs of each specific program. Our various partners have included programs at Dine College (the Navajo tribal college), CU-D, CU-B, Regis University, and the Denver Public Schools. The goals of these partnerships are to increase the number of URM students who can experience a meaningful exposure to biomedical research and who may dedicate themselves to a career in clinical or translational science. All of the programs have their own primary sources of funding from agencies such as the NIH and the Howard Hughes Medical Institute, and several receive institutional support. Our role in these programs is to improve their efficiency by eliminating redundancies in the process of identifying suitable mentors, to provide funding for additional qualified students, and to enrich the quality of the programs by expanding the educational opportunities and experiences for their students. We have also strengthened the integration of these outstanding students into the academic and clinical translational community at CU. Our CCTSI sponsored Pipeline Programs are directed by Dr. Dominic Martinez, who also serves as the Director of the Office of Diversity and Inclusion for CU-D.

The following describes future plans for each of the Pipeline Programs and the role of the CCTSI:

a. The American Indian and Alaska Native Collegiate Partnership: With the assistance of Dr. Spero Manson, Distinguished Professor and Director of the Centers for American Indian and Alaska Native Health (CAIANH), the ETCD established an exciting partnership with Dine College in Tsaile, Arizona, the oldest and largest Tribal College in the United States. Located on the Navajo nation, Dine College previously developed an NIH supported 10-week summer research enhancement training program (SREP) in public health research methods. The SREP introduces American Indian and Alaska Native undergraduate students to the research process and to health professions, providing a foundation for basic public health research and evaluation. Using state of the art scientific methods, the SREP integrates concepts of holism, balance/harmony, kinship, and relatedness; values shared by American Indian and Alaska Native people generally and these students in particular. The SREP has been remarkably successful and to date has trained 48 American Indian and Alaska Native undergraduate students in health disparities research and led many to pursue advanced studies at other institutions across the country. The CCTSI will continue to support for the Dine College SREP in the following ways:

1. The Dine College SREP program has more qualified applicants than funded positions. The CCTSI will provide stipends for two additional students to participate in the Dine College SREP each summer. To date the CCTSI has supported a total of six additional SREP students (2 students per year for the last three summers).

2. We also will sponsor one CU-D faculty member to spend two days at Dine College at the beginning of the SREP program. In general, we have selected one of our KL2 scholars or a member of the ETCD leadership council to be the visiting faculty member. The goal is to teach the students how to pursue a clinical translational research career including discussing barriers that might be encountered. The faculty member will also assist students with the selection of their summer research project.

3. During the last week of the summer session, two additional CU-D faculty members will visit Dine College to help the students with the analysis of their research projects and their presentations.
During the next 5 years, The CCTSI-American Indian and Alaska Native Collegiate Partnership will be expanded to include undergraduate students from the Pine Ridge Reservation in South Dakota. Initially, faculty members from Pine Ridge Oglala Lakota College will participate, observe, and learn about the Dine College SREP with the goal of replicating this program on their campus the following summer. For this new Pine Ridge program, the ETCD will provide funding for students in their summer research program and support CU-D faculty members to visit the Oglala Lakota College and provide guidance and support for the student’s research projects. Additionally, students from both these summer programs will formally visit the CU-D campus each year to present their research to distinguished members of our faculty and also meet with our TL1 and KL2 scholars. During this visit, students will meet with leaders from the CCTSI, Deans and leaders from Centers for American Indian and Alaska Native Health to learn about opportunities at CU-D in clinical and translational research.

**b. The Summer Undergraduate Minority Mentoring in Translational Science (SUMMiT) Program**

In 2009, the ETCD created the Summer Undergraduate Minority Mentoring in Translational Science (SUMMiT) partnership to assist promising URM students with an interest in a clinical and translational sciences career. The SUMMiT is a collaborative program that builds on the structure of existing summer research internship programs at CU-D. Many of these preexisting programs are funded by NIH supported mechanisms (Table 39). The primary goal of SUMMiT is to quantitatively and qualitatively enhance the summer undergraduate research experience of URM students with a focus on the unique needs of Hispanic, Native American, and Alaskan Native students.

The SUMMiT program will provide the following additional resources to the existing internships.

1. **Career Development Sessions**: Selected trainees from programs will participate in targeted career development sessions including: A Translational Research Fair, Networking with Campus Leadership, and Resume Development workshops. These sessions will specifically build academic persistence and are designed to incorporate the students into the university fabric. For example, the students will meet with the Dean of Admissions of the Medical School to discuss what graduates schools desire in their applicants.

2. **Additional Student Stipends**: CCTSI will continue to fund summer stipends for URM students.

3. **Evaluation support for the partnered program**: Many of these existing programs expressed the need for enhancement of their tracking and evaluation systems. We have and will continue to sponsor the CCTSI T&E

<table>
<thead>
<tr>
<th>Table 39: Summer Internship Programs</th>
<th>Campus</th>
<th>Sponsored/Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graduate Experience for Multicultural Students</td>
<td>CU-D</td>
<td>NHLBI</td>
</tr>
<tr>
<td>Link to Advancement in Biomedical Research Career Opportunities and Training Section</td>
<td>CU-D</td>
<td>NIGMS</td>
</tr>
<tr>
<td>Summer Undergraduate Research in Pharmacology</td>
<td>CU-D</td>
<td>American Society for Pharmacology</td>
</tr>
<tr>
<td>Undergraduate Pre-Health Program (UPP)</td>
<td>CU-D</td>
<td>ODI and KP</td>
</tr>
<tr>
<td>Student Cancer Research Fellowship Program</td>
<td>CU-D</td>
<td>NCI</td>
</tr>
<tr>
<td>Undergraduate Research Opportunity Program</td>
<td>CU-D/CU--B</td>
<td>Campus Funding</td>
</tr>
<tr>
<td>Building Research Achievement in Neuroscience</td>
<td>CU-D</td>
<td>NIH</td>
</tr>
<tr>
<td>Undergraduate Research Practicum in Psychiatry and Behavioral Sciences</td>
<td>CCH</td>
<td>Department Funding</td>
</tr>
<tr>
<td>Clinical Undergraduate Research Experience</td>
<td>CU-B</td>
<td>Howard Hughes</td>
</tr>
<tr>
<td>Summer Education and Training Program in Schizophrenia</td>
<td>CU-D</td>
<td>Department Funding</td>
</tr>
</tbody>
</table>
Core to create and administer evaluation tools for a variety our partners. In addition, this team will continue to implement specific tracking measures to assist the long term follow up of their students.

4. **ETCD Faculty support of the partnered programs:** Members from the ETCD Executive committee will continue to serve on the Selection Committee and Internal Advisory Committee for several of these programs.

5. **Website support:** The CCTSI Translational Informatics program has and will continue to assist our partners with their website development. Importantly, we linked all of these summer research internships onto the CCTSI website thereby creating the first comprehensive single resource for students interested in applying to these summer programs.

6. **TL1 trainee mentors:** Students in the pipeline programs will continue to work in labs with trainees in the TL1 program. This will provide an opportunity for the pipeline students to become familiar with the career paths of PhD students in clinical translational sciences.

Since the start of the SUMMiT program, the CCTSI has supported 47 funded and 137 unfunded students (overall 184 URM undergraduate students have benefited from the SUMMiT program) (Table 40). Funded students received their summer stipend from the CCTSI. Unfunded students did not receive CCTSI stipend but attended all career development sessions. CCTSI will continue to fund 15-20 students per year in the next grant cycle.

<table>
<thead>
<tr>
<th>YEAR</th>
<th>FUNDED</th>
<th>UN-FUND</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>12</td>
<td>24</td>
<td>38</td>
</tr>
<tr>
<td>2011</td>
<td>16</td>
<td>58</td>
<td>74</td>
</tr>
<tr>
<td>2012</td>
<td>21</td>
<td>55</td>
<td>76</td>
</tr>
</tbody>
</table>

### c. CREATE Health Scholars (CHS) Program

This is a year-long program with a one-month summer intensive experience for undergraduate students from colleges throughout Colorado. Participating undergraduate students strengthen their applications to professional schools and programs by receiving hands-on training and exposure to a variety of health careers, and through advanced professional school examination practice. For example, students participate in clinical simulations, cadaver lab, heart and brain dissection, job shadowing and by launching a student-driven research projects that address local health issues. We have had over 120 participating students since 2010 and have demonstrated significant increases in these students’ scores in algebra, anatomy & physiology, biology, chemistry, organic chemistry, and physics in both pre- and post-tests as well as in DAT, MCAT, PCAT, and GRE practice test scores. CCTSI will continue to support students in this program.

### d. Regis University Masters of Science in Biomedical Sciences Research Externship

This partnership was established between CCTSI and Regis University in 2011. The goal is to provide access and research experiences at CU-D for Regis students enrolled in the Masters of Science Biomedical Program. The main objective is to establish connections and contacts at CU-D for these students and increase the knowledge and consideration for the Doctoral and/or professional programs on campus. Students will be selected by the Internship Coordinator at Regis University based on interest and past research experience. Students will complete the following training as part of their participation: Chemical Waste Management, Blood Borne Pathogen, and Lab Safety. Fifteen students have participated in this 12 week, 10-15 hours per week experience (9 students in 2011-12, and 6 in 2012-13) and the CCTSI will continue to support this program.

### e. The Denver Student Training in Research Science (STaRS) Program

One of the newest CCTSI programs targets traditional URM high school junior and seniors from CEC Middle College of Denver, Denver East High School, and Denver School for Science & Technology-Stapleton Campus. These schools were selected by the Denver Public School administration because of their rank among the most ethnically diverse schools in the state of Colorado and the great potential of their students (Table 41). The STaRS program has two distinct tracks for students interested in clinical and translational research. The short-term objective for both tracks is to create a positive exposure for URM junior and senior high school students that are beginning to explore career and education options in clinical-translational science. The long-term objective of the STaRS program is to increase the diversity of the future clinical and translational workforce. In order to create a pool of participants and recruit them to the program, we will work closely with key staff and faculty at each respective high school to identify top caliber URM students. Since its inception in 2011, a total of 66 URM high students have participated in the STaRS program.
All students will complete an application form and a formal interview process. Selection criteria include the maintenance of at least a 3.3 GPA, and the completion of advanced science courses (AP, Honors, or College equivalent). In addition, a parent or guardian must make a written commitment to the program. The advanced track (fall, spring & summer term) will pair students with a CU-D researcher for an 8-10 week laboratory research experience. On average students will devote 8-10 hours per week to the program. Students will participate in training prior to the start of their experience that covers HIPAA, professionalism, Chemical Waste Management, Blood Borne Pathogen, and Lab Safety. During the laboratory experience, participants will learn basic laboratory skills and gain insight on the biomedical and translational research projects conducted in their respective laboratories. The investigators and their research teams will stimulate intellectual curiosity in the students by teaching them the importance of research, specific laboratory techniques, and how to develop a scientific question. In general students from Denver East High School and the Denver School for Science and Technology will participate in this advanced track experiences. (See Table 42)

The preliminary track (only offered in the spring term) involves exploratory workshops focused on clinical and translational research, and includes field trips to the CU-D medical campus, and guidance workshops on educational paths for clinical and translational research careers. Students will complete HIPAA and professionalism training. In general students from the CEC Middle College will participate in preliminary track experiences. However, certain exceptional students that previously participated in preliminary track may subsequently participate in advanced track. In the future, the STaRS program will expand beyond a one-year program for juniors and include advanced course work and research experiences during their senior year. For many students who develop an interest in science, receiving positive feedback through involvement in a science fair is of great benefit. Therefore, we will provide support for STaRS students to present at the Denver Metro Science Fair.

### Table 41: Description of the High School

<table>
<thead>
<tr>
<th>High School</th>
<th>Description of the High School</th>
<th>Demographics</th>
<th>Free or Reduced Lunch</th>
<th># of STaRS students in 2011-2012</th>
<th># of STaRS students in 2012-2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEC Middle College (n=387)</td>
<td>Denver’s only career and technical magnet high school offering college and career-oriented experiences.</td>
<td>Hispanic 87.1% AA 2.6%, NA 0.5%</td>
<td>88.89%</td>
<td>20</td>
<td>22</td>
</tr>
<tr>
<td>Denver East High School (n= 2313)</td>
<td>Inter-city Denver public high school.</td>
<td>AA 26.4%, Hispanic 21.7%, NA 0.7%</td>
<td>35.5%</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Denver School for Science &amp; Technology(n=495)</td>
<td>Charter School focused on Math, Science, &amp; English. Goal is to graduate 100% of students and attend college.</td>
<td>Hispanic 38.4%, AA 25.3%, NA 0.6%</td>
<td>44.04%</td>
<td>3</td>
<td>11</td>
</tr>
</tbody>
</table>

### Table 42: Description of the Two Denver STaRS Research Tracks

<table>
<thead>
<tr>
<th>Advanced Track</th>
<th>Preliminary Track</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goal: Exposure to biomedical or translational research. To increase research and career options awareness</td>
<td>Goal: Exposure to basic research principles through exploratory simulations. To increase research and career options awareness.</td>
</tr>
<tr>
<td>Target Audience: URM high school juniors &amp; seniors</td>
<td>Target Audience: URM high school juniors &amp; seniors</td>
</tr>
<tr>
<td>Duration: 8 weeks, 8-10 hours per week</td>
<td>Duration: Spring Semester, 4 exploratory activities, 2 visits to CU Medical Campus, Denver Science Fair judge experience.</td>
</tr>
<tr>
<td>Trainings: Chemical Waste Management, Blood Borne Pathogen, Professionalism, &amp; Lab Safety, and HIPAA.</td>
<td>Trainings: HIPAA and Professionalism</td>
</tr>
<tr>
<td>Skills Gained: Gel electrophoresis, Immunocytochemistry, DNA extractions, and other translational science techniques</td>
<td>Skills Gained: DNA extractions, basic dissection, learn how to determine the significance of research projects</td>
</tr>
</tbody>
</table>

The preliminary track (only offered in the spring term) involves exploratory workshops focused on clinical and translational research, and includes field trips to the CU-D medical campus, and guidance workshops on educational paths for clinical and translational research careers. Students will complete HIPAA and professionalism training. In general students from the CEC Middle College will participate in preliminary track experiences. However, certain exceptional students that previously participated in preliminary track may subsequently participate in advanced track. In the future, the STaRS program will expand beyond a one-year program for juniors and include advanced course work and research experiences during their senior year. For many students who develop an interest in science, receiving positive feedback through involvement in a science fair is of great benefit. Therefore, we will provide support for STaRS students to present at the Denver Metro Science Fair.

### E. EVALUATION OF TL1 AND PIPELINE PROGRAMS

**TL1 program:** To evaluate the impact of the TL1 program, the Clinical Research Appraisal instrument described previously will be used as a pre/post measure to assess fellows’ self-efficacy regarding clinical and translational research core competencies. In addition, annual key informant interviews with fellows will explore: 1) general satisfaction with and feedback on the program (specifically, perceived strengths or elements that have been particularly impactful and ways the program could be improved); 2) perceptions regarding the value of mentoring triangles and their influence on fellows’ research, research interests and educational as well as career goals; 3) where they would place their research interests and endeavors on the
T1-T4 continuum; and, 4) career goals and aspirations. During the first year, evaluators will conduct a feasibility study, using previous TL1 cohorts, to examine if it is useful and feasible to obtain transcripts to compare the courses taken by TL1 fellows with other PhD students in their same doctoral program to determine if there are qualitative differences following fellows’ engagement with the TL1 program (i.e., if the training and educational paths begin to diverge, with a path that is more translational in nature beginning to surface following selection as a TL1 fellow). As students graduate, their dissertations will be examined through document review/content analysis for inclusion of clinically relevant topics; the evaluation and tracking program will develop a protocol/template for standardizing this process. Longitudinal tracking of TL1 graduates (through annual interviews or surveys) will examine whether they continue their education/training in programs specifically designed to advance clinical and translational research core competencies and whether they pursue careers in academic research, and the degree to which this research addresses clinically relevant topics. TL1 program participants’ metrics will be compared to their doctoral peers who are matched on key characteristics, such as gender, race/ethnicity, and program completion to access the differential impact of specialized preparation on fellows’ research portfolios, maturation as a scientist, and research productivity.

**Case Study:** from a STaRS instructor about one of the students: Chloe Vasilakis stood out from the beginning. As one of the Denver STaRS participants from the CEC Middle College of Denver, she excelled in the workshops, took lead in group activities, asked appropriate high level questions, and challenged her peers to look at the discussion topics from different perspectives. Her eager attitude prompted us to invite Chloe to subsequently participate in the “Research Experience” track and spend eight weeks in a research setting over summer. Chloe was paired with Dr. Emily Gibson, from the Bioengineering Department. Chloe described her STaRS experience as “eye opening experience that expanded my horizon to the vast fields of research. The STaRS program had such a positive impact on my outlook on the importance of research in advancing medicine”. Chloe graduated from high school with a 3.67 GPA. She is currently a freshman at Colorado State University studying Microbiology. Chloe will be applying to one of the research focus programs sponsored by CCTSIs SUMMIT to continue her interest in clinical and translational research. Eventually she would be an excellent candidate for our TL1 program.

**Pipeline Programs:** Evaluation of pipeline programs will focus on examining the effectiveness of the ETCD Program on recruiting and retaining diverse students who, demographically, have been historically under-represented in the biomedical research enterprise and who experience differential attribution rates across critical education, training and career development milestones. Every effort will be made to conduct key informant interviews and/or focus groups with previous pipeline participants to explore the impact and influence of having participated in a pipeline program. Assuming that at least some of these individuals will have participated in more than one pipeline program, evaluators will examine dose-response (i.e., is there an association between the number of programs and duration of participation and continued engagement in STEM education and relevant training career development programs. Interviews will explore relevant opportunities that were available to students as context (i.e., to assess whether there were adequate structural supports available that made it possible for students to pursue their interests and actualize their potential in STEM education and ultimately clinical and translational research). Since the time from enrollment in pipeline programs until attainment of a clinical research degree is long, the evaluation will focus on intermediary outcomes (e.g., continued engagement in the pipeline through selection of relevant courses and participation in internships, career aspirations, etc.). An outgrowth of this work, to carefully document the journeys of pipeline participants longitudinally, may be the discernment or classification of different pathways that may be used to validly predict the future attainment of a degree relevant to clinical and translational research. This work will be published and shared with the CTSA consortium through the Evaluation and ETCD KFCs. More immediately, evaluation findings will be used to inform the refinement of pipeline programs to increase the likelihood of diverse participants pursuing a career in clinical and translational research.

**F. MILESTONES AND IMPLEMENTATION TIMELINE.** Milestones and a timeline for the implementation of our future programs are displayed in **Table 43.**

<table>
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<tr>
<th>Table 43. TL1 and Pipeline Program Timelines</th>
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<tr>
<td>TL1 Programs</td>
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<tr>
<td>1. Research Methodology Enrichment Track</td>
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<td>2. Clinical Research Educational Program</td>
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<td>3. Team Science Lecture Series</td>
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<tr>
<td>Pipeline Programs</td>
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<tr>
<td>1. Development of the Pine Ridge Oglala Lakota College program</td>
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</tbody>
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1. Development of the Pine Ridge Oglala Lakota College program
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