

Executive Summary: Clinical Research Task Forces
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On September 20, 2004, Wendy Baldwin, Ph.D., executive vice president for research, and Jay A. Perman, M.D., dean of the College of Medicine, convened a Clinical Research Summit to set an agenda for the review of clinical research at the University of Kentucky. The Summit was attended by over 30 participants representing UK HealthCare, the six health sciences colleges, University Hospital, KMSF, the Offices of Sponsored Projects Administration, Sponsored Program Development and Research Integrity, University legal representation, units supporting and engaged in clinical research and the training programs dedicated to clinical research training (Appendix A).

This summit was chaired by John Thompson, M.D., interim associate dean for clinical research in the College of Medicine. Dr. Thompson noted that a similar broad-based review of clinical research at UK in 1997 brought about many changes to facilitate the conduct of clinical research at UK, including the creation of the Kentucky Center for Clinical Research Investigator Services (KCCRIS), predecessor to the University of Kentucky Clinical Research Organization (UKCRO).

The Clinical Research Summit of September 2004 considered numerous avenues of investigation and review. The resulting Clinical Research Summit Agenda raises questions related to University policies and procedures, investigator issues, operational norms, and the roles and relationships of units involved with or engaged in clinical research. To initiate review of these issues, Dean Perman appointed a Clinical Research Task Force corresponding to each area. C. William Balke, M.D., senior associate dean for research in the College of Medicine, charged these Task Forces in November 2004. The Task Force on Investigator issues was chaired by Dr. Tom Foster, College of Pharmacy, and co-chaired by Roxane Poskin, UKCRO; the Task Force on Operational Norms was co-chaired by Shirley Warren, UKCRO and Dr. John Slevin, Neurology; the Task Force on Policies and Procedures was co-chaired by Dr. David Watt, associate provost for academic affairs, and Dr. Dan Wermeling, College of Pharmacy; the Task Force on Roles and Relationships was chaired by Dr. James Ferguson, III, chair of Obstetrics and Gynecology and co-chaired by Dr. Jane Harrison, College of Medicine. Representation on the task forces came from across the University.

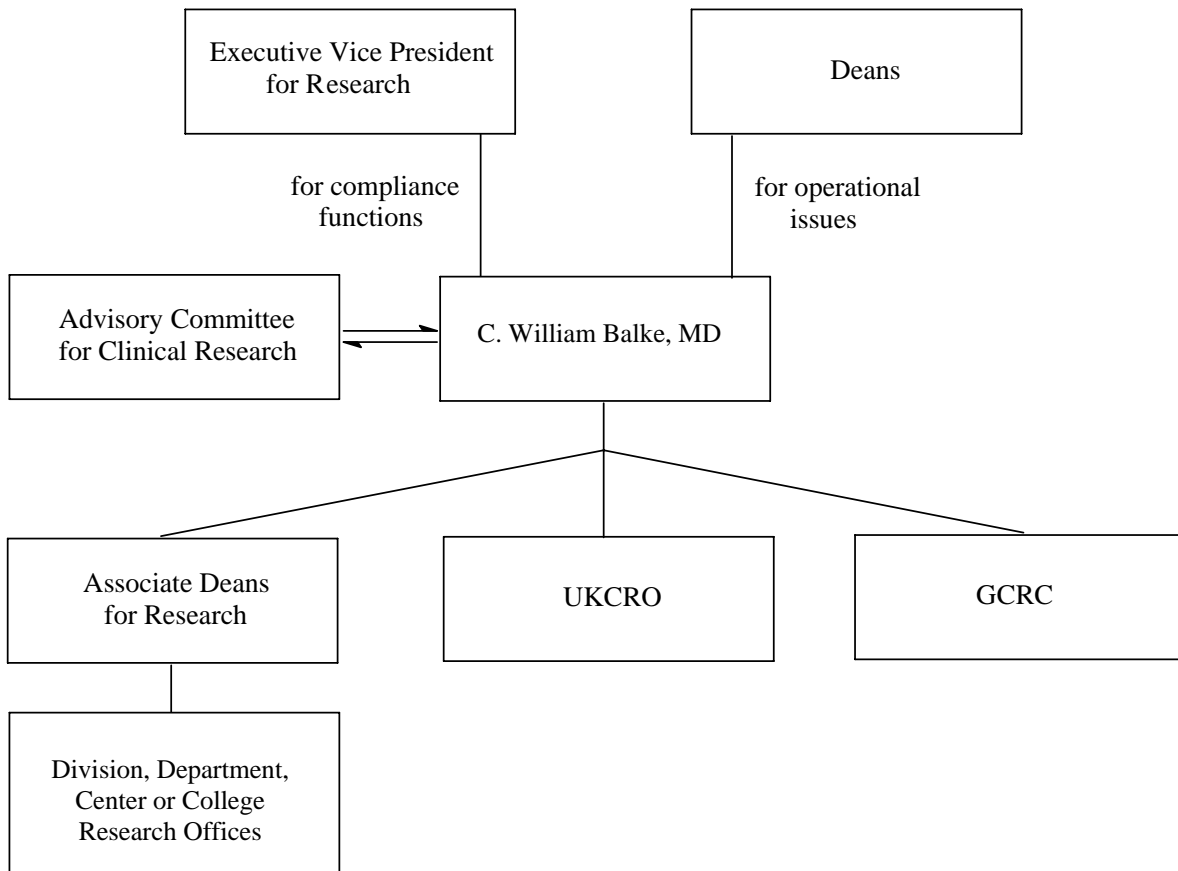
The Clinical Research Task Forces met during 2004-2005 and each issued a report with recommendations to address the issues in their areas. Although each task force began with a different set of questions, their thoughtful and thorough review resulted in a consistent set of recommendations. The Task Force reports call for centralization of the governance, administration, educational programs and operational infrastructure to support clinical research. They highlight the need for centralized electronic infrastructure (hardware, software and databases) to advance and monitor the conduct of clinical research. And they call on the University to assign a top priority to funding development of these recommendations.

Clinical Research Task Force Recommendations:

I. Advisory Committee for Clinical Research:

Create a central institutional decision-making body responsible for establishing university policies, operational norms and business practices directing how all clinical research will be conducted within the University.

The Policies and Procedures Task Force recommends the following governance structure:



Individual Task Forces provide varying proposals on the functioning of this central administrative body. The Policies and Procedures Task Force recommends that Dr. Balke report to the Executive Vice President for Research for compliance issues and to the deans of the colleges engaged in clinical research for operational issues related to clinical research. Additional committee members may serve on an expanded committee to address specific issues or subcommittees may be dedicated to specific areas, such as regulatory issues.

The Operational Norms Task Force recommends establishment of an Executive Clinical Research Advisory Committee comprised of deans and department chairs responsible for financial issues related to clinical research. In their structure, a Clinical Research Oversight Committee with additional faculty members active in clinical research will be responsible for 1) risk management, 2) fiscal management, and 3) establishing best practices for clinical research.

The Task Forces on Policies and Procedures and Roles and Relationships recommend a careful evaluation of governance needed for clinical research conducted in departments and centers outside the six health sciences colleges to ascertain the nature of inclusive governance required to address the needs of these organizations. However, the need for inclusion must be weighed against the need for a small committee capable of functioning in a timely manner.

The Advisory Committee for Clinical Research will be responsible for creating and maintaining an official web site of all policies and procedures pertinent to clinical research, similar to the web sites of the University of Minnesota and the Oregon Health and Science University. This is critical to managing the wealth of policies initiated and overseen by many different committees, colleges and administrative offices throughout the University.

In addition, the Advisory Committee for Clinical Research will be responsible for conducting an annual assessment of clinical research at the University.

II. Definition of Clinical Trials and Clinical Research and Determination of Units engaged in Clinical Research

The Advisory Committee for Clinical Research will review definitions of clinical research (NIH, Graylyn Development Conference, Association of Colleges of Medicine) and either select one or develop a University-wide definition to be used to identify units engaged in clinical research and therefore subject to compliance, monitoring and regulatory requirements. Care should be given to distinguish clinical research from clinical trials and different definitions of each term developed.

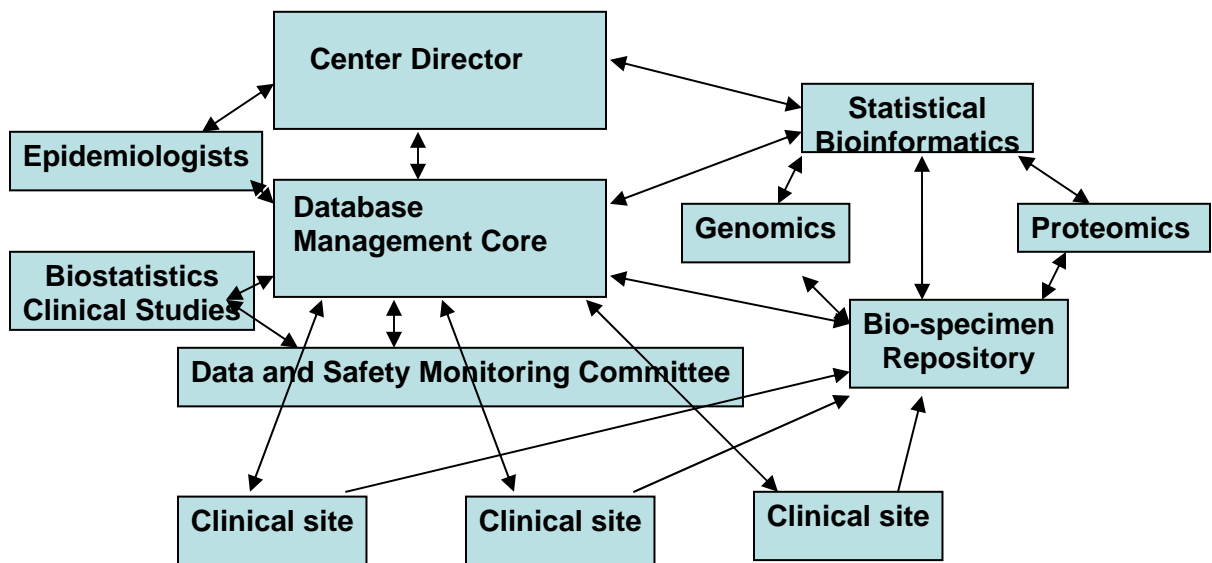
In the absence of campus-wide definitions for clinical research and clinical trials, it is difficult to inventory the clinical research enterprise. Once a definition has been agreed upon, it will be used to more clearly define and shape the clinical research enterprise. It will be the basis for determining what should be classified as clinical research, for example, on the University Internal Approval Form. It will also serve as the basis for a more exhaustive inventory of units involved with or engaged in clinical research. Such an inventory is essential in developing an expanded centralized clinical research organization to serve the needs of the entire University community and in considering the parameters of a broad communications plan for the clinical research enterprise.

III. Expanded Centralized Organization to Provide Needed Services

Expand the existing clinical research organization to include a clinical data management-biostatistics center, centralized data safety monitoring and additional expertise in such areas as clinical pharmacology, investigational drug services and dietary services with the goal of establishing a full service operation to support virtually all aspects of clinical research.

The Task Force on Operational Norms provides this diagram of the interactions of an expanded CRO structure, with all elements supported by electronic infrastructure:

Translational Research Structure



According to the Task Force on Operational Norms, the key element in this expansion is a Data Management Core requiring a minimum of 2,000-2,500 sq ft dedicated space with a budget of \$680,000-\$880,000 to bring it on line and an additional \$450,000-\$600,000 in operational expenses.

The second key element is an expanded Biostatistical Core, with a projected 5 full time faculty and 5 MS level biostatisticians, divided between a bioinformatics core and a clinical trials biostatistics core, at a projected cost of \$1.5 million and a projected implementation timeline of 1.5 years.

A Bio-specimens/Tissue repository is another key component of this expansion to preserve the specimens collected in clinical trials for later investigation. This repository could follow models already in place in Markey Cancer Center and the Department of Pathology.

Development of a University-level Data Safety Monitoring Committee is seen by the Operational Norms and Investigator Issues Task Forces as a necessity, regardless of the expansion of other services, because this committee is needed to meet increasingly stringent data safety requirements imposed by NIH and other granting agencies. Models have already been developed and could be implemented within a six-month time frame. However, such a University-level committee will need to operate under the umbrella of a broader organization, such as an expanded UKCRO, for authority and visibility.

IV. Expanded Electronic Infrastructure

Identify and implement a centralized electronic clinical trials software system for regulatory, study management, patient information, study populations, and fiscal compliance. This software would be required for all clinical research and be compliant with the NCI Cancer Center Support Grant Guidelines.

In addition, resolve existing electronic infrastructure issues:

- a. Electronic registration system for patients involved in clinical research trials is still not available and is still a top priority.
- b. Access to patient databases is needed for investigators with appropriate credentials to search for study subjects through all patient entry portals. The VA offers a model of such a system, with the resulting efficiency and ease of identifying potential research subjects.
- c. Electronic communication infrastructure is needed to support efficient conduct and coordination of multi-center regional or national clinical trials.

Although expansion of electronic infrastructure has been under consideration for many years, the University is still faced with fragmented data storage in databases that do not communicate with each other, as well as inadequate systems to register, identify, and access potential and actual study subjects. Resolving the issues related to electronic infrastructure so that all elements of the clinical/translation structure are appropriately supported electronically is crucial to UK's ability to take the next steps in developing clinical research by initiating and overseeing regional and national multi-center trials.

V. Education Program

Develop a coordinated program of education that can be continuously monitored and assessed.

Components of the Program include a continuum of training with the core representing minimal requirements for all clinical research investigators and the levels based on the following categories, as recommended by the Task Force on Investigator Issues:

Core Program:

- Human Subjects Protection
- Responsible Conduct of Research
- Fiscal Compliance
- Navigator Trial Conduct at UK

Level I: Potential requirements dependent on job functions

- Occupational Health and Safety
- Environmental Management
- Radiation Safety
- VAMC requirements

Level II: Optional training programs in good clinical practice

- UKCRO Clinical Research Updates
- GCRC Scientific Exchange Seminar Series
- Sponsored Program Development Workshops
- ASTeCC Seminar Series

Level III: Scientific research professional development education

- Academic Curriculum: Certificate in Clinical Research, MPH in Clinical Investigation,
- COBRE: Biologic Basis of Oral/Systemic Diseases, Molecular Mechanisms of Human Disease, Nutritional Sciences and Obesity, Women's Health
- K-12: Building Interdisciplinary Research Careers in Women's Health (BIRCWH)
- K-30: Career Training in Clinical & Translational Research
- Physician-Scientist and Clinical Research Scholars (College of Medicine)

Communication is a key to making this continuum of educational programs available to young investigators and research staff working with them. An incentive program to permit researchers to "test out" of required trainings would enable them to move on to building their skills and careers through professional development opportunities.

VI. *Research Resources Issues:*

- a. Develop a Rapid Response IRB to rapidly schedule and review protocols where time elements for initiating the research is critical, such as in multi-center clinical trials where subject accrual times are of short duration.
- b. House Core Services together, including:
 - o Office of Sponsored Programs Administration (OSPA),
 - o Institutional Review Board (IRB),
 - o General Clinical Research Center (GCRC), and
 - o Clinical Research Organization (CRO).

Summary Statement

There is a strong and positive history of success in multiple avenues of clinical research at the University of Kentucky. And even in the midst of the Task Force investigations, development of clinical research infrastructure is underway. A Clinical Research Training Retreat in September 2005 provided and gathered information about the needs of clinical investigators at UK (Appendix B) and a search for an assistant dean for clinical research in fall 2005 will conclude by December 31, 2005.

However, the members of the Clinical Research Task Forces express their concern that UK is at a critical juncture in the evolution of its clinical research enterprise. The stringencies of new regulatory requirements, the perceptions—often negative—in the broader community concerning clinical trials, the new directions in clinical research resulting from NIH Roadmap initiatives, all add to the pressures already too apparent to clinical researchers. If UK is to move forward and take a leadership role both regionally and nationally in clinical research, it must first have its own policies, procedures, and infrastructure clearly defined and operational. It is with this goal that the Clinical Research Task Forces submit these reports for your review, consideration and action.

Recommendations of the Clinical Research Task Forces Timeline for Implementation

- Winter 2006:** Town Meetings to review Task Force recommendations and implementation timetable
- Winter 2006:** Appointment and inauguration of Advisory Committee for Clinical Research
- Spring 2006:** Review and development of definitions of clinical research and clinical trials by Advisory Committee for Clinical Research
- Spring 2006:** Alignment of UKCRO and GCRC
- Spring 2006:** Educational programs reviewed, aligned and publicized; MPH in Clinical Investigations developed
- Spring 2006:** Inauguration of Data Safety Monitoring Committee
- Spring 2006:** Development of Rapid Response IRB
- Fall 2006:** Data Management Core added to UKCRO/GCRC
- Fall 2006:** Review of UK policies and procedures by Advisory Committee for Clinical Research
- December 2006:** Official Web site for clinical research developed
- January 2007:** Biostatistical Core added to UKCRO/GCRC