University of Kentucky
Clinical and Translational Science Award Planning Grant

Overall Aims

This proposal outlines a comprehensive planning process for the design and implementation of a Clinical and Translational Science Award (CTSA) Program at the University of Kentucky (UK). The planning process will align UK's ongoing restructuring of its clinical and translational research enterprise with the goals and objectives of the National Institutes of Health's (NIH) Roadmap CTSA initiative. The structure of UK's emerging CTSA Program will subserve its overall function of improving the quality and accelerating the pace of the University's clinical and translational discovery. As such, UK's CTSA Program goals are:

1. The establishment of the UK Center for Clinical and Translational Science (the UK Center), which will serve as the "academic home" for the distinct discipline of clinical and translational research. In UK's tradition of Centers, the UK CTSA Program will include dedicated faculty and staff members who will conduct original research, develop graduate and postgraduate training curricula, and lead programs that integrate clinical and translational science across multiple UK departments, colleges, institutes and centers, and hospitals.
2. The aggregation and integration of the essential infrastructure and core services required for the efficient and ethical conduct of first-rate clinical and translational research by investigators in the UK Center. The co-localization of these key resources in the UK Center will lead to natural synergies of existing resources and talent, thereby furthering the Center's overall function.
3. The development of integrated training mechanisms required for the adequate preparation of future generations of clinical and translational scientists at multiple levels of career development.

Specific Objectives of the planning process for the UK Center include the following:

1. Identifying the clinical and translational science communities served.
2. Cataloging the existing mechanisms for the conduct of and training in clinical and translational research.
3. Identifying the strengths and weaknesses of each of these existing mechanisms.
4. Identifying new programs needed to meet the aforementioned goals of the UK Center.
5. Developing the UK Center's content, governance, administration, and evaluation.
6. Managing the institutional and cultural changes that are anticipated to occur with the establishment of a bonafide University Center for clinical and translational research.

Outline of the Proposal

1. **Introduction**
    a. Working definition of clinical research
    b. Working definition of translational research
    c. Rationale for the imperative for a transformative change in clinical and translational science.
2. **"The way we were…": University of Kentucky's Substrate for Clinical and Translational Research** demonstrates the availability of
    a. Most of the "building blocks" necessary to support a distinct discipline for clinical and translational science at UK;
    b. The depth and breadth of clinical and translational research upon which a comprehensive University Center must be founded; and
    c. A unique institutional culture of collaboration and cooperation required to create a new paradigm for clinical and translational science.
3. **"What we are becoming…": UK's Clinical & Translational Research Summit** describes UK's ongoing planning process for the restructuring of our clinical and translational enterprise; demonstrates commitment from all facets of the University for the UK Center; and summarizes the resources UK has committed both to the planning process and the UK Center.
    a. Executive Summary of UK's 2004-2005 Clinical and Translational Research Summit
    b. Progress Report on the implementation of the recommendations from the Clinical and Translational Research Summit
    c. Clinical & Translational Research Summit – "What Remains to Be Done - The Year Ahead"
4. **Concluding Summary: UK Clinical and Translational Science Center and Planning Grant**

Abbreviations & Acronyms that appear frequently in this application:
AHEC, Area Health Education Center; ***API***, Academic Performance Institute, Inc.; ***ASTeCC***, Advanced Science and Technology Commercialization Center; ***BIRCWH***, Building Interdisciplinary Research Careers in Women's Health; ***COBRE***, Center of Biomedical Research Excellence; ***COHR***, Center for Oral Health Research; ***COPS***, Circles of Power Leadership Development Program; ***CPST***, Center for Pharmaceutical Science and Technology; ***CRO***, Clinical Research Organization; ***CTSA***, Clinical and Translational Science Award; ***EVP***, Executive Vice President; ***FDA***, Food and Drug Administration; ***GCRC***, General Clinical Research Center; ***HEEL***, Health Education through Extension Leadership Program; ***IRB***, Institutional Review Board; ***KAN***, Kentucky Ambulatory Network; ***KSCHIRT***, Kentucky Spinal Cord and Head Injury Research Trust; ***Ky-CARAT***, Kentucky Consortium for Applied Oral Health Research and Treatment; ***NIH***, National Institutes of Health; ***ORAU***, Oak Ridge Associated Universities; ***ORI***, Office of Research Integrity; ***ORLD***, Office of Research and Leadership Development; ***ORNL***, Oak Ridge National Laboratory; ***NCI***, National Cancer Institute; ***NSF***, National Science Foundation; ***SCoBIRC***, Spinal Cord and Brain Injury Research Center; ***SES***, socioeconomic status; ***SKYCAP***, Southeast Kentucky Community Access Program; ***SWOT***, Strengths, Weaknesses, Opportunities, and Threats; ***UK***, University of Kentucky; ***UK-AGTC***, University of Kentucky Advanced Genetics Technology Center; ***UKCRO***, UK's Clinical Research Organization; ***UKCMC***, University of Kentucky Chandler Medical Center; ***UofL***, University of Louisville; ***VAMC***, Veterans Affairs Medical Center.

1. Introduction: Working Definitions & The Imperative for Change

1.a. Definition of Clinical Research

For many reasons, the lay public and the scientific community have traditionally compartmentalized biomedical science into 2 broad categories: basic science and clinical science. This oversimplified categorization has some usefulness in delineating the meaningful differences between these 2 areas of science with respect to (1) the requisite education and training required of its participants, (2) the resources required, (3) institutional infrastructure, and (4) funding mechanisms. More recently, and particularly in the postgenomic era, the growing complexity of biomedical science has been accompanied by the emergence of new subsets of clinical research, including (1) patient-oriented research, (2) epidemiologic and behavioral studies, and (3) outcomes research and health services research. For the purposes of the UK Center and our planning process, we define clinical research broadly along the NIH PHS 398 guidelines to include all the aforementioned subsets of clinical research.

1.b. Definition of Translational Research

In the wake of recent advances in genomics, proteomics, informatics, imaging, and other novel methodologies, a new category of research, translational science, has evolved, and it is considerably broader than the subtypes of clinical research mentioned above. The term *translational research* has grown to embody 3 areas of translation. One area is the process of applying discoveries at the bench or preclinical studies to the development of clinical trials and studies in humans. The second area involves the translation of the results of clinical trials to changes in the delivery of clinical care in the community. A third and novel area of translation involves taking observations at the bedside and in the clinic back to the laboratory to drive mechanistic basic science investigations. So defined, translational research has the potential for enormous impact on the advancement of the public health.

1.c. Imperative for Change: The Potential Impact of Clinical and Translational Research on the Public Health

The enormous impact of clinical and translational research is, perhaps, best illustrated by the work of Michael Brown and Joseph Goldstein on the regulation of cholesterol metabolism. Their work began with the *clinical observation* of advanced atherosclerosis in a pediatric patient. Their dogged pursuit of the "why," or the mechanisms that underlay this pivotal observation, led to a series of basic science studies culminating in the following observations: (1) that the uptake of cholesterol-containing particles, namely low-density lipoproteins (LDL), is mediated by cell surface receptors, and (2) that the complete or partial lack of LDL receptors is the underlying mechanism of severe hereditary familial hypercholesterolemia characterized by premature atherosclerosis, myocardial infarction, and stroke. Their work earned them the Nobel Prize in Medicine or Physiology in 1985 and has resulted in new principles for the treatment and prevention of atherosclerosis and in the development of lifesaving, cholesterol-lowering statin drugs that are used by millions of people worldwide. This example illustrates clearly the impact of a bidirectional scientific approach that began at the bedside, led to mechanistic studies at the bench, and finally led to dramatic improvements in patient care at the bedside and in the clinic.

Considering the huge impact of this example, it is highly desirable to identify the factors that were required for its accomplishment and to duplicate them across the entire spectrum of biomedical research. Unfortunately, most of the notable examples of high-impact clinical and translational research are not the products of systems set up to promote discovery of this breadth and impact but rather seem to result from the serendipity of a clinical observation made by an investigator with the "stubbornness," persistency, and skills needed to take that observation to its mechanistic conclusion and then back again to change patient care. Clearly, the creation of an "academic home" for

the distinct discipline of clinical and translational science staffed by a new workforce of clinical investigators who lead multidisciplinary research teams is a key step in systematizing and codifying this process and thereby accelerating the pace of discovery of new knowledge in the prevention, detection, diagnosis, and treatment of disease and the translation of these discoveries into applications that will improve the health of the nation.

2. "The way we were…": University of Kentucky's Substrate for Clinical and Translational Research
Prior to the initiation of the restructuring of its clinical and translational research activities in 2004 (see **3.** below), UK, like many research-intensive institutions, supported a number of different programs dedicated to all aspects of clinical and translational research. In aggregate, these programs represent UK's clinical and translational research capability and infrastructure. Several of UK's most prominent programs are summarized below and illustrate (1) the depth and breadth of the subject areas that are needed to sustain a CTSA-like program; (2) the considerable research support and productivity of the UK faculty in each of these programs; and (3) UK's existing culture of cooperation and collaboration as evidenced in many of the following programs and centers conducting clinical and translational research and research training.

The University of Kentucky
The University of Kentucky is a public, research-intensive, land-grant university dedicated to enriching people's lives through excellence in teaching, research, and service. The University, as the flagship institution, plays a crucial leadership role in the Commonwealth of Kentucky by promoting human and economic development that improves lives within Kentucky's borders and beyond. Founded in 1865, the University has grown over the years into a comprehensive public institution of higher learning, with 16 Colleges (including 6 professional schools), 93 undergraduate programs, Master's degrees in 99 fields, and doctoral degrees in 66 programs and 4 first professional programs. The University enrolls more than 25,000 students and awards approximately 5,200 degrees annually. The UK student body represents 115 foreign countries, all 50 states, and each of the 120 counties of the Commonwealth of Kentucky. Additionally, thousands more people are educated through continuing education programs. Approximately 1,900 full-time faculty members and 9,000 full-time staff are employed by the University.

In fiscal year 2005, UK researchers brought in a record $274 million in extramural funding for grants and contracts. This is the fourth consecutive year that UK has exceeded $200 million in sponsored project awards, and this figure represents a 15% increase since FY 2004.

Most of UK's grants and contracts come from federal agencies. In FY 2005, awards from federal agencies totaled $152.2 million (a 6% increase over 2004) and accounted for 55.5% of UK's total awards. The primary federal agencies funding research at UK are the Department of Health and Human Services (which includes the 27 centers and institutes in the National Institutes of Health), the National Science Foundation, the US Department of Agriculture (USDA), the Departments of Education, Energy, and Defense, and the Small Business Administration.

UK also receives grants and contracts from in-state agencies and organizations. These awards totaled $71.2 million in FY 2005 (a 53% increase over 2004). Finally, UK receives research funds from business and industry ($17.6 million in 2005, a 9% increase from 2004), and from philanthropic foundations ($33.0 million).

With respect to national licensing income and patent rankings, UK ranks 17th among land-grant universities, 34th among public universities, and 57th overall (Source: The Association of University Technology Managers annual ranking of licensing income & patents, FY 2002). UK ranks 10th in the nation among all universities for the number of start-up companies formed per $10 million in research spending, according to the *Chronicle of Higher Education*.

Overall, UK is currently ranked 36th among public research universities and 52nd among public and private universities in research and development expenditures by the National Science Foundation. UK is one of 59 public universities in the country and the only university in Kentucky to be designated a *Research University of the First Class* by the Carnegie Foundation.

2.a. University of Kentucky Chandler Medical Center
The University of Kentucky Chandler Medical Center (UKCMC) was established in 1957 on the UK campus and consists of the Colleges of Medicine, Dentistry, Nursing, Pharmacy, Public Health, and Health Sciences. The UKCMC is one of only 10 academic health centers nationwide to house all 6 schools of the health professions. In

addition to these 6 Colleges, UKCMC also includes the University of Kentucky Hospital, the University of Kentucky Children's Hospital, the Lexington Veteran's Affairs Medical Center (VAMC), the Kentucky Clinic, and several Centers of Excellence and Institutes, such as the Sanders-Brown Center on Aging, the Linda and Jack Gill Heart Institute, and the Kentucky Neurosciences and Orthopaedics Institute.

2.a.1. College of Medicine
Established in 1956, the UK College of Medicine is dedicated to the health care needs of Kentuckians through integrated programs in health care delivery, education, and research. In spite of its relative youth, the College of Medicine has achieved early prominence in all 3 components of its mission. With respect to biomedical research, the College of Medicine ranks 31st among public medical schools in NIH funding. Among public medical schools, the Department of Behavioral Science (psychology category) ranks first; the Department of Physical Medicine and Rehabilitation ranks eighth; the Department of Molecular and Biomedical Pharmacology ranks 10th; the Department of Neurology ranks 13th; the Department of Anatomy and Neurobiology and the Department of Molecular and Cellular Biochemistry rank 14th; the Department of Obstetrics and Gynecology ranks 15th; the Department of Microbiology, Immunology, and Molecular Genetics ranks 17th; and the Department of Pathology ranks 20th. In FY 2005, the College of Medicine was awarded $122.9 million from all sources in support of research and research training. Currently, the College of Medicine has numerous NIH-funded programs supporting basic, clinical, and translational research and training programs, including an NIH K30 program, an NIH GCRC, and many institutional training awards (e.g., 10 T32 awards, a BIRCWH award [K12] in Women's Health, a Center of Biomedical Research Excellence [COBRE award in Women's Health, and a COBRE award in The Molecular Basis of Human Disease).

In addition to the traditional basic science and clinical departments, the College of Medicine has several main research areas and centers that have achieved regional or national prominence and have acquired substantial NIH support for their research activities. A representative sample of UKCMC's NIH-funded clinical/translational research centers that have particular relevance to UK's CTSA initiative includes the Markey Cancer Center, the Sanders-Brown Center on Aging, the Linda and Jack Gill Heart Institute, the Graduate Center for Nutritional Sciences, the Spinal Cord and Brain Injury Research Center, the Center for Biomedical Engineering, the Center for Advancement of Women's Health, the Center of Excellence in Rural Health, and the Department of Behavioral Science.

2.a.1.1. The Markey Cancer Center. From its roots as the McDowell Cancer Network, the Markey Cancer Center was established in 1986 to expand the network's registry to include the elements of cancer research and education. The Markey Cancer Center conducts research across the entire spectrum of malignant diseases, with studies ranging from cancer prevention and control to early diagnosis to advanced treatment and supportive care. Broadly focused areas of current emphasis include the following cross-disciplinary matrix of biomedical sciences applied to various organ systems: cancer prevention and control, tumor immunology, cancer causation and tumorigenesis, molecular biology and genetics, drug discovery and experimental therapeutics, cell proliferation and apoptosis, breast cancer, prostate cancer, lung cancer, gastrointestinal cancers, gynecologic cancers, hematologic malignancies, head and neck cancers, and brain cancers. The Markey Cancer Center currently has 411 active clinical trials and has been ranked among the top 20 cancer centers for the last several years by *US News and World Report* on the basis of peer-reviewed funding.

2.a.1.2. The Sanders Brown Center on Aging. Established in 1963, the Sanders Brown Center on Aging is responsible for research, education, and service programs in aging. More than 150 faculty researchers and staff from many disciplines work together to explore the aging process and its implications for society. The Sanders-Brown Center is one of the original 10 NIH-funded Alzheimer's Disease Research Centers, one of 19 national Geriatric Education Centers, and one of 5 Commonwealth of Kentucky Centers of Excellence.

2.a.1.3. The Linda and Jack Gill Heart Institute. The Linda and Jack Gill Heart Institute was founded in 2000 by the Gill Foundation as a center of excellence for the clinical services, education, and research in the general field of cardiovascular diseases. The research activities of the Institute are organized into 3 NIH-funded focus groups: (1) The Atherosclerosis/Lipoprotein/Vascular Biology Focus Group is a multidisciplinary group of 12 faculty members whose scientific interests intersect on the common themes of inflammation, vascular biology, and atherosclerosis. (2) The Vascular Biology Focus Group includes 4 investigators interested in the related topics of neural control of cardiac function and ischemia. (3) The Institute of Molecular Medicine consists of 14 faculty and staff members

whose research activities include basic and translational investigations of the mechanisms that underlie the abnormalities of contraction seen in heart failure and of electrical signaling characteristic of cardiac arrhythmias.

2.a.1.4. The Graduate Center for Nutritional Sciences. The Graduate Center for Nutritional Sciences offers multidisciplinary MS and PhD training programs. The Center has 56 faculty members from 8 UK Colleges: Agriculture, Health Sciences, Arts and Sciences, Dentistry, Education, Human Environmental Sciences, Medicine, and Pharmacy. The Center has numerous training and research opportunities in basic, clinical, and translational NIH-funded projects in the agricultural, biological, behavioral, clinical, medical, social, and molecular nutritional sciences.

2.a.1.5. The Spinal Cord and Brain Injury Research Center. The Spinal Cord and Brain Injury Research Center (SCoBIRC) was established in 1999 to promote both individual and collaborative studies on injuries to the spinal cord and brain that result in paralysis or other loss of neurological function. The SCoBIRC faculty includes 22 researchers and clinicians from a variety of disciplines, working together to promote multidisciplinary interactions and the cross-fertilization of ideas. NIH-funded research studies range from fundamental neuroscience projects to clinical studies and outcomes research. SCoBIRC focus areas include treatments for minimizing damage and promoting repair mechanisms after spinal cord or brain injury; strategies for promoting neuronal regeneration, including gene therapy; studies aimed at understanding the mechanisms involved in axon guidance and myelination; and implementation of advanced control systems for functional neuromuscular stimulation.

2.a.1.6. Kentucky Spinal Cord and Head Injury Research Trust. In August 1999, the legislature of the Commonwealth of Kentucky established the Kentucky Spinal Cord and Head Injury Research Trust (KSCHIRT) to promote spinal cord injury research at the University of Kentucky and the University of Louisville (UofL). Dedicated fines for failure to wear seat belts and speeding violations are deposited into this Trust. The Trust has provided UK with matching funds for 5 endowed chairs in spinal cord research, for start-up funds for faculty members, and for a yearly gift to fund SCoBIRC predoctoral and postdoctoral fellows. In addition, funds from KSCHIRT are distributed to UK and UofL spinal cord researchers through an NIH-style proposal/award process.

2.a.1.7. The Center for Biomedical Engineering. Established in 1988, the Center for Biomedical Engineering offers educational and research opportunities in a variety of areas, ranging from biomaterials to biomechanics to systems physiology. The Center has 4 main focus areas: (1) Biomaterials and Tissue Engineering—involves the development of novel biomaterials and surface modification strategies for controlling cellular events at the bone-implant interface; (2) Bioelectromagnetics—investigates mechanisms underlying the stimulation of growth and regeneration with electromagnetic fields; (3) Biomechanics—focuses on the application of mechanical engineering principles to biofluids and soft and hard tissues; and (4) Cardiovascular and Neural Control—combines experimentation and computational modeling of cardiorespiratory interactions and cardiac rhythm dynamics. In addition to its extensive interactions and collaborations with all UKCMC Colleges, the Center houses 15 independently funded laboratories conducting applied and clinical research in the aforementioned focus areas.

2.a.1.8. Center for Advancement of Women's Health. The Center for Advancement of Women's Health was established by the UK Board of Trustees in October 2000 with the mission of integrating research and education services with the delivery of clinical care. The research centerpiece of the Center for Advancement of Women's Health is the Kentucky Women's Health Registry, open to all women in the Commonwealth between the ages of 18 and 89. The Registry includes self-reported information on demographic factors, health behaviors, health status, clinical symptoms, and medical diagnoses. Conducted annually, the survey allows for cross-sectional and longitudinal epidemiologic studies of the relationships between environment, health behaviors, clinical symptoms, and disease. Prospective cohorts are assembled from Registry participants, and the Registry increases the participation of women in research of all kinds. Women participating in the Registry have the opportunity to participate in research studies after providing separate consent. Consistent with its mission, the Center supports career development and mentoring for junior MD and PhD faculty members interested in research careers related to women's health through an NIH-funded BIRCWH (K12) award and a COBRE Award in Women's Health.

2.a.1.9. The Center of Excellence for Rural Health. The Center of Excellence for Rural Health embodies a novel approach to improving rural communities, simultaneously addressing health, education, and economic issues. The Center uses a combination of academic training courses, health policy research, and community outreach programs

to improve the well-being of rural residents and the quality of rural health care facilities. Since its creation by legislative mandate in 1990, the Center has graduated 338 students from its academic programs, approximately 80% of whom now practice in rural Appalachia, primarily in Central Appalachia. The Center was ranked as the best rural health program in the US by the national Rural Health Association (2000), and the UK College of Medicine was ranked ninth among medical schools with rural health programs in 2003 by *US News and World Report*.

Since 1994, The Center's lay health worker programs—Kentucky Homeplace and the Southeast Kentucky Community Access Program (SKYCAP)—have linked tens of thousands of medically underserved rural residents with available health and social services that they otherwise would probably have had to do without. During calendar year 2004 alone, Kentucky Homeplace provided services to 14,956 clients in 58 rural counties and accessed more than $19.6 million worth of medications for those clients. The Center's other outreach initiative, the State Office of Rural Health, has helped establish 3 rural health networks across Kentucky, aided nearly 25 rural hospitals in converting to more reimbursement-friendly critical access licensure, and provided other forms of technical assistance to dozens of other rural hospitals, clinics, and health care organizations.

2.a.1.10. The Department of Behavioral Science. Founded in 1959, the Department of Behavioral Science is the first such department to be included in any medical school in the US and ranks second in the country in NIH funding to medical school psychology departments. The Department serves as UK's nexus for research and training in medical behavioral science. The Department occupies 7,500 square feet in a dedicated building that houses 4 research laboratories: the Residential Research Facility, the Behavioral Physiology Core Laboratory, the Communication and Emotional Research Laboratory, and the Laboratory of Human Behavioral Pharmacology. These laboratories facilitate collaborations between clinical researchers in the Markey Cancer Center, the Sanders-Brown Center on Aging, the Center on Drug and Alcohol Research, and the Center for Drug Abuse Translation Research. In addition, the Department has numerous educational initiatives for both predoctoral and postdoctoral trainees; these initiatives are supported by training grants from the National Institute of Mental Health, the National Institute of Drug Abuse, and the Department of Defense.

2.a.2. College of Dentistry

Founded in 1962, the UK College of Dentistry is recognized as one of the nation's outstanding dental institutions and is ranked near the top 20 of US dental schools in 2005 in terms of peer-reviewed research funding. Established in 2000, the Center for Oral Health Research (COHR) supports 4 major themes of clinical and translational science: (1) Infection/Inflammation, which focuses on the systemic sequelae of chronic oral infection in severe periodontal disease; (2) Health Services Research, with multiple projects related to dental health in rural communities and historically underserved populations; (3) Orofacial Pain, which focuses on the development and refinement of the diagnosis and treatment of orofacial pain; and (4) Craniofacial Bone Biology, a transdisciplinary program with the Colleges of Medicine and Pharmacy and the Center for Biomedical Engineering that is focused on understanding the biological basis of and the development of more effective therapies for craniofacial bone anomalies or trauma, and the development and evaluation of structural bioresorbable products for tissue engineering and therapeutics. In FY 2005, COHR faculty members were awarded more than $5.9 million in research grants and contracts. The College of Dentistry actively participates in collaborative projects with other UK Chandler Medical Center (UKCMC) investigators, projects that yielded an additional $2.4 million in FY 2005 alone. Currently, the College of Dentistry has 16 NIH-funded programs, including a Dental Research Core for the UKCMC's GCRC and an NCRR-funded COBRE Award on the molecular mechanisms by which oral diseases affect other health problems, including HIV, atherosclerosis, gestational diabetes, and viral or bacterial interactions in chronic disease.

2.a.3. College of Nursing

The UK College of Nursing was established in 1960 as one of the initial colleges of the UKCMC. In 2004, the program was ranked 29th in the nation (out of more than 250 eligible master's degree programs) by *U.S. News & World Report* and ranked 20th among colleges of nursing affiliated with public universities. The college has 52 full-time faculty members; of these, 54% are doctorally prepared. The College supports a robust basic, clinical, and translational science research program with 24 active peer-reviewed awards with total revenues of $8.5 million.

2.a.4. College of Pharmacy

Established in 1870 as the Louisville College of Pharmacy, the College of Pharmacy became a division of UK in 1947 and became part of the newly developed UK Chandler Medical Center (UKCMC) in 1966. It is ranked eighth

among all colleges of pharmacy in the US on the basis of its accomplishments in both education and research by the *U.S. News & World Report* polls of colleges of pharmacy.

The research programs represent the full spectrum of basic, clinical, and translational science and have generated an average of $12.4 million per year over the last 3 years. NIH funded support has increased by 26%, from $9.6 million in FY 2002 to $12.2 million in FY 2005. This funding covers the entire breadth of drug discovery and development: the discovery of new drugs and their targets; the mechanisms of drug action; delivery of drugs to their site of action; evaluation of pharmacokinetics, pharmacodynamics, and drug metabolism; clinical studies; and drug-related outcomes (cost, clinical, and humanistic).

In 1986, the College initiated the Center for Pharmaceutical Science and Technology (CPST), which today is a fully integrated analytical and formulation development and pharmaceutical clinical supplies manufacturing facility. A new aseptic processing facility for human clinical supplies manufacturing opened this year at the University's Coldstream Research Park. The CPST has 4 primary missions: (1) to enrich the education of UK students through specialized educational and training programs related to pharmaceutical technologies, (2) to provide expertise to students and faculty members involved in translational research that requires the manufacture of pharmaceutical products, (3) to support the extensive infrastructure required to manufacture drug products for clinical trials through grants and contracts with academic institutions, biotechnology and pharmaceutical companies, and federal agencies such as the National Institutes of Health, and (4) to enhance economic development in the Commonwealth. CPST has completed more than 200 projects and grants.

2.a.5. College of Public Health

Founded in 2004, the College of Public Health has 20 full-time faculty members and 60 faculty members from other Colleges with secondary appointments in the College of Public Health. The College offers programs leading to 3 degrees: Master of Public Health (MPH), Master of Science in Public Health (MSPH), and Doctor of Public Health (DrPH). The College also coadministers the MD/MPH dual-degree program with the College of Medicine. The College has a robust research program, and in its inaugural year its full-time faculty members have a total of 48 peer-reviewed grants with a total of $4.7 million in direct costs. The College is organized into 6 departments: Health Behavior, Biostatistics, Preventive Medicine and Environmental Health, Epidemiology, Health Services Management, and Gerontology. In addition, the College supports 4 transdisciplinary research centers: (1) The Kentucky Injury Prevention Research Center is a partnership between the College and the Kentucky Department for Public Health that combines investigation and research with practical, community-based public health initiatives such as pediatric and adolescent injury prevention, trauma registry, and traumatic brain and spinal cord injury surveillance. (2) The Southeast Center for Agricultural Health and Injury Prevention is funded by the National Institute for Occupational Safety and the CDC and is one of 9 national centers of excellence for occupational health and safety within the agricultural industry. Areas of active research include pesticide exposures, suicide among agricultural workers, and health access among Latino agricultural workers. (3) The Graduate Center for Gerontology provides advanced interdisciplinary training in gerontology; research on aging and health considered from the cellular to the societal perspective; and service and policy research aimed at improving the quality of life of elder citizens of the Commonwealth of Kentucky. (4) The Center for Drug Abuse Translation Research has received continuous funding from the National Institute on Drug Abuse since 1987 and was the first such center established by NIDA. Its overall goal is to examine the intersection of biological, psychological, and social factors as they relate to the initiation and continuation of drug use and abuse and to develop and test communication and other intervention strategies for drug abuse prevention.

2.a.6. College of Health Sciences

Established in 2002, the College of Health Sciences has more than 50 full-time faculty members distributed across 9 distinct programs organized into 2 departments: the Department of Clinical Science and the Department of Rehabilitation Services. Although relatively young, the College supports a budding clinical and translational research program with a total of $1.7 million (direct costs) in NIH support and multiple ties to other UK health-related College research programs.

2.b. College of Education

The College of Education was the first College of Education to receive the certification of the National Council for Accreditation of Teacher Education, which has been renewed annually. It maintains a wide array of educational and

outreach research programs to improve the conduct of education and associated activities in a variety of settings to a diverse population. The Departments of Education Psychology & Counseling, Kinesiology, and Special Education & Rehabilitation Counseling are actively engaged in clinical and translational research, bringing in $2.96 million in peer-reviewed resources in FY 2005 and averaging approximately $3 million annually over the past 5 years. The Department of Curriculum and Instruction and the Department of Education Policy Studies and Evaluation are particularly interested in the issues of effective curriculum development and curriculum evaluation, respectively. Because the UK CTSA initiative involves novel curricular elements, faculty members from the College of Education will provide invaluable help in the design, implementation, and iterative evaluation of this curriculum.

2.c. College of Agriculture
The College of Agriculture has 29 departments, 6 of which are actively engaged in clinical and translational research projects using one or more of the University's programs or core facilities (see below). The peer-reviewed research programs of these 6 departments generate more than $2 million (direct costs). In addition, these departments support a number of community engagement programs, including coordination of the Health Education through Extension Leadership (HEEL) Program through the Agriculture Extension Offices located throughout the state.

2.d. College of Arts & Sciences, Department of Psychology
The Department of Psychology is home to the Clinical Psychology Rehabilitation Program, which is ranked 18th among public universities and 26th among both public and private universities in terms of peer-reviewed grant awards, publication productivity, and impact factor. Currently, the Department of Psychology has a total of 29 active peer-reviewed grant programs for a total of $3.1 million (direct costs); 23 of the 29 are funded by the NIH, one is funded by the NSF, and the other 5 are funded by philanthropic organizations.

2.e. UK Research and Core Facilities for Clinical and Translational Research
UK's research facilities are located predominately on its 814-acre urban campus in Lexington, Kentucky, and include 75 specialized research centers and 33 core research facilities. These facilities are housed in 26 main buildings and include an approximate total of 1,650,000 assignable square feet. In addition, UK maintains additional offsite research facilities dedicated to specialized research activities, including the Coldstream Research Campus (735 acres, see below), Spindletop Conference and Research Facility, the Kentucky Agricultural Experiment Station (1,300 acres), the UK Animal Research Center (1,500 acres), and the Robinson Forest (14,800 acres). The UK Chandler Medical Center (UKCMC) occupies 39 acres on the south end of the UK campus and has an approximate total of 339,000 net assignable square feet in 15 main buildings for basic, clinical, and translational research activities. All of the UKCMC Colleges, health care facilities, and the VAMC are in close proximity, and all but the College of Pharmacy are physically interconnected by pedestrian walkways that facilitate multidisciplinary collaborations and interactions. Of UK's specialized research centers and core facilities, the following facilities are of particular relevance to UK's CTSA initiative.

2.e.1. General Clinical Research Center (GCRC). Continuously funded by the NIH since 1985, the UK GCRC provides an excellent environment for investigations into the causes, progression, prevention, control, and cure of human disease and provides an optimal setting for controlled clinical investigations. Its resources are available to all clinical investigators throughout the University, and it emphasizes robust collaborations between basic and clinical scientists. Its mission is to develop, promote, and maintain a national core of expert clinical investigators, to train other health professionals in clinical research, and to provide resources to advance scientific knowledge that may be translated into new or improved methods of patient care. The GCRC provides both inpatient and outpatient services to the entire clinical research community of UKCMC. The inpatient unit is located on the fifth floor North wing of the University Hospital and occupies a total of 4,344 square feet with a reception area for patients and their families, a registration area, 8 rooms for 16 patient beds (double occupancy; 14 JCAHO-accredited beds), specimen-processing facilities, 2 metabolic kitchens, biostatistics and bioinformatics facilities, a gene therapy room, and administrative offices. The outpatient unit is located on the second floor of the Kentucky Clinic, immediately adjacent to the UK Clinical Research Organization (UKCRO; see below), and includes 4 dedicated outpatient rooms for a total of 500 square feet. The University Hospital and the Kentucky Clinic are interconnected by enclosed pedestrian walkways to the VAMC and all of the UKCMC Colleges except the College of Pharmacy. In addition, the GCRC has a newly funded (2005) Dental core that is supported, in part, by the GCRC and the College of Dentistry's COBRE Award. The Dental Core occupies an additional 6,085 square feet and has a waiting room; the examination rooms of the Delta Dental Clinic (4 rooms; 2000 square feet); 3 clinical research operatives and 3 treatment rooms; research

rooms; a core laboratory; and offices for the core laboratory technician, 4 study coordinators/research hygienists, 3 part-time interpreters for Hispanic patients and their families, and one research associate clinician. The GCRC also sponsors 2 GCRC CReFF scholars, and the Mentored Medical and Dental Student Awards currently support the training of 6 (3 dental and 3 medical) students in clinical research.

2.e.2. UK Clinical Research Organization (UKCRO). Established in 2002, the UKCRO currently amalgamates several of UKCMC's formerly independent clinical research organizations into a single organization designed to provide the entire UK clinical and translational research community with the infrastructure needed to support the outstanding conduct of industry-sponsored clinical research trials. The UKCRO is located on the second floor of the Kentucky Clinic and occupies a total of 3,985 square feet, with a reception area for patients and their families, patient registration, 7 outpatient examination rooms (with one additional "swing" room), facilities for handling and processing specimens, 2 infusion rooms, and administrative offices. UKCRO administrative and support functions are housed in an additional 700 square feet in the newly constructed Wethington Health Sciences Building. The UKCRO is interconnected by enclosed pedestrian walkways to the VAMC and all of the UKCMC Colleges except the College of Pharmacy. The UKCRO provides essentially "one-stop shopping" for all services required for the execution of high-quality clinical research. Importantly, the UKCRO is highly integrated with the GCRC, both physically (their outpatient facilities are immediately adjacent) and through educational activities for both investigators and support staff.

2.e.3. Advanced Science and Technology Commercialization Center (ASTeCC). ASTeCC, funded by the US Economic Development Administration and the Small Business Administration, is UK's showplace for multidisciplinary research, technology transfer, and new business start-ups. The ASTeCC program combines a research facility at which fundamental discoveries are made and a commercialization center at which these discoveries become products in the marketplace. The $17-million, 80,000-square-foot ASTeCC building, located in the heart of the UK campus, features 2 types of laboratory space: faculty laboratories and laboratories for high-tech business start-ups that have a connection to UK faculty members or staff or that have licensed UK intellectual property. Faculty members with laboratories in ASTeCC represent all colleges throughout the University, and faculty all across campus use ASTeCC as a hub for technology-transfer activities and as a source of information about new businesses. ASTeCC also houses a number of shared research resources (e.g., the Center for Micromagnetic and Electronic Devices, the Mass Spectrometry Facility, and the Nuclear Magnetic Resonance Facility) for the entire UK community.

ASTeCC has 2 objectives: to foster interdisciplinary collaborations with economic development potential, and to facilitate the commercial development of the discoveries made by UK's research faculty members, staff, and students. ASTeCC's interdisciplinary research is concentrated in 5 focal areas: (1) biotechnology: health and agricultural, (2) medical devices and instruments, (3) advanced materials, (4) nanotechnology applications, and (5) drug discovery and delivery systems. ASTeCC currently houses 6 start-up companies, and 23 businesses have "graduated" from the facility since its inception in 1994.

2.e.4. UK Coldstream Research Campus. The UK Coldstream Research Campus is situated within minutes of UK's main campus on 735 acres housing 11 research buildings with more than 50,000 square feet of assignable research space. Along with ASTeCC, the Coldstream Research Campus provides the infrastructure for the Coldstream Commercialization Program, offering UK faculty members and students the opportunity to benefit from the commercialization of their research. This environment supports the entire life cycle of a technology company, from start-ups to emerging and mature technology-based companies and research centers. Presently, the Coldstream Research Campus employs more than 700 persons in 26 companies at various stages of development and independence.

2.e.5. The UK Advanced Genetic Technologies Center (UK-AGTC). UK-AGTC, supported by the FDA and NSF, provides high-throughput genetic analysis with strong collaborative links to UK campus resources devoted to transcriptomics, proteomics, bioinformatics, and structural biology. UK-AGTC serves researchers from the UK campus and the region. UK-AGTC is a core-type facility that uses robotics and high-throughput tools to provide the most cost-effective facilitation of cutting-edge research. Laboratory database management suites enhance the ability to customize these processes and to store, organize, and then disseminate the large volume of data (460,800 bases of DNA per day) to their owners via Web-based applications.

2.e.6. The UK Biostatistics Consulting Service. The UK Biostatistics Consulting Service is supported jointly by the Colleges of Medicine and Public Health. This multidisciplinary unit provides a broad array of biostatistical and epidemiological consulting services to the entire UKCMC community. In addition to biostatistical support and consulting, the service also provides assistance with experimental design, data analysis, and power analysis for intramural and extramural grants. The service also organizes and delivers short courses on statistical methods and computing that are interfaced in the curriculum of the UK K30 award and the educational activities of the GCRC and UKCRO.

2.e.7. Additional Core Facilities. Other core facilities available to serve basic, clinical, and translational researchers include the **UK Microarray Core Facility** (provides expertise in Affymetric chips and custom cDNA microarrays), the **Flow Cytometry Core Facility** (for sorting and analysis of single-cell populations for membrane, cytoplasmic, and nuclear antigen expression, light-scattering properties, DNA content, cell cycles, and apoptosis, as well as intracellular biochemical changes such as calcium flux and pH), the **UK Imaging Facility** (provides expertise in sample preparation for and use of a variety of laser scanning confocal microscopes), the **UK Electron Microscopy Facility** (provides expertise with sample preparation and access to 2 transmission electron microscopes, 2 scanning electron microscopes, and an atomic force microscope), a **Magnetic Resonance Imaging and Spectroscopy Center** (1.5- & 3.0-Tesla MR imagers dedicated to research), and the **UK Mass Spectrometry Facility**.

2.f. UK Clinical Facilities For Clinical and Translational Research

In addition to housing the Colleges of all 6 health professions, the UKCMC includes integrated facilities for the delivery of health care, education, and clinical and translational research. The UKCMC includes the University of Kentucky Hospital, a teaching hospital; the UK Children's Hospital; the Markey Cancer Center; the Kentucky Clinic; and the VA Medical Center. All of these facilities provide tertiary clinical care in all medical specialties and provide the clinical substrate for UK's depth and breadth of clinical and translational research and clinical research training.

2.f.1. UK Hospital. The UK Hospital is a 473-bed academic tertiary referral center founded in 1962. The Hospital is part of the UK HealthCare patient enterprise, encompassing the UK Hospital, Kentucky's only level 1 Trauma Center with dedicated helicopter transport service; UK Children's Hospital; 4 Kentucky Clinic outpatient facilities with more than 80 specialty programs; and 140 outreach/community programs and clinics. The UK Hospital is supported by 630 faculty physicians, approximately 500 resident physicians, and a staff of approximately 3,200 health professionals. The UK Hospital provides tertiary clinical care for all Kentucky residents and residents of surrounding states (predominantly Southeastern Ohio, West Virginia, and Tennessee) and several foreign countries. During FY 2005, the total number of admissions was 22,269, with 266,245 outpatient visits and 42,909 emergency department encounters. These numbers reflect an increase of more than 10% in both inpatient and outpatient encounters per year for each of the last 5 years.

2.f.2. UK Children's Hospital. The UK Children's Hospital is currently ranked 28th among the nation's pediatric hospitals by *US News and World Report* America's Best Hospitals. The Children's Hospital is a state-of-the art 40,000-square-foot hospital with 132 beds, including a 12-bed PICU; a 50-bed NICU organized in a modular format; 44 acute-care (non-ICU) rooms; a 26-bed normal newborn nursery; a separate area containing 8 to 10 beds for 23-hour admissions/observation; children's playrooms; and expanded family consultation and waiting rooms. The hospital admits approximately 6,200 patients per year, with approximately 3,100 non-ICU floor admissions, 600 PICU admissions, 900 NICU admissions, and 1,600 admissions to the newborn nursery. Patients are admitted by pediatrics, pediatric surgery and the other surgical subspecialties, neurology, and pediatric dentistry.

2.f.3. The Markey Cancer Center. (see **2.a.1.1.** above)

2.f.4. The Kentucky Clinic. The Kentucky Clinic is centered at UKCMC and also has 3 satellite sites that provide outreach services to minority and disadvantaged populations. The Kentucky Clinic at UKCMC is designed to provide total ambulatory health care through a multitude of clinics, X-ray facilities, clinical laboratories, and a patient pharmacy. More than 400 physicians and dentists from more than two dozen specialties see patients at this site. Kentucky Clinic North in downtown Lexington provides health care to a predominantly African American community; Kentucky Clinic South at 2400 Greatstone Point provides care for predominantly middle class patients; and

Kentucky Clinic Berea specializes in providing a full spectrum of outpatient cancer care within the rural communities around Lexington. In FY 2005, there were more than 703,532 patient visits at all 4 Kentucky Clinic sites.

2.f.5. Veterans Affairs Medical Center. The Lexington Department of Veterans Affairs Medical Center (VAMC) is a 2-division medical center. Acute medical, neurological, surgical, and psychiatric services are provided at the Cooper Drive Division, located adjacent to UKCMC. The Leestown Division, 5 miles from Cooper Drive, provides extended care, psychiatric services, and nursing home care. The Leestown Division also includes primary care, ambulatory surgery, a women's health center, a telephone care program, a geriatric evaluation unit, a hospice, and several outpatient mental health services, including substance abuse treatment and posttraumatic stress care.

The Lexington VAMC serves as a teaching facility, affiliated with the UK Colleges of Medicine and Dentistry, for the training of more than 490 medical and dental residents in 49 accredited specialty/subspecialty programs. Yearly, the Lexington VAMC cares for more than 25,000 veterans and has more than 5,400 admissions and 200,000 outpatient visits. The VAMC has more than 1,400 professional, technical, and support personnel reinforced by more than 600 volunteers committed to serving veterans. The Lexington VAMC is a fully accredited, 209-bed acute medical and surgical care facility offering primary and specialized outpatient services and a 198-bed nursing home care unit. The VAMC also supports an outreach clinic and operates mobile medical clinics in 7 locations throughout Eastern and Central Kentucky. A community-based outpatient clinic has been opened in Somerset, Kentucky.

2.f.6. The Center of Excellence in Rural Health. (See also **2.a.1.9.** above.) Situated in Hazard, Kentucky, the Center of Excellence in Rural Health is housed in a newly constructed $13.1-million building with more than 57,000 square feet that houses the UK Family Medicine Clinic and its family practice and dental residency programs, nursing laboratories, a radiographic simulation area, clinical laboratories, and classrooms with distance-learning capability. With 129 employees, the Center exploits its rich participatory lay network to penetrate every rural county and community in Kentucky. Thus, the center provides UK clinical and translational researchers with unprecedented access to special populations of relatively isolated low socioeconomic status (SES) and of ethnic and racial diversity (see below).

2.f.7. General Clinical Research Center. (See also **2.e.1.** above.) The UK GCRC currently supports clinical and translational investigators from 8 UK colleges (Medicine, Dentistry, Nursing, Arts and Science, Engineering, Health Sciences, Education, and Pharmacy), 21 departments (Internal Medicine, Oral Surgery, Pharmacy Practice and Science, Psychiatry, Kinesiology, Neurology, GI, Neurosurgery, Neurology, Nursing, Behavioral Science, Nutrition, Radiology, Pediatrics, Biomedical Engineering, Cardiology, Ophthalmology, Urology, Pediatric Psychiatry, Stroke, and Bone Marrow Transplant), and 2 Research Centers (Alzheimer Disease and Cancer).

2.f.8 Kentucky TeleCare Network. The Kentucky TeleCare Network, based at UK, is a telemedicine network of interactive videoconference-based devices situated in health care facilities across the state. This network provides the core of the Kentucky TeleHealth Network, a statewide tele-health network located in more than 70 health care facilities. The network uses high-speed communications lines to link interactive videoconferencing systems and electronic medical peripheral devices.

2.f.9. Office of Research Integrity (ORI). The Office of Research Integrity is UK's central facility that supports 7 federally mandated review committees: 3 Medical and 2 Nonmedical Institutional Review Boards (IRBs), the Institutional Animal Care and Use Committee (IACUC), and the Radioactive Drug Research Committee (RDRC). The University Veterinarian provides guidance in animal care. ORI also supports the institution in promoting ethical conduct of research and educating UK students and employees regarding research misconduct regulations, data ownership, and animal care regulations. ORI delivers many of these services via Web-based applications. ORI maintains an extensive education and training program in all facets of basic and clinical research, programs that are integrated into and coordinated with the education modules of the GCRC and UKCRO, the educational activities of UK's 10 T32 training grants and 3 COBRE awards, and the K30 certificate and master's programs.

2.f.10. Oak Ridge Associated Universities (ORAU) and Oak Ridge National Laboratory (ORNL). Established in 1946, Oak Ridge Associated Universities (ORAU) is a consortium with 91 doctorate-granting members and 10 associate members. ORAU members are found in 28 states plus the District of Columbia, Puerto Rico, and the United Kingdom. UK was one of the founding members of the ORAU. The ORAU offers member institutions the

opportunity to expand patient databases for clinical and translational research by providing access to (1) the human subjects database of DOE-wide research projects and programs involving human subjects, (2) the core services of ORNL, including the mammalian genetics and genomic facility (phenotype screening, genomics/transcriptomics, proteomics), and (3) computational biology services (analysis and annotation of genomes).

2.g. UK Centers and Programs of Excellence

2.g.1. The Kentucky Consortium for Applied Oral Health Research and Treatment (Ky-CARAT). With a $1.3-million federal grant, the COHR of the College of Dentistry developed a consortium of established medical centers and facilities in South-Central Appalachia to provide clinical and translational research training and to develop the infrastructure for clinical and translational research at these rural sites. Initial projects target relationships between oral infections and general health; the first pilot studies involve a cohort of expectant mothers in Appalachia and their young children. Under the auspices of Ky-CARAT, research networks of practicing dentists and physicians have formed in rural Kentucky, thereby further increasing the capability to conduct community-based clinical and health services research. These networks include community-based faculty in the Colleges of Medicine and Dentistry with practices in rural Kentucky who participate in the Kentucky Area Health Education Center (AHEC) Program, and the primary care practitioners and researchers of the Kentucky Ambulatory Network (KAN) (see below). These unique partnerships strongly position the College of Dentistry to conduct oral health disparities research in rural, community-based settings.

2.g.2. Kentucky Ambulatory Network (KAN). KAN is an NIH-funded primary care practice-based research network established in the fall of 2000. It is administered through UK's Department of Family Practice and Community Medicine, in cooperation with the University of Louisville (UofL) and the Kentucky Academy of Family Physicians. KAN seeks to enhance the ability of office-based clinicians to deliver high-quality primary health care to their patients through collaborative research conducted in primary care practices and translation of research to the clinical care delivered in these practices. KAN emphasizes the prevention and management of common health problems in Kentucky and their broader implications. The practice-based research conducted by KAN and its affiliated investigators is supported by several federal and foundation grants (Health Resources and Services Administration and the Agency for Healthcare Research and Quality, the Robert Wood Johnson Foundation, and the American Academy of Family Physicians).

As of July 2004, KAN included 130 community-based primary care clinicians located in central and Eastern Kentucky; 36 UK and UofL Family Practice faculty members; all 7 Kentucky Family Practice Residency programs; and 37 health services researchers and academicians at UK and UofL who represent a broad array of other fields of expertise, such as public health and health services. Approximately 75% of KAN's community-based clinicians practice in rural, medically underserved areas, where they provide care to an estimated 280,000 people.

2.g.3. NIH K30 Curriculum. Career Training in Therapeutics and Translational Research is an NIH-funded K30 Clinical Research Curriculum Award supported jointly by the Colleges of Medicine and Pharmacy. It provides career development and mentoring opportunities to clinician scientists interested in pursuing careers in clinical or patient-oriented/translational research. The program provides 2 years of structured training, consisting of didactic coursework and a formal mentored research experience tailored to the needs of individual scholars, leading to a certificate in clinical research. In 2005, the University and the College of Medicine made a long-term commitment to continue this program (at the current level of NIH funding) after the initial period of seed funding from the NIH has ended (August 2006). This UK commitment of $200,000 per year for 5 years (total commitment of $1 million) has led to revitalization of the training program and expansion of the curriculum to meet the needs of participants from all UK Colleges interested in clinical research. The new curriculum will be offered in July 2006 and will be incorporated into MPH and MSPH degrees offered jointly by the Colleges of Medicine and Public Health.

2.g.4. Building Interdisciplinary Research Careers in Women's Health (BIRCWH, NIH K12). The BIRCWH Program provides career development and mentoring opportunities for a total of 15 junior MD and PhD faculty members interested in establishing research careers related to women's health. An NIH-funded K12 program, it received a competitive renewal of $2.5 million in October 2005. The BIRCWH curriculum involves 2 to 3 years of an individually structured program consisting of a mentored research experience, didactic courses, and participation in seminars, journal clubs, and symposia. The program is closely linked to the GCRC and the K30 program, and all of these programs benefit from shared missions and resources. In its first 5 years (2000-2005), the UK BIRCWH

Program had remarkable success, including (1) the recruitment of highly qualified scholars (6 basic scientists and 9 clinical scientists from a pool of 48 applications) for all 15 positions (31% acceptance rate); (2) the retention of 14 scholars in academic careers; and (3) the funding of 16 peer-reviewed research grants by 15 scholars, including 4 NIH R01s and 1 NSF award (total direct costs of $7.7 million), with 6 additional awards in review.

2.g.5. Center of Biomedical Research Excellence in the Molecular Basis of Human Disease (NIH COBRE Award). This is a 5-year, $10-million award (Fall, 2004) to the Department of Molecular and Cellular Biochemistry to support multidisciplinary research and mentoring teams to develop faculty biomedical research expertise and competitiveness within the thematic research focus of the molecular basis for human disease. The program provides salary and equipment support for 5 junior faculty members, research support for their senior faculty mentors, and 4 shared core facilities: an administrative core, a cell culture core, an imaging core, and a proteomics core. The educational activities of this program are delivered through UK's K30 program.

2.g.6. Center of Biomedical Research Excellence in Oral Disease (NIH COBRE Award). This is a 5-year, $10.9-million award (Fall, 2004) to the College of Dentistry to support multidisciplinary research and mentoring teams to develop faculty biomedical research expertise and competitiveness within the theme of the effect of oral diseases on other health problems, including HIV, atherosclerosis, gestational diabetes, and viral/bacterial interactions in chronic disease. The program provides salary and equipment support for 10 junior faculty members and research support for their senior faculty mentors. The educational activities of this program are tightly interfaced with UK's K30 curriculum and faculty development activities.

2.g.7. Center of Biomedical Research Excellence in Women's Health (NIH COBRE Award). UK's first COBRE award, this 5-year, $8.3-million award (Fall, 2000; competitive renewal to 2008) furthers the understanding of the unique role of sex and gender, female reproductive hormones, and selective estrogen receptor modulators in the manifestation of health and disease. This focus is used as a platform for developing promising junior investigators and enhancing their success in competing for NIH funding. During its first funding period (2000-2004), 9 of the program's scholars received NIH peer-reviewed awards; 3 proposals are pending review; and the scholars have generated 67 peer-reviewed publications and 35 presentations.

2.g.8. Circles of Power Leadership Development Program (COPS). COPs targets women and underrepresented minorities with leadership potential for participation in an 8-month mentor-centric program that provides leadership knowledge and skills and a framework for applying them in work and life experiences. The speakers and facilitators are both internal and external to the UK academic community and include influential academic, business, and political leaders. COPS offers a 3-phase process that includes the establishment of a network of colleagues, training in management theory, and collaborative "shadowing" experiences. Graduates of the COPS program have the opportunity to practice these new skills through the leadership (with the tutelage of their mentors) of their research teams. COPS graduates have gone on to such senior leadership positions as College Deans and University Provosts across the country. Women identified as potential leaders are also encouraged to apply for national leadership programs such as Executive Leadership in Academic Medicine.

2.h. Availability of "Special" Populations for Clinical and Translational Research.
Special Populations of Low Socioeconomic Status: Appalachia.
Appalachia has long been a region with high rates of poverty, isolation, and poor health. Even though these rates have been halved since the inception of President Johnson's "War on Poverty" in the mid-1960s, the region still has substantial economic, educational, and health disparities. In particular, Appalachian Kentucky continues to have among the poorest socioeconomic indicators in the United States. Its per capita income is approximately 40% lower than the US average, the poverty rate is almost twice as high as the US average, the unemployment rate is 50% higher than the US rate, and, among those aged 25 or older, the proportion of Appalachian Kentucky residents with at least a high school diploma is 22% lower than the national proportion. The socioeconomic indicators for Appalachian Kentucky are also considerably lower than those for Kentucky as a whole.

The US Department of Health and Human Services considers rural Americans a "special population" (Appalachia Leadership Initiative on Cancer. Sowing Seeds in the Mountains: Community Based Coalitions for Cancer Prevention and Control, in Portnoy B [ed]: *Healthy People in Rural Areas by the Year 2000*. Bethesda, MD, National Cancer Institute; 1994). Rural Americans tend to be older, poorer, less educated, and more likely to be medically

uninsured than their urban counterparts. Rural communities also have higher rates of chronic illness and disability and report poorer overall health than do residents of urban communities. Systemic factors such as lack of public transportation, fewer community services, and a shortage of health care providers all contribute to suboptimal health care access among rural Americans. Although these characteristics are common in much of rural America, Appalachian Kentucky, a largely rural population, represents an extreme version of these characteristics.

As estimated from the 2000 Census, Appalachian Kentucky's population in 2002 was 1,150,413, or 28.1% of Kentucky's total population of 4,092,891. The vast majority (97%) of Appalachian Kentucky residents are white. The next most common racial/ethnic group is African American, composing 1.7% of the Appalachian population in Kentucky. All other racial groups combined account for 1.3% of the population. Fewer than 1% of Appalachian Kentuckians identified themselves as Hispanic, compared with 12.5% nationwide. It is clear that the region's racial and ethnic composition differs from that of the United States.

Although the population of Appalachian Kentucky is primarily white, the population is nevertheless culturally quite diverse. The literature on Appalachian culture is rife with stereotypes about this population. There is a common view that the population is homogenous and that the effects of poverty outweigh all other explanations of health disparities. Finally, the stereotypical view of Appalachia is that antagonism toward "outsiders" is an insurmountable barrier. To reduce health disparities, programs and research must acknowledge the barriers to health care (poverty and low education levels) but must also recognize that the Appalachian population is quite heterogeneous and that, to be successful, a community-based, participatory approach to research is needed.

Although these populations are regionally unique, clinical and translational research in these communities will clearly have national applicability to all 2,308 nonmetropolitan (rural) counties in the United States and especially to the 442 high-poverty counties, which tend to have the highest illness and death rates and the poorest quality-of-life measures. "If anything is unique about Appalachia, other than the stereotypical image developed and maintained in the wider culture, it may be the way that the region isolates and magnifies so many of the problems and the potential solutions that are more generic to American society" (Sowing Seeds in the Mountains: Community-Based Coalitions for Cancer Prevention and Control, The Appalachia Leadership Initiative on Cancer [ALIC], NIH/NCI).

Consequently, Central Appalachia has the potential to be a particularly fertile incubator for programs that promote clinical and translational research. The key factors supporting this assertion are (1) the presence of relatively isolated, low-SES populations of striking racial and ethnic diversity; (2) the preponderance of diseases that are uniquely endemic in this region, including cancer; neurological disorders; cardiovascular, metabolic, and genetic diseases; and dental problems; (3) the superimposition of a variety of tertiary problems, such as poor access to health care services and disparities in health care delivery; and (4) the presence of numerous participatory community-based programs for health care delivery that will expedite access to the special populations of the region for clinical translational research programs. UK's clinical and translational researchers have access to the unique and culturally diverse adult and pediatric populations in Appalachia through UK's extensive rural outreach programs described above, including the Kentucky Ambulatory Network (KAN), the UK Center of Excellence in Rural Health, and the UK Dental outreach program (Ky-CARAT). These programs exploit extensive lay participatory networks to engage these populations and involve them in all aspects of clinical and translational research.

2.i. Summary

As indicated by the "inventory" above, the University of Kentucky, like many research-intensive academic institutions, has a number of separate programs supporting various aspects of clinical and translational research. Although most of these programs could boast considerable success in the achievement of their goals, their disease- and discipline-specific focus fosters a culture of detachment and isolation that prevents them from taking maximal advantage of the economies of scale that accompany shared resources, the identification and sharing of best practices, and, most important, the incubation of an *esprit de corps* or culture characteristic of a distinct discipline. In June 2004, 4 accumulating forces combined to drive UK to embark on a bold reassessment of its clinical and translational activities with the goal of transforming the institution's overall approach to clinical and translational science. The 4 forces were (1) the recruitment of new and visionary leadership at all levels of the University, from the President's Office through the leadership of most of the UK Colleges engaged in clinical and translational research; (2) the President's promotion of the Kentucky Legislature's mandate that UK emerge by the year 2020 as a "top 20" public research university in terms of peer-reviewed NIH revenue; (3) the multidisciplinary and

translational opportunities stimulated by recent advances in genomics, proteomics, informatics, and other novel methodologies; and (4) the NIH Roadmap initiative. The Clinical and Translational Research Summit and the related activities described below are the products of the triangulation of these forces at UK.

3. "What we are becoming…": UK's Clinical & Translational Research Summit

In spite of its past successes in clinical and translational research (see **2.** above), UK recognized that a different paradigm is needed to accelerate the pace of discovery of new knowledge that will improve the public health. Clearly, this new paradigm depends on nurturing the translational interface between basic and clinical science through collaborative multidisciplinary teams both for the conduct of research and for research training. To remain at the leading edge of clinical and translational research, UK has invested considerable time and resources to examine and reinvent (when necessary) its entire clinical and translational research and research training enterprises with the aim of identifying best practices and exerting economies of scale that can be applied across the University. In essence, the Research Summit served as a classic SWOT (Strengths, Weaknesses, Opportunities, and Threats) analysis. This ongoing process is described below and demonstrates UK's investment in and commitment to clinical and translational research.

It is important to point out that this Summit and its related activities are tangible evidence of unwavering institutional leadership and support for the planning and establishment of the UK Center. This institutional commitment is driven by the senior leadership of the University President's Office and includes the Offices of the Deans of all of the UK Colleges engaged in clinical and translational science; the directors and senior leadership of all the aforementioned institutes and centers (see 2. above); and the senior leadership of the core facilities, hospitals and clinic services (see also 2. above). Consistent with the RFA guidelines and directions of the NIH's Program and Review officers, we have included only a letter from UK's President that underwrites this institutional support. We believe that the changes accomplished to date (see 3.b.) and those in the planning stages (see 3.c.) demonstrate the integrity of this institutional support for our Center.

In June 2004, Wendy Baldwin, PhD, Executive Vice President for Research, and Jay A. Perman, MD, Dean of the College of Medicine and Vice President for Clinical Affairs, initiated a review of clinical and translational research at UK. A broad-based review of clinical research had been conducted in 1997-1998, with specific topical reviews in subsequent years. Given new leadership in both the College of Medicine and the University's Office of Research, and in preparation for establishing the Office of the Senior Associate Dean for Clinical Research in the College of Medicine, a review of clinical and translational research was timely and was built on the results of previous reviews.

As a first step, the leadership conducted a survey of researchers, administrators, and support staff in departments, centers, and administrative offices across the University that were engaged in or involved with clinical research so that a comprehensive agenda of relevant items and issues pertaining to clinical and translational research could be developed. All of the suggested agenda items were discussed at a University-wide Clinical Research Summit held on September 20, 2004, which involved 35 participants from 22 different UK colleges, administrative offices, clinical research centers, and educational programs. The wide range of issues identified during the initial phase of this process limited the task of this meeting to the review and approval of an agenda that would serve as the basis for a university-wide examination of clinical and translational research.

After the Clinical Research Summit, Dean Perman appointed 4 task forces to address the main areas of UK's clinical and translational research agenda: (1) The **Institutional Policy and Procedures Task Force** focused on the myriad issues related to the setting of institutional policies governing components of the clinical and translational research enterprise, the "measurement" of clinical research, monitoring and oversight, etc. (2) The **Operational Norms Task Force** examined the issues pertaining to regulatory and fiscal compliance, data management, quality assurance, etc. (3) The **Roles, Relationships, and Coordination Task Force** concentrated on the coordination and integration of all units involved with clinical research. (4) The **Investigator Task Force** was concerned with the spectrum of issues related to accessibility, training, education, and support. Each task force and its relevant subcommittees were given 3 charges: (1) to assess what currently existed in each area, with the anticipation that the resulting inventory would shape the next steps in each discussion; (2) to determine the critical path that an individual investigator must follow if he or she is to understand what is necessary and available within the institution to regulate and support the conduct of clinical research, with an analysis in each instance of the gaps in service and communication that create confusion and inefficiencies; and (3) to recommend what should exist to facilitate the

proper conduct of first-rate clinical and translational research. Each task force and their relevant subcommittees were asked to deliberate from the perspective of promoting the simplification, coordination, and streamlining of policies and procedures at all levels so as to enhance the safety and effectiveness of clinical and translational research. The task forces and their component committees met during 2004-2005 and completed their reports in September 2005; their cumulative recommendations were distributed throughout the University community in December 2005. Not surprisingly, this report was prescient of many of the components of the NIH's CTSA Program and has become UK's blueprint for our ongoing transformation of clinical and translational research.

3.a. Clinical & Translational Research Summit – Executive Summary

Although each of the 4 task forces of the Research Summit began with a different set of questions (see above), their thoughtful and thorough review resulted in a consistent set of recommendations that address the key components of the content, governance, administration, and evaluation of UK's clinical and translational enterprise.

1. **Content**. The Summit report recommended the creation of a University-level Center for clinical and translational research. This Center would represent the merging of the multiple and separate programs that currently exist at UK for clinical and translational research and research training. The structure of the Center would be driven by the functionality of the Center's key components.
    a. **Clinical Research Organization (CRO)** serves as a "one-stop-shop" for all of the components required for the conduct of high quality clinical and translational research. Forged from the UKCRO and the GCRC, the Center would provide these services through distinct but functionally integrated units.
        i. **Project Initiation/Management Unit** serves as the initial point of contact for clinical and translational investigators. It assists investigators and their clinical coordinators in preparing and reviewing all documents necessary for the initiation, approval, and maintenance of all clinical and translational research projects. In addition, this unit assigns and manages discretionary monies (i.e., seed funds) for the support of pilot and collaborative clinical and translational projects for the acquisition of preliminary data in preparation for submission of a research grant application.
        ii. **Clinical Operations Unit** provides operational support for all aspects of clinical research. It maintains new state-of-the-art inpatient and outpatient facilities that are equipped to support phase I through IV clinical trials and provides support for investigator-initiated research involving human subjects. In addition, this unit assists investigators with subject/patient recruitment, particularly for studies requiring special populations; provides biostatisticians and epidemiologists for consultation on study design, data analysis, etc; and provides special services for investigators pursuing FDA submissions, patent applications, etc. Importantly, this unit provides logistic support for clinical and translational research programs with our community partners and community-based clinical and translational research faculty members.
        iii. **Clinical Research Marketing Unit** develops an aggressive marketing plan in collaboration with other UK resources and maintains the Center's Web page, newsletter, and Web-based recruitment programs. This unit is responsible for all aspects of community outreach such as (1) programs designed to raise the community's awareness of and trust in UK's clinical and translational research programs; (2) strategies for patient/subject recruitment; and (3) cultural sensitivity training for faculty and staff members engaging community populations and particularly the region's "special populations".
        iv. **Clinical Research Compliance Unit** assists investigators in complying with all regulatory and fiscal requirements of all clinical and translational research protocols.
        v. **Clinical Research Education Unit** ensures that all of the Center's staff and students who participate in clinical and translational research receive the appropriate education and training needed for the conduct of high-quality and ethical clinical and translational research.
        vi. **Core services** would support the aforementioned functional units and include the following:
            1. **Data Management Core** is responsible for developing a centralized software platform that integrates all of the existing and new systems needed for clinical and

translational research and allows connectivity with other research partners such as the NIH, industry partners and sponsors, community-based partners, research networks, etc. To be effective, this platform must be compatible with the hospital's electronic medical record and be compliant with the cancer center support grant guidelines of the National Cancer Institute (NCI).

2. **Biostatistics/Informatics Core** provides investigators with expertise in research design, data analysis, and the ethical conduct of research. This unit also provides genomics and proteomics services and a biospecimen repository.
3. **Epidemiology Core**
4. **Data and Safety Monitoring Committee**

b. **Research Education, Training, and Career Development** program of the proposed Center brings together the disparate educational and training activities of existing programs (GCRC, UKCRO, K30, BIRCWH K12, 10 T32s, 3 COBREs, the UK intramural Physician Scientist Program, and the Dean's Clinical Research Scholars Program) to form a continuum of horizontally and vertically integrated educational and training experiences and opportunities that are accessible by researchers at a wide variety of career development stages. These experiences would share the common principle of a mentor-centric, multidisciplinary team-based approach. The Center's "menu" of educational opportunities includes the following:

i. **MPH,** a traditional public health curriculum with a clinical research track offered by the College of Public Health.
ii. **MSPH,** a science-based curriculum in clinical research offered jointly by the Colleges of Medicine and Public Health.
iii. **Certificate in Clinical Investigation** targeted at PhD trainees, junior faculty members, and community practitioners who need training in clinical research to be effective partners in clinical and translational research teams in UK-based and community-based initiatives.
iv. **Certificates** of training in the regulatory aspects of clinical research for all faculty and staff members engaged in any facet of clinical and translational research.
v. **"Survival Skills"** courses encompassing formal and informal training and experiences in areas of career development such as leadership training, grantsmanship, manuscript preparation, etc.

2. **Governance & Administration**. The Summit report strongly recommended that UK's clinical and translational research Center be led by a program director with (a) scientific and administrative qualifications as a productive clinical/translational investigator and (b) the institutional rank and experience to effectively forge collaborations and inspire cooperation between all of the UK constituencies involved with clinical and translational research. They recommended that the Center director report directly to the office of the President in the context of the Executive Committee for Clinical and Translational Research.

a. **Executive Committee for Clinical and Translational Research** would be chaired by the University Provost. Its roster would include leaders of all the key stakeholders in the University's clinical and translational mission, including the Center Director, the Executive Vice President (EVP) for Research, the EVP for Health Affairs, the EVP for Finance and Administration, and the Deans of the UK Colleges that engage in clinical and translational research, including to date the Colleges of Medicine, Dentistry, Pharmacy, Nursing, Health Sciences, Public Health, Agriculture, Education, and Arts and Sciences. This committee would meet quarterly and provide general oversight for UK's Clinical and Translational Research Center; facilitate the alignment of University and College resources to the clinical and translational research program; allocate faculty "lines"; and develop University-compliant policies for appointment, promotion, and tenure in the Center.
b. **Operational Committee for Clinical and Translational Research** would be chaired by the Center Director and would include the directors of all of the key components of clinical and translational research on campus, including the General Clinical Research Center (GCRC), the UKCRO, the UK K30 program, the Core Services, and the associate deans for research from all of the colleges (see above) engaged in clinical and translational research. This committee would meet monthly and be responsible for (1) the center's administrative policies and procedures, (2) establishing and monitoring appropriate advisory or subcommittees, and (3) implementing an assessment and evaluation component for all of the center's activities at all levels.

3. **Evaluation.** The Summit report was emphatic about the necessity for both ongoing and periodic assessment of the Center's achievement of its objectives. The recommended governance structure (see above) will allow "real-time" evaluation at the institutional level (e.g., the Executive Committee for Clinical and Translational Research) and at the operational level (e.g., the Operational Committee for Clinical and Translational Research). In addition, the Summit report contains the expectation that each functional unit and educational module will have its own evaluation and oversight committee, as do all currently active UK programs supporting clinical and translational research. In addition, the Summit report underscored the necessity for external oversight and recommended periodic (at a minimum, yearly) reviews of all aspects of the Center's activities by an external advisory committee who will report to the Executive Committee for Clinical and Translational Research.

3.b. Clinical & Translational Research Summit – Progress Report

It is clear from the Executive Summary that the Clinical and Translational Research Summit was closely aligned with the collective consciousness that generated the NIH's CTSA RFA. Many of the provisions of the Summit report have been implemented either at the time they were being formulated by the 4 individual task forces and their subcommittees during 2004-2005 or after the formal release of the Summit report in December 2005. The changes that have been or are being made are indicated below. The number and extent of these changes and the resources involved clearly demonstrate UK's unwavering institutional commitment to the Center. **[As noted above in the introduction to this section, we have not amended this application with letters from the many University components that have come together to contribute resources to this initiative because of the proscriptions in the planning grant RFA and our discussions with NIH Program and Review officers. In aggregate, UK has committed more than $12 million in support of salaries and programs for the UK Center and has provided nearly 20,000 square feet of space (see below) for the Center's administration, operations, and educational, training, and career development functions.]** The next section (**3.c.**) outlines the tasks remaining for the year of planning for the roll out of UK's CTSA Center.

1. **Content**. UK is well along in the process of creating a University-level organization for clinical and translational research, following the tradition of UK University Centers that provide the "home," both physical and intellectual, for dedicated faculty members (both primary and secondary appointments) and staff who (1) conduct original research and engage in related patient care, (2) develop and deliver graduate and postgraduate training experiences, and (3) lead broad-based programs across multiple departments, colleges, clinical and research institutes, and hospitals and clinics.
    a. **Center's Clinical Research Organization and Investigational Patient Care Unit** represents the gradual "merging" of the GCRC and the UKCRO to better serve as a "one-stop shop" for all of the components required for the conduct of high-quality clinical and translational research.
        i. **GCRC**. The program director and leadership team of UK's GCRC were transitioned in Fall 2005-Winter 2006 to persons who share the transformative vision, mission, and strategy embodied in the Summit Report. This transition has led to the following:
            1. Creating joint leadership representation with the UKCRO and UK's K30 program (see below);
            2. Restructuring administrative, operations, and core laboratory services to serve the key functions of supporting the clinical research needs of UK investigators and protecting the human subjects that voluntarily participate in the clinical research efforts at UK;
            3. Partnering with the UKCRO and K30 programs for conferences, seminars, and monthly "Grand Rounds" for clinical and translational research;
            4. Establishing and rolling out standardized hospital charges for inpatient research beds of $200 per day;
            5. Establishing and rolling out a standardized fee schedule for research-related hospital and laboratory services at the Medicare rate.
        ii. **UKCRO**. The executive director and senior leadership of the UKCRO were also transitioned in Fall 2005-Winter 2006 to persons who share the transformative vision, mission, and strategy embodied in the Summit Report. New leadership has driven the following initiatives to date.

1. Consolidating many of the individual investigator- or discipline-based clinical research organizations at UK into the UKCRO;
2. Expanding each of the functional units of the UKCRO (Project Initiation/Management Unit; Clinical Operations Unit; Clinical Research Marketing Unit; Clinical Research Compliance Unit; Clinical Research Education Unit [see **3.a.** above]);
3. Expanding the responsibilities of the Clinical Research Marketing Unit (see above) to include ***all*** clinical and translational researchers at UK, including GCRC investigators;
4. Initiating "in-reach" activities for University practitioners and "outreach" activities for community-based practitioners interested in clinical and translational research;
5. Expanding the Clinical Research Compliance Unit by hiring (October 2005) a full-time compliance officer and assuming responsibility for all regulatory and fiscal compliance requirements of ***all*** clinical and translational research protocols across campus; and rolling out University-wide policies and procedures for fiscal compliance that govern all clinical and translational research;
6. Colocalizing key personnel (e.g., contracting, grants management) from the Office of Sponsored Projects Administration (OPSA) and ORI to new and expanded UKCRO/GCRC space.

b. **Research Education, Training, and Career Development Program** of the Center represents the consolidation and integration of key educational and training activities of existing and newly created programs across the University to form a continuum of horizontally and vertically integrated educational and training experiences and opportunities that are accessible to researchers at a wide variety of career development stages. These experiences share the common principle of a mentor-centric, multidisciplinary team-based approach.

   i. We are in the final stages of a comprehensive search for a director of the Center's education, training, and career development activities and anticipate appointing in March 2006 a person who shares with the new GCRC and UKCRO directors the transformative vision, mission, and strategy embodied in the Summit Report. This person will have leadership responsibilities in the GCRC that will enable him or her to align the GCRC's educational programs under the umbrella of the Center's programs. He or she will assume responsibility for several educational, training, and career development initiatives that have been implemented during the course of the Summit process.

      1. **K30 Program**
         a. The University and the College of Medicine have committed full funding ($185,185 in direct costs per year for 5 years, for a total commitment of $925,925 through 2011) for the K30 program after the completion of NIH support in August 2006.
         b. In July 2006, the program will offer an MPH degree and an MSPH degree, both offered jointly by the Colleges of Medicine and Public Health and targeted at UK's junior faculty members and senior fellows interested in clinical and translational research careers.
         c. In July 2006, the program will offer a redesigned Certificate in Clinical Investigation targeted at PhD trainees and junior faculty members who need to be conversant in the lexicon of clinical research if they are to be effective partners in clinical and translational research teams; and to community practitioners who partner with UK investigators in a variety of community-based clinical and translational research initiatives.
      2. **The Physician Scientist Program**, offered by the College of Medicine and supported by the UK Hospital, provides salary and project support for promising clinically trained investigators who want to pursue careers in translational science. Modeled after the NIH K08 award, the program provides project and 75% salary support for up to 3 years to prepare recipients to submit competitive applications for individual NIH K01 and K08 awards. The program supports 2 new scholars per year.
      3. **The Dean's Clinical Research Scholars Program**, also offered by the College of Medicine, it provides project and 75% salary support for clinically trained investigators who are devoted to careers in patient-oriented research. Like the

aforementioned Physician Scientist Program, this program enrolls 2 new scholars per year and provides support for up to 3 years to prepare recipients to submit competitive applications for individual NIH K01 or K23 awards.

4. **Office of Research and Leadership Development (ORLD)** is being established by pooling dedicated resources from the GCRC, UKCRO, and BIRCWH K12 programs. The overall goal of ORLD is to provide the career development necessary for the critical transition from training to independence as a clinical or translational researcher. ORLD will be located in the Center's new space (see below) and will have a dedicated staff to provide investigators and trainees with the following key services:
    a. **Grant Development** – through a series of formal workshops and individual tutorials.
    b. **Manuscript Preparation** – through a series of workshops and individual tutorials with a staff member who is a professional medical editor.
    c. **Research Skills** – formal courses and workshops, informal seminars, and individual tutorials on the "survival skills" necessary for a career in clinical and translational science, such as sensitivity training, presentation skills, and responsible conduct of research.
    d. **Mentoring**. ORLD will assume responsibility for all aspects of the mentoring process that is fundamental to all of the Center's training and educational activities, including the following key components:
        i. The formalization of the mechanisms (1) by which mentors are paired with prospective trainees; (2) for the development of "mentor teams" for each trainee; (3) for the "real-time" evaluation of the mentor-trainee axis; and (4) by which fractures in particular mentor-trainee relationships will be recognized and corrected.
        ii. The standardization of (1) the criteria required to mentor trainees at specific levels of career development; (2) the selection of mentors; and (3) the ongoing evaluation of mentor performance.
        iii. The development of mentors from former trainees through formal and informal career-development activities.
        iv. The codification of appropriate recognition and rewards for successful mentoring, most importantly at the level of the Center's appointment, promotion, and tenure guidelines.
5. **Research Subject Advocate** (RSA) and associated staff will be located in the research education, training, and career development unit of the UK Center to maximize their function and minimize any conflicts that might develop with proximity to ORI or the compliance functions of the Center.
6. **Leadership Development** will expand Circles of Power (COPS, see **2.g.8.** above), UK's leadership program for women and underrepresented minorities, and offer it to all trainees with leadership potential.

2. **Governance & Administration**.
    a. **UK Center's Senior Leadership** is described briefly below. All members will continue to actively participate in national forums for their respective units and will transition to National Steering Committee and subcommittee service as these are developed. This participation will be essential for sharing best practices and adopting uniform policies and procedures for a national standard for the conduct of and training in clinical and translational research.
        i. **Program Director**. The Principal Investigator of this application, C. William Balke, has been designated as the Program Director for UK's Center for Clinical and Translational Science. As is evident from his NIH biosketch, Dr. Balke is a productive and well-funded translational investigator who also has, as the College of Medicine's Senior Associate Dean for Research, the administrative experience and qualifications needed to direct large, multidisciplinary programs. With the arrival of UK's new Provost in July 2006, Dr. Balke will assume the rank of Vice Provost for Clinical and Translational Science, reporting directly to

the University Provost. This rank will enable Dr. Balke to effectively forge collaborations and inspire cooperation between all of the UK constituencies involved with clinical and translational research.

ii. **GCRC Director**. Leslie J. Crofford, MD, is Gloria W. Singletary Professor of Internal Medicine. She brings broad basic, translational, and clinical science experience to the leadership of the UK Center application. In addition to her role as Program Director of the GCRC, Dr. Crofford is Division Chief of Rheumatology and Director of the Center for the Advancement of Women's Health. She has been continuously funded by NIH since leaving the intramural program of NIAMS in 1993. Her research has always been patient-oriented but has ranged from the most basic investigations of lipid mediators of inflammation in synovial tissues of patients with inflammatory arthritis to animal models to studies of the physiology of pain in human subjects. Dr. Crofford has had substantial experience as a mentor, holding a K24 award and serving as principal investigator of a T32 award for the Training of Arthritis Research Scientists. She is also principal investigator of the Kentucky Women's Health Registry, which aims to facilitate recruitment of women to clinical studies and to provide a dataset for clinical epidemiologic studies.

iii. **UKCRO Director**. John Novak, BDS, LDS, MS, PhD, was appointed Director of the UKCRO and Assistant Dean in the College of Medicine in November 2005. He is Professor of Periodontics and Associate Director, Center for Oral Research, UK College of Dentistry. He is also Director of the UK Delta Dental of Kentucky Clinical Research Center. Dr. Novak supervises a large NIH-funded clinical and translational research program in oral health and the impact of oral health on systemic illnesses. His research program involves extensive interfaces with a number of UK Colleges and Centers, including obstetrics, aging, cardiology, pediatrics, and the intramural programs of NIH.

iv. **Assistant Director for Clinical and Translational Research**. Geanie Umberger, PhD, MPH, RPh, was appointed as Assistant Director for Clinical and Translational Research in January 2006. Her unique background in the Colleges of Pharmacy, Public Health, and Medicine and her many years of industry experience with Bristol Myers-Squibb will be invaluable in extending the collaborations required to complete the development of the UK Center for Clinical and Translational Science. She has expertise with (1) industry-sponsored clinical trials; (2) basic science and NIH-funded investigator-initiated clinical studies; (3) education and outreach to the community, both clinicians and the lay public; and (4) teaching and mentoring students at all stages of career development. She provides oversight for a number of education and training programs and support for the development of this application and the Center.

b. **Executive Committee for Clinical and Translational Research** has been constituted and will begin its quarterly meeting schedule with the arrival of the new Provost in July 2006. Its roster includes leadership representatives from all of the key stakeholders in the University's clinical and translational mission, including the Provost, the Center Director, the Executive Vice President (EVP) for Research, the EVP for Health Affairs, the EVP for Finance and Administration, and the Deans of the UK Colleges that engage in clinical and translational research, which to date include the Colleges of Medicine, Dentistry, Pharmacy, Nursing, Health Sciences, Public Health, Agriculture, Education, and Arts and Sciences.

c. **Operational Committee for Clinical and Translational Research** has been constituted and has been meeting weekly during the Center's planning process since January 2006. As recommended by the Summit, the committee is chaired by the Center's Program Director and includes the newly appointed directors of the key components of clinical and translational research on campus, including the General Clinical Research Center (GCRC), the UKCRO, and the UK K30 program. Most of the accomplishments enumerated in section **3.b.** above are the direct result of the activities of this operations committee.

d. **Space and Facilities.** The University has committed 10,000 square feet of assignable space, in a soon to be vacated building for the physical "home" of the Center. This space is in addition to the existing 9,612 square feet dedicated to the combined operations of the GCRC and UKCRO. Occupancy is scheduled for the end of 2006. The building is strategically located near the Kentucky Clinic, which houses the contiguous outpatient facilities of both the GCRC and UKCRO. (The

inpatient beds of the GCRC are on the 5th floor of University Hospital and are easily accessible from the Kentucky Clinic via an enclosed pedestrian walkway.) This "Centers" home is ideally suited for locating all of the administrative, educational, and regulatory operations of the Center in close proximity to operational units of the CRO and investigational patient care units.

e. **Evaluation.** The Summit report was emphatic about the necessity for both ongoing and periodic assessment of the Center's achievement of its objectives. The recommended governance structure (see above) will allow "real-time" evaluation at the institutional level (e.g., the Executive Committee for Clinical and Translational Research) and at the operational level (e.g., the Operational Committee for Clinical and Translational Research). In addition, the Summit report expects that each functional unit and educational module will have its own evaluation and oversight committee, as do all currently active UK programs supporting clinical and translational research. The Summit report also underscores the necessity for external oversight and recommends periodic (at a minimum, yearly) reviews of all aspects of the Center's activities by an external advisory committee who will report to the Executive Committee for Clinical and Translational Research. In addition, all academic programs will be subject to the 6-year programmatic review required by University accreditation.

3.c. Clinical & Translational Research Summit – "What Remains to Be Done - The Year Ahead"

Continuing the momentum of UK's Clinical and Research Summit, we are dedicating the next year to completing the adjustments necessary to create an integrated CTSA Program at UK. The following items represent the main tasks that remain to be competed, along with our strategies for accomplishing them.

1. **Identification of the clinical and translational science communities served by the UK Clinical and Translational Research Center.** The Summit process has brought together a vast array of UK faculty, staff, and administrators from 22 different UK colleges, administrative offices, clinical research centers, and educational programs. Although this process has clearly identified the UK constituencies that will be served, the UK Center as conceived above can be expected to have an impact far beyond the UK campus. Without exaggeration, the UK Center will touch virtually everyone in the Commonwealth of Kentucky and the region by virtue of (1) the impact of its clinical and translational research discovery on the delivery of health care in the region; (2) the engagement and participation of the community health care providers in its discovery and educational missions; (3) the impact of the first 2 activities on the economy in the Commonwealth; and (4) the "connectivity" of UK's Center to other clinical and translational research centers across the nation and the NIH. Consequently, a critical aspect of our planning process is to develop mechanisms whereby these critical constituencies can be involved in a substantive way in the creation, implementation, operations, and ultimately the evaluation of the UK Center. To engage the first 3 groups, we are planning a series of Town Hall meetings described below.
    a. **Town Hall Meetings** will be held every other month for the next year and are scheduled at a variety of locations, including the UK campus, the state capital in Frankfort, and various community locations throughout the state. They will be staffed by members of the Operational Committee for Clinical and Translational Research (see **2.b.** above). The meetings will be approximately 2 to 3 long, and the format will include brief presentations about UK's 2020 mandate, the Clinical and Translational Research Summit recommendations and how these further the 2020 mandate, and key elements of the UK Center for Clinical and Translational Research. The remainder of each meeting will be devoted to input from participants regarding any and all aspects of UK's emerging initiative. The proceedings of each meeting will be broadcast in real time throughout the Commonwealth by the Kentucky TeleCare Network (see **2.f.8.** above), thereby amplifying the scope of the audience and the potential of the meeting's impact. The content of the discussions of each meeting will be transcribed and made accessible on the Web page of the UK Center for Clinical and Translational Science sponsored by UK's EVP for Research. Most important, these Town Hall meetings will generate task-delimited working committees that will be assembled from key members of the audience and the Center's Operational Committee to address specific concerns, identify viable solutions, and build those solutions into the ultimate shape and form of the UK Center. This level of outreach and engagement over the next year will obviously be important for the final "shape" of the UK Center, but we intend to continue to ground the UK Center in the reality of the populations served by continuing these outreach activities annually.
    b. **Web Site and Electronic Formats.** The Summit report called for one Web site as the repository of all UK policies and procedures and a directory of all information related to the conduct of clinical and

translational research at UK. This site is currently in the planning stages. With regard to the connectivity of the UK Center with the larger clinical and translational research community and the NIH, we have already committed to electronic formats and products that are compatible with the main platforms of the NCI, NIH, and others. During the past 18 months, UK has purchased and is rolling out the following data management systems: **Eclipsys®** electronic patient record and clinical software system; in-house development of an **Electronic Patient Research Database; BRAAN2** for electronic IRB submissions, evaluation, and tracking**;** and **Oncore** for the Markey Cancer Center.

2. **Cataloging the existing mechanisms for the conduct of and training in clinical and translational research.** The inventory of the existing mechanisms at UK that are either involved in or support clinical and translational research was largely accomplished during the Summit process. As can be seen in section **2.**, UK has virtually all of the building blocks for the development of an integrated center for clinical and translational research, with the exception of an integrated electronic platform linking the clinical and translational research activities to the mainstream of clinical care. This need is addressed below.

3. **Identification of the strengths and weaknesses of these existing mechanisms**. The Clinical and Translational Research Summit also identified the strengths and weaknesses of the mechanisms and programs identified in section **2.** above. With few exceptions (see below), most of UK's existing clinical and translational research programs and support services are quite successful, as judged by their productivity and accomplishments as supported by successful peer review (e.g., T32s, COBREs) and recent successful competitive renewals (e.g., T32s and BIRCWH). The main weakness identified was the loss of synergy caused by the existence of separate programs that often duplicate services and resources. This is the primary reason that the Summit recommended a University-wide colocalization of the programs and services needed in the UK Center for Clinical and Translational Research. In addition, 3 of the component programs were identified as needing attention, though for very different reasons.
    a. The **UKCRO** was identified as the primary clinical research organization at UK, but its effectiveness was limited by (1) the presence of multiple investigator- and department-specific CROs across campus, and (2) the size of professional staff and facilities that lagged behind growing demand for service (i.e., yearly doubling since 1992). Consequently, over the last 6 months, a national search resulted in the hiring of a new director, Dr. John Novak (see NIH biosketch), who is a productive and well-funded clinical scientist with the administrative experience and organizational skills needed to mold the UKCRO into a campus-wide resource for clinical and translational research. In the first 6 months of Dr. Novak's tenure, the UKCRO has either absorbed or assumed oversight control of many of the individual CROs that existed in separate divisions and departments; the staff has been increased by 44% (total of 26 personnel); and the space has doubled to a total of 9,612 square feet. These changes were needed to keep pace with the markedly increased use of the UKCRO by existing and newly recruited faculty members engaged in clinical and translational research in the Colleges of Medicine, Dentistry, Pharmacy, Health Sciences, Nursing, and Public Health.
    b. The Summit Report identified the **GCRC** as underperforming on the basis of a consistently less-than-budgeted use of inpatient, outpatient, and core laboratory services by UK's large and growing base of NIH-funded clinical and translational investigators. This underperformance was attributed to the absence of a culture of investigator-focused service and communication. As a result, the Dean initiated a national search for a new Program Director with the vision and commitment needed to reform the GCRC along the suggestions of the Summit Report. In January 2006, Dr. Leslie Crofford assumed the directorship of the GCRC on the basis on her qualifications (see NIH Biosketch) as a highly productive and well-funded clinical investigator; her administrative expertise in directing large institutionally based programs; and her leadership abilities necessary for the team forming the UK Center for Clinical and Translational Science. With newly committed resources from the College of Medicine, Dr. Crofford is restructuring the leadership and staff of the GCRC to align with the service-oriented goals of the UK Center.
    c. The **K30 program**, though successful with respect to its original mission, was identified in the Summit Report as being currently too narrow in its offerings with regard to the diversity of educational programs and the career and leadership development aspects required for scope of the UK Center. The Center's Operational Committee has broadened the scope of the K30 program to include the elements described above. Importantly, the resources have been committed, and these

programs are now either in place or in the process of being offered. The Center's Operational Committee is currently in the final stages of recruiting the inaugural leader of this new unit and is considering a field of candidates with (1) proven credentials as productive and funded clinical or translational scientists; (2) a track record of mentoring trainees at multiple levels of career development; (3) experience in administering board-based training programs; and most important (4) a vision in common with the members of the Center's Operational Committee with regard to the discipline of clinical and translational science.

4. **Identification of new programs needed to meet the goals of the UK CTSA Center.** The Clinical and Translational Research Summit Report identified several important mechanisms that are not currently present and will be required if UK's Center is to achieve the expectations of the Summit report and the NIH's CTSA RFA.
    a. **Biomedical informatics core** has long been recognized as a pressing need, a need emphasized by each of the Summit reports. At present, bioinformatics expertise is scattered and isolated in different departments and colleges. As the cornerstone for communication of clinical and translational discovery, bioinformatics must take center stage in our planning process. This bioinformatics core will contain a director and master's-level support staff, as well as a data warehouse for all clinical and translational research data, including an electronic research patient data repository.
    b. **Centralized electronic record keeping and data management platform** is needed to unify the following key elements of a robust clinical and translational research program: (1) the hospital's and clinic's electronic medical record and (2) clinical trials software for study management, patient data, patient recruitment, and regulatory and fiscal compliance. In January 2006, a working group led by the Center's Operational Committee was convened to inventory the systems currently in use at UK that require compatibility and interface and to determine the features that the system would need to provide. With this information and the goal of establishing a bioinformatics network in mind, potential vendors that could partner with UK and develop a bioinformatics network have been identified. One vendor, Academic Performance Institute, Inc. (API), was recently awarded a contract by ORI to supply an IRB software system, BRAAN2, currently used by a number of university IRBs. UK has entered into discussions with API to develop a global system capable of interfacing all of the different clinical, research, and support units, as well as community partners.
    c. **Predoctoral training and educational programs** will be developed and based on the models already in place in UK's 10 discipline-based NIH T32 training programs and the GCRC's predoctoral training component. These programs will draw on the curriculum developed for the K30 program and the MPH and MSPH degrees to integrate predoctoral students across the spectrum of UK's professional and graduate programs. Our goal is to establish the vertical and horizontal integration of clinical and translational training experiences to stimulate the pipeline of clinical and translational researchers.
    d. **Clinical and Translational Research Methodologies** are currently taught in courses offered by the Colleges of Medicine, Pharmacy, and Public Health, and the Department of Statistics in the College of Arts and Sciences. However, our planning process must identify a core of researchers with the vision to develop novel methodologies, study designs, and ways of involving the unique populations available to UK researchers in clinical and translational research. Their efforts will also focus on development of didactic courses that will be incorporated in the academic programs associated with the UK Center.

5. **Development of the Program's Content, Governance, Administration, and Evaluation.** As is evident from the discussion above, the main components of the content, governance, and administration of the UK Clinical and Translational Research Center have been conceived and are either in place or should be implemented within the next several months. The evaluation component is essential for the conduct of the UK Center and will be formulated during our planning process over the next year. Both the Executive and Operational Committees view this component as essential for the proper functioning of the UK Center and will use its recommendations in an iterative way to keep the development of the UK Center true to its mission and to provide the direction for "mid-course" corrections should they prove necessary. Overall, the Operational Committee will develop evaluation and oversight mechanisms for the center as a whole and also for each of the Center's key components. With regard to the Center as a whole, oversight will be

provided by both internal and external committees. The internal oversight committee will be chaired by the EVP for Research and will consist of the Center's program director and the directors of the Center's key functional components. This group will meet every 6 months and will issue a written report to the Center's Executive and Operational Committees with the expectation of a timely written response addressing the identified weaknesses and deficiencies. The external committee will be chaired by the Provost and will consist of several members of UK's leadership who are not involved with the Center (such as Deans of UK Colleges that do not conduct clinical and translational research) and several external members, preferably from the CTSA-like programs of other Universities or the NIH. This committee will meet annually and will issue a written assessment of the fidelity of the Center to its mission and goals to UK's President, Dr. Lee Todd. This report will be included in noncompetitive progress reports and the competitive renewal applications for the funding of components of UK's Center.

6. **Managing the institutional and cultural changes that are anticipated to occur with the establishment of the UK Clinical and Translational Research Center.** The degree of cultural adjustment associated with the transformative changes involved in the creation of the UK Center for Clinical and Translational Science cannot be overstated. The formalization of a new discipline of clinical and translational science represents a true paradigm shift in the culture of this University. However, it is important to point out that both the direction and the pace of these changes are being driven in large part by UK's recognition of the need for and its readiness for changes of this magnitude. Consequently, the main challenge for the UK Center will be managing the cultural changes associated with the constituencies outside UK that will be served by UK's Center (see above). The Town Hall meetings and the working committees and groups that will be formed as a consequence of these meetings will provide a number of opportunities at several levels for engaging and involving all members of our greater community in the creation, management, and ultimate evaluation of the UK Center for Clinical and Translational Science.

4. Concluding Summary: UK's Clinical and Translational Science Center and Planning Grant

On the basis of the NIH's Roadmap initiatives, UK recognized in 2004 that a new and quantitatively different structure was needed for the governance, support, and facilitation of clinical and translational research. The Summit process guided UK to the same conclusions that the NIH reached with its CTSA initiative, namely that a distinct discipline of clinical and translational science absolutely requires the synergy of previously disparate resources and services. Remarkably, the discussion of how clinical and translational research should be organized at UK has engaged researchers from across the health sciences colleges and across the many multidisciplinary programs and centers at UK. The unique perspectives of such a diverse assembly—from the Colleges of Agriculture, Arts and Sciences, and Education to the 6 health sciences Colleges to community-based health care professionals—have shaped and energized these efforts. These collaborations have created a shared culture of innovation and risk-taking that will serve us well as we advance to our goal of establishing UK's Center for Clinical and Translational Research.

The University of Kentucky is now well along in the process of transforming its clinical and translational research activities into a new and distinct discipline of clinical and translational science. New leadership has been put into place at all levels; multilevel organizational bodies have been conceived and appointed and are now operational; the governance and reporting relationships of the Center have been established; institutional commitment and support have been solidified; and resource allocation is under way. This process has been informed by the highest commitment and support of UK's senior leadership, who have already allocated more than $12 million in support of salaries and programs for the UK Center and provided nearly 20,000 square feet of space for the Center's administration, operations, and educational, training, and career development functions. The planning process described in this application will complete UK's transformation of its clinical and translational research activities and will thereby change for the better the University's entire discovery mission.