

**Final Report of the
Clinical/Translational Research
Task Force**

Submitted to President David Skorton
March 2006

Task Force Members

Jordan Cohen, College of Pharmacy (Co-Chair)

David Johnsen, College of Dentistry (Co-Chair)

M. Kathleen Clark, College of Nursing

Ed Dove, Biomedical Engineering

Mary Gilchrist, Hygienic Laboratory

William Haynes, Carver College of Medicine

Raymond Hohl, Carver College of Medicine

Gary Hunninghake, Carver College of Medicine

Donna Katen-Bahensky, Univ. of Iowa Hospitals and Clinics

Joel Kline, Carver College of Medicine

Allyn Mark, Carver College of Medicine

Brad Phillips, College of Pharmacy

Jean Robillard, Carver College of Medicine

Clark Stanford, College of Dentistry

Charlotte Talman, Clinical Trials Office

James Torner, College of Public Health

David Wynes, Research Administration

Dennis Domsic, Office of the Provost (Ex Officio)

FINAL REPORT
of the
Clinical/Translational Research Task Force

Table of Contents

	Page
I. Executive Summary, Including Major Recommendations	1
II. Specific Recommendations—Resources For Personnel, Facilities, IT	3
III. Introduction	3
A. Charge to the Task Force	3
B. Objectives for the Task Force	4
C. Vision, Mission and Goals for Clinical/Translational (C/T) Research at the University of Iowa (UI)	4
IV. Internal and External Assessment	5
A. List of Existing Clinical Research Entities at UI	5
B. Summary of Survey to Faculty Conducting Clinical Research (See Appendix I for a more detailed report of the survey.)	13
C. Status of Information Technology (IT) Planning for Electronic Medical Record and Clinical Research	17
D. Institutions Sampled (Listing)	18
V. Infrastructure Elements for Clinical/Translational Research	18
Sections include: 1) facts and trends potentially affecting recommendations; 2) general recommendations; and 3) specific recommendations, including programmatic essentials, infrastructure, financing and governance.	
A. Institutional Review Board(s)	18
B. Subject and Minority Recruiting	23
C. Faculty Development	29
D. Clinical Trials Unit, Including Facilities and Staff Support	34
E. Budgeting	36
F. Clinical Research Coordinators: Training and Availability	39
G. Biostatistics Support	42
H. Preclinical and Clinical Development of New Therapies and Diagnostics	47
I. Role and Dynamics of Current Clinical Research Leaders in a Governance Structure	50

	Page
J. Role of Smaller Units in Clinical and Translational Research	52
K. IT System for Clinical and Translational Research	55
L. Community	59
VI. Interface with the Clinical and Translational Science Award (CTSA) Program	69
A. The Next Paradigm for Clinical/Translational Research	69
B. Overall Summary of the CTSA Assessment	70

APPENDICES

1. [Survey of Clinical Researchers](#)
2. [Discussion Matrix on Governance](#)
3. [Task Force Members](#)
4. [Specific Recommendations—Resources for Personnel, Facilities, IT](#)

I. EXECUTIVE SUMMARY

The Task Force was charged by President Skorton in February, 2005 with several outcomes, including developing a detailed plan for a Center for Clinical Trials with a business plan. The Task Force met bi-weekly and developed the following

assumptions/observations:

- In defining the charge, the Task Force emphasizes that this work would incorporate a new paradigm in clinical/translational (c/t) research that enables UI to expand both the quantity and quality of clinical research studies, whether supported by the NIH or by industry, while maintaining compliance with federal regulations and institutional policies.
- The Task Force was timely in light of the local and national attention being paid to transforming clinical research in this country and the recently released NIH initiative – the Institutional Clinical and Translational Science Award (CTSA).
- Several active high quality UI clinical research programs are relatively independent and loosely configured. While these c/t research activity centers are relatively autonomous, they are not at all hostile silos.
- Several issues that needed to be addressed at an institutional level were identified. These issue areas appear as Report sections listed in the Table of Contents.
- The lack of available baseline resource data demonstrates a diffuse structure and composition of clinical research at UI, and makes it difficult to create a definitive business plan.
- After review of several other institutions which have reengineered clinical research, the Task Force quickly concluded that there is not a single model that has been successful and that all institutions continue to refine their approach. Clearly consistent with the experience at UI, a strong central commitment to hard work, cooperation and resources are required.
- The UI critical mass of senior faculty clinical researchers is marginal for the kind of transformation reflected by the CTSA Program; however other than Michigan, UI is positioned as well as any Big Ten University in NIH training support.
- Major change in c/t research for UI is extremely important as is determining a high level reporting structure for c/t research and a formal working relationship among current c/t research leaders.
- There is a need to establish a formal process for involving Iowa communities in c/t research.
- UI has formidable assets for a new paradigm in translational research including strong individual units, UI “excitement” to move in this direction, our own hospital, a single location and potential to be the dominant clinical/translational research entity for a state.
- The need to strengthen the UI clinical research program is highly consistent with the Battelle Initiative for Economic Development and will facilitate the further development of the four UI-based platforms currently under consideration for funding by the Iowa Department of Economic Development.

Process:

The Task Force assigned report sections based on the issue areas identified early in the process (see Table of Contents). Each section included related background information and recommendations, both programmatic and financial. In the midst of the Task Force activities, NIH announced the elimination of the General Clinical Research Center Program and the creation of the new Clinical and Translational Science Awards Program. The Task Force decided to continue its work toward improving clinical/translational research for UI and at the same time, work to support the CTSA effort headed by Gary Hunninghake.

The Task Force developed an extensive list of specific recommendations for each of the elements and issue areas listed in the Table of Contents. This list of recommendations captures the scope of the task ahead in establishing a University entity in c/t research.

The Strategic Recommendations of the Task Force are:

- Value clinical/translational research as a central part of our mission, as a component of patient care quality, as integrated with our clinical educational program, and as an element to support economic development.
- Assign a top strategic priority for the Institute for Clinical and Translational Research. Prioritization will be needed for UI as a whole, for the Carver College of Medicine, for UI Hospitals and Clinics, and for other units.
- Invest to build and transform the clinical and translational research infrastructure, organization and culture; this is essential in order to survive and prosper as a premier academic research university.
- Support the UI application for a NIH CTSA. Failure to become one of the 60 funded centers is unthinkable as a Research 1 University.
- Capitalize on the strengths and interactions of the Health Sciences Colleges, the UIHC, the Colleges of Engineering, Liberal Arts and Sciences, and others to advance clinical/translational research.

The Operational Recommendations are:

- Establish a UI Institute for Clinical/Translational Research reporting to one or more senior UI officials.
- Constitute a council of c/t research leaders to advise on policy and to facilitate resolution of identified problems.
- Enhance our c/t infrastructure by increasing staffing and providing support in the areas of IRB activities, budget development for studies, faculty mentoring, staff training, data networking, biostatistics, etc.
- Enhance monitoring and compliance activities of c/t research to identify barriers and opportunities.
- Expand and renovate central and satellite facilities for c/t research.
- Develop a network of community-based partners.

- Establish c/t research informatics at UI. Essential components include a director, an integrated network with the UIHC electronic medical record and other relevant computerized systems which are accessible to current UI c/t researchers.
- Create faculty appointments in c/t research and increase educational opportunities in this field.
- As a basis for a business plan, assemble baseline data on current resources committed for clinical research, including faculty, staff, facilities and program support.

UI is positioned to transform our clinical and translational research to a new level and become a national model. Successful development of a UI Clinical/Translational Research Center/Institute represents an enormous commitment to c/t research as a UI strategic priority. This will require administrative centralization, resource reallocation, enormous logistical effort and a shift in faculty culture. All of these are critical steps and all these things need to happen.

II. SPECIFIC RECOMMENDATIONS—RESOURCES FOR PERSONNEL, FACILITIES, IT (See Appendix 4)

III. INTRODUCTION

A. Charge to the Task Force

President Skorton appointed the Clinical Trials Center Task Force in early 2005 to: (1) assess current UI activities related to clinical trials and clinical research; and (2) gather internal and external information to allow development of a long term plan for enhancing clinical trial and clinical research activity at UI. The specific *charge* was as follows:

- Complete a detailed plan, including a business plan, for a Clinical Trials Center
- Define the types of clinical trials to be included in the Clinical Trials Center
- Benchmark with other clinical trials centers around the country
- Review best practices
- Conduct site visits, if needed
- Gather and analyze internal and external data
- Present the plan to the President and other relevant groups

The Task Force was co-chaired by Deans Jordan Cohen (Pharmacy) and David Johnsen (Dentistry) and was comprised of senior representatives from a wide range of University colleges and programs. (Membership listed in Appendix 3).

The Task Force met bi-weekly from late March, 2005, through February, 2006. Much of the time was spent reviewing current activities related to clinical trials and clinical research, gaining an understanding of infrastructure needs to support clinical trials/research, evaluating IT and facilities needs to support clinical trials/research, and assessing current practices for placing and conducting clinical trials by the pharmaceutical/biotechnology industry. In light of the new NIH CTSA program, a substantial amount of time was spent discussing how activities and planning at UI related to the clinical research and training, as well as, translational research at the NIH and beyond.

B. Objectives for the Task Force

Two main *objectives* for the Task Force were identified:

1. Develop recommendations to strengthen our clinical trials and research infrastructure across all colleges, departments and organized research units engaged in these activities. This will include core resources, facilities, organizational and reporting structures and funding.
2. Articulate a vision and matrix structure to position UI as a national leader in performing translational research, in training outstanding clinical investigators, and in developing cutting-edge therapies and treatments.

C. Vision, Mission and Goals for Clinical/Translational Research at UI

Vision:

UI will be viewed as a national leader in conducting clinical research to promote scientific discovery, educating and training of future clinical investigators, and improving patient care and outcomes.

Mission and Goals:

Organize our activities and resources in the areas of clinical trials, clinical and translational research so as to:

- 1) Enhance and facilitate clinical research at UI
- 2) Develop new preventive and therapeutic interventions
- 3) Evaluate the efficacy and effectiveness of preventive interventions
- 4) Develop novel methods for evaluating new interventions

- 5) Train researchers, methodologists and clinicians across all health science disciplines in the conduct of clinical trial research according to Good Clinical Practice standards (GCP's)
- 6) Coordinate small- to large-scale clinical trials of new interventions
- 7) Participate in networks of researchers in the development and evaluation of new interventions and compete for major industrial and federal funding
- 8) Provide a supportive infrastructure and facilities for design, implementation, evaluation and delivery of new interventions

IV. INTERNAL ASSESSMENT

The Task Force agreed that the scope of work would encompass clinical trials and clinical research sponsored both by industry and NIH and that any recommendations for changing current processes or structure would reflect the needs and unique requirements of the individual programs and investigators conducting such studies. Examples of existing programs with external requirements include the NIH funded General Clinical Research Center (GCRC) and the Holden Comprehensive Cancer Center's NCI Cooperative Cancer Study Group (CCSG). A faculty survey was developed to ascertain current strengths and weaknesses in our ability to support clinical trials and clinical research at UI, and the survey was distributed to faculty across all of the Health Sciences Colleges as well as relevant departments in all other colleges. (Survey results shown in Appendix 1)

A. List of Existing Clinical Research Entities at UI

1. General Clinical Research Center (GCRC)

This center is one of 80 across the country and has been continuously funded by the NIH for more than 40 years. The grant resides in the College of Medicine with the Dean as PI, has a unique Dental GCRC component and serves investigators across UI. It is very highly regarded nationally and is seen as one of the most effective such centers in terms of productivity and publications per dollar of NIH funds invested. It serves primarily NIH-funded clinical research and provides protocol review as well as access to several core services including biostatistics, pulmonary physiology, specialty clinical laboratory, nutritionists and kitchen, bone scanning, ultrasound and EEG monitoring.

Challenges include:

- Physical space limitation in terms of age, location and amount, specially for ambulatory studies

- Recruitment of subjects in general and diversity a particular challenge
- Outpatient growth
- Limited staff and time to assist, mentor and develop young investigators
- Limited ability to provide administrative support to investigators
- Cost structure of non-GCRC clinical laboratory support and diagnostic testing
- NIH currently examining future mission and scope of GCRC programs with an eye towards enhancing the translational research agenda

Opportunities include:

- Genotyping, and imaging cores would be very helpful as translational science progresses
- Enhanced informatics capabilities
- Developing and moving therapies emerging from the clinic to the IND phase by partnering with our drug manufacturing and CBB FDA facilities
- Great benefit from many of the core service capabilities of an expanded Clinical Trials Unit including administrative assistance, recruitment, nurse coordinators, and internal marketing

2. Clinical Trials Office (CTO)

The CTO was established in 1998 and reports directly to the Vice President for Research. It provides the UI interface for all industry-sponsored clinical and pre-clinical studies that involve the evaluation of a company product or technology (drug, device, vaccine, procedure, etc.). The CTO serves investigators of such studies in all UI departments by: negotiating the terms and conditions of industry contracts; serving as a resource for the clinical trials process; coordinating activities with the Human Subjects Office; informing the faculty of clinical trial opportunities; and developing marketing programs to increase clinical trials at UI. The current staffing level consists of a director, a program associate, and an administrative assistant. During the past fiscal year, the CTO processed a total of 286 contracts (135 for new studies; 54 contract amendments; 97 confidentiality agreements).

Challenges include:

- Competition from sites dedicated solely to conducting clinical trials in terms of expediency and pricing of contracts

- Recruitment of subjects difficult for many trials in subspecialty areas
- Limited staff and space for CTO
- Decreasing number of faculty interested in conducting industry-sponsored clinical trials
- Difficulty in expediting trials through UI processes
- Mergers of pharmaceutical companies causing a decrease in number of clinical trials
- Actual enrollment in trials is lower than target, so revenue is lower than awarded amount
- Lack of study coordinators and difficulties related to hiring
- Lack of facilities for more complex protocols (such as Phase I studies and inpatient studies)
- Negative national media coverage of pharmaceutical research practices

Opportunities include:

- Potential economies of scale by consolidating core services to serve all UI investigators
- High level of collegiality and collaboration across medical and basic science disciplines could lead to more investigator-initiated studies
- Highly competent core (although, small in number) of nationally-certified clinical trials coordinators
- Integration of resources could attract drug development interest
- Exceptional commitment on the part of Iowans to participate in important clinical trials

3. Prevention Intervention Center (PIC)

Initially established within the College of Medicine in 1992 and then moved with the Department into the College of Public Health, the PIC has focused on multi center trials for industry and federally funded trials with long standing funding for the Women's Health Initiative Study from the NIH. Funding has totaled nearly \$40M over the years but has trailed off recently with the conclusion of some of the major longitudinal studies. While housed centrally on campus, the center operates off campus facilities and clinics in Cedar Rapids, Davenport and Des Moines. Support services include bone density, ECG and phlebotomy while contracting for blood chemistry and radiography. The Center has a full-time staff of 41, involves investigators from 6 departments and has significant interactions with other centers.

Challenges include:

- Limited number of investigators
- Seeking major new initiatives and funding
- Limited infrastructure support for recruitment, laboratory, diagnostics, administrative function
- Need for additional IRB resources

Opportunities include:

- Build on an existing national reputation with both NIH and industry
- Build on existing and strong links with leading clinical investigators on and off campus
- Help expand our efforts in disease prevention and outcomes assessment – post marketing studies

4. Holden Comprehensive Cancer Center Clinical Research Enterprise (HCCC)

This is a highly organized clinical research unit that allows coordination and tracking of all cancer-related studies and is linked closely with NCI Cooperative groups including Children's Oncology Group, Leukemia Group B, Surgical Adjuvant Breast and Bowel project, and the Radiation Treatment Oncology group. Nearly all trials are coordinated with the GCRC, although the HCCC has a separate protocol review structure. Industry trials have a lower priority than federally-funded studies, but they are an important part of the work of the HCCC. Current staffing includes fractional salary coverage for principal investigators and support staff totaling 1.5-2.0 FTE's. Funding comes from a variety of sources including CCSG, College of Medicine, NCI Spore Grant, and an endowment and totals \$870,000 this year.

Challenges include:

- Very modest and highly stretched infrastructure
- Need to stimulate and develop new investigators and investigator-initiated trials
- Administrative support to expedite contracting, budgeting, and IRB resources
- Recruiting of subjects

Opportunities include:

- Build on highly interdisciplinary structure
- Build on strong track record – seen as good value from industry

- Well defined structure and strong linkages externally
- Potential to benefit from enhanced core infrastructure services
- Critical in the overall goal to portray the institution as a place for advanced care and cutting edge therapies

5. Imaging Clinical Trials Center

Human Imaging

A very large and diverse array of human imaging facilities and capabilities exist at Iowa which are becoming an increasingly important part of clinical trials for new therapies. This activity is supported by substantial NIH funding as well as significant industry linkages and contract. Used by most clinical departments, the full-size, large-animal Magnetic Resonance (MR), Computed Tomography (CT), Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), X-ray, and ultrasound imaging devices are also available for human clinical and research.

- **MR.** The MR is an 8000-square-foot, state-of-the-art facility, containing 200 square feet of lab space for image processing. The MR includes a 1.5T General Electric LX CV/I capable of real-time imaging for cardiovascular research and functional brain mapping; and 1.5T Siemens Symphony, two 1.5T Siemens Avanto, and 3.0T Siemens Trio MR scanners which support echo-planar, spectroscopic and chemical shift imaging. These scanners all have dedicated times available for researchers. Another 3.0 T Siemens Trio MR scanner, recently acquired through a NCRH High End Instrumentation Grant, will be wholly dedicated to researchers. The MR scanners offer a full barrage of specialized imaging sequences and quantitative image analysis packages. Pulse programming environments exists for both the GE and Siemens systems, allowing custom sequence and image reconstruction tools to be developed. Additionally, a Helium polarizer and transporter module are available for pulmonary MR studies.
- **PET, PET-CT.** The PET Imaging Center is a self-contained laboratory encompassing approximately 7000 square feet space for production of radionuclides, synthesis of radiopharmaceuticals, quantitative PET scanning for research and clinical activities and analysis of PET imaging information.

- Siemens/CTI Biograph Duo PET-CT system is the main clinical PET scanner. Rapid two slice CT data are acquired.
- Siemens/CTI HR+ PET system is used for all research studies offering a number of acquisition modes (static, dynamic, list mode, gated).
- Space is available and prepared for the installation of an additional PET/CT scanner to be delivered within the next calendar year. This scanner will be used for research as well as clinical studies.
- Scanditronix MC-17F two particle cyclotron is used for routine production of positron emitting nuclides. Routine production of carbon-11, nitrogen-13, oxygen-15, vanadium-48, and fluorine-18 are performed. The cyclotron is completely automated for normal operation. The fully-equipped clinical radiochemistry laboratory, cold chemistry lab (non-radioactive chemistry area), and physics and electronics labs provide the necessary support for translational research.
- **CT.** As essential to translational imaging research, the following CT resources are dedicated to researchers:
 - A 16-slice Siemens CT scanner. Several research software packages are licensed to the system for lung imaging, musculoskeletal imaging, perfusion, and virtual colonoscopy evaluation. This scanner is used for basic, translational, and clinical trials research with CT imaging. A 2500 square foot CT imaging research facility supports the efforts of a Biomedical Research Partnership (BRP) project. Directly opposite the computer facility is the Environmental Health Sciences Research Center exposure chamber facility with associated pulmonary function lab.
 - 64-slice Sensation MDCT scanner with 0.30s rotation time fitted with a newly designed Straton X-ray Tube. With help from Siemens, this system has been modified to allow movement between an internal and external cardiac gating mode by flipping a switch within the scanner. In turn, the gate signal is derived from our custom-built physiologic monitoring system. An additional mode of respiratory gating has been created to allow slower pitches down to 0.1, permitting retrospective respiratory gating protocols and incremental stepping of the table. For the next 6 years, Siemens will maintain the CT research facility at pre-beta, state-of-the-art levels.
 - The following equipment is also available: an Xe gas re-breathing delivery system; a high pressure Med Rad contrast injector; a

- bronchoscopy cart; several high-end animal and human respirators; a mobile digital fluoroscopy unit allowing catheterization procedures in the scanner, and human and animal preparation suites.
- **Nuclear Imaging**
 - The Nuclear Medicine clinic has over 6,000 square feet of space with 1 Siemens Diacam gamma camera, 1 Siemens LEM mobile gamma camera, 1 Siemens whole-body dual gamma camera system, 3 Siemens dual detector SPECT systems (one with profile attenuation correction option) and 1 GE dual detector Hawkeye SPECT/CT system. A complete software system for image analysis, archiving and presentation integrates the clinical, translational, and basic research imaging.
 - A high speed autoradiography (Typhoon) system is used for validation of nuclear imaging techniques with reusable exposure plates and resolution of 250 microns. System is capable of measuring both gamma and beta radiation.
- **Ultrasound.** A large variety of state-of-the-art 2D+time and 3D+time ultrasound imaging scanners is available for clinical as well as research purposes.
- **Optical Imaging**
 - The Iowa Comprehensive Lung Imaging Center (I-CLIC) facility has developed a high-resolution microscopy imaging system integrated with a vibrating microtome for acquiring images of excised lung tissue.
 - A large scale digital cell analysis system was developed to facilitate real-time imaging of living cells under controlled stress conditions. The system consists of a computer-controlled microscope and a moving support table.

Strengths, Weaknesses and Opportunities

1. Cross-talk between relevant groups is still limited. This is mainly caused by the absence of a common “home.”
2. Physicians working in the more specialized fields of medicine have not been made fully aware of the improved capabilities of imaging available in other medical specializations. Consequently, common medical imaging and image analysis needs are not identified or understood among clinicians.

3. While medical imaging researchers are, to some extent, cross-fertilizing individual medical specialties by identifying common needs, such cross-fertilization is not systematic.
4. Even when physicians are fully aware of the available technology, utilization may be difficult because of technological obstacles, including, but not limited to: lack of data-accessing and data-sharing capabilities, difficulties in utilizing available single-purpose quantitative medical image analysis software, the practical impossibilities of modifying existing analysis software to fulfill even slightly different tasks, and non-transparency of the reported results.

The development of a strong Clinical Trials Institute of the type proposed in this report will result in new methods for animal and/or human imaging, quantitative analysis and its use in epidemiologic and clinical trials, and effective translation of research results obtained under controlled conditions to clinical medicine.

6. **Center described by Dr. Gary Hunninghake in Department of Medicine**

Overall Summary and Recommendations

Significant reorganization of the clinical and translational research and training infrastructure is essential for the survival of the University of Iowa as a premier Institution for Biomedical Research. The NIH Roadmap has mandated a new emphasis on bench to bedside research coupled with mechanisms to implement these studies into patient care in the community. It is expected that this research will be interdisciplinary and involve multiple Colleges within a research community. Therefore, it is mandatory that an Institute for Clinical and Translational Research is created which can bring multiple disciplines together to achieve these goals. This effort must be supported by significant Institutional resources and space and be empowered to carry out the mission of the Institute to improve research and training related to clinical and translational research at the University of Iowa.

Summary

- Much of the clinical and research infrastructure for clinical and translational research at the University of Iowa either does not exist or is not well designed to facilitate clinical studies.

- There is no integration of training programs for clinical and translational research.
- There is little or no structure to facilitate development of faculty and trainees who wish to conduct clinical and translational research.
- There are no uniform policies that guide the design, budgeting, and implementation of industry supported trials. Nor is there space (inpatient or outpatient) that directly supports these studies.
- Bioinformatics necessary to support clinical research is lacking.
- There are few mechanisms to stimulate interdisciplinary and intercollegial research programs.
- There are few mechanisms to foster partnerships and build trust with community physicians and include them in our clinical research enterprise.
- There are few mechanisms that allow for follow-up health care when a clinical trial or treatment ends.
- Expectation should be set across the entire research community that study results and outcomes should be shared with research participants and the larger community promptly and consistently.
- The new NIH roadmap puts increased emphasis on clinical and translational research and training. The infrastructure for this research and training will be supported, in part, by a new NIH CTSA grant that will replace the current GCRC and NCRR K- and T- awards. This grant requires a home (Department, Center, or Institute) for clinical research and training. It also mandates significant Institutional support and that the approach to research and training cross disciplinary and Collegiate lines and involve the community.

Recommendations

- The mission of the Institute for Clinical and Translational Research should be broadly related to clinical and translational research and training and include community involvement. It will require significant institutional and state resources and space. The Institute for Clinical and Translational Research and must be empowered to create change necessary for the clinical and translational research mission of the University of Iowa. To function in an optimal manner, the functions of the Institute will need to be broader than those proposed in the NIH CTSA grant. The mission of the Institute should include:
 1. Serving as the home for the functions of the CTSA.
 2. Integrating clinical and translational research training.

3. Integrating functions that support clinical and translational research, including regulatory support and drug development, essential research core support, pilot grants, and informational technology.
4. Providing an academic home and supportive environment for faculty across the university interested in clinical and translational research, including support for career development.
5. Serving as the engine to bridge basic and clinical research, and to bring these discoveries to Iowa communities.
6. Serving as the engine to develop multidisciplinary research and training programs.
7. Developing partnerships with industry for research.
8. Developing innovative programs to educate the community and to involve them in education and research programs focused on clinical and translational research.

7. Health Services Research Center

Center for Research in the Implementation of Innovative Strategies in Practice (CRIISP)

CRIISP was established in June 2004 through a \$3.6 million award from the Department of Veterans Affairs (VA) as a Center of Excellence in health services research. CRIISP's goals are to: 1) advance understanding of fundamental barriers to the adoption of evidence-based practices; and 2) test novel interventions to improve quality and costs in a variety of practice settings. CRIISP represents a close partnership between the VA and health services research programs at UI in Medicine, Public Health, Nursing, and Public Policy. Projects are designed by interdisciplinary teams, incorporate a spectrum of quantitative and qualitative methods, and emphasize clinical conditions for which there is both evidence to achieve a national consensus regarding best practices and clearly demonstrated gaps between evidence and practice. In addition to developing innovative research, CRIISP actively supports the career development of junior investigators through mentoring by Senior Scientists and research seminars. CRIISP investigators currently hold 6 career development awards (from the VA, NIH, and Robert Wood Johnson Foundation) and are principal investigators on 10 investigator-initiated research awards from the VA, NIH, and AHRQ. Lastly, CRIISP has funded postdoctoral fellowship training programs for physicians and PhD scientists that support 6 positions.

Strengths and Opportunities:

- ◆ Strong, critical mass of VA and UI investigators and methodologists with structured process for facilitating development of new proposals;
- ◆ Close partnership between the VA and UI and seamless interface;
- ◆ Increasing focus by NIH on implementing evidence into clinical practice and on building community partnerships;
- ◆ Development of partnerships with health care systems and insurers to implement strategies for improving quality and efficiency;
- ◆ Development of methodological cores in key areas (e.g., health economics, behavioral health) to support research by other UI faculty;
- ◆ Synergize with Institute for Clinical Practice to promote community-based research to improve practice;
- ◆

Challenges:

- ◆ Difficulty in accessing minority populations, which is essential for NIH-funded patient-oriented research;
- ◆ Need for integrated clinical information system with electronic medical record, clinical decision support, and easy to access clinical data;
- ◆ Relative lack of senior physician health services investigators to mentor junior faculty;
- ◆ Lack of a strong partnership between UI Healthcare and the State's major private insurer to support collaborative health services research mobilize large populations of patients;
- ◆ Physical space limitations and inability to house all CRIISP investigators together in common space;
- ◆ Difficulties in gaining IRB approval for studies seeking to evaluate and improve clinical care processes.

B. Summary of Survey to Faculty Conducting Clinical Research
(See Appendix I for a more detailed report of the survey.)

A comprehensive user survey was developed and distributed to all faculty across the Health Sciences Colleges as well as relevant faculty in other UI colleges. There were 136 responses representing 10 colleges, 45 departments and 36 divisions. The goal of the survey was to ascertain the current level of clinical trials/research activity among faculty, identify the perceived problems interfering with successful conduct of clinical research, and assess receptivity to a more

centralized approach to facilitating clinical trials at UI. One notable finding from the survey was the revelation that an estimated \$4.2M in funding was lost within the past two years for various reasons including declining the terms of the study, early withdrawal of the study, delays in UI procedures leading to problems in starting studies and recruiting subjects. Highlights of the survey included:

1. Priority rankings of areas where improvements could be made to facilitate clinical trials/research:
 - More rapid IRB review
 - Administrative assistance
 - Availability of study coordinators/PAs
 - Subject identification and recruitment
 - Less bureaucracy internally
 - Dedicated outpatient space
 - Separate research database
 - Fairer pricing on clinical testing
 - Dedicated inpatient space

2. Priority ranking of reasons for not doing clinical research:
 - Lack of resources
 - Insufficient time
 - Lack of collaborators

3. Priority ranking of most appealing elements of a centralized clinical research support service:
 - Assistance in writing IRB applications and documents
 - Proposal preparation
 - Data management
 - Study coordination
 - Subject recruitment assistance
 - Budget administration
 - Safety monitoring
 - Laboratory support
 - Outpatient facilities
 - Protocol design
 - Inpatient facilities
 - Nutritional support
 - Others – training, marketing, access to minority populations, access to core facilities, less administrative hassles, seed funds to help develop clinical investigators, facilitate collaboration

4. Advantages of establishing off-site facilities –
 - Convenience for subjects
 - Access to larger and more diverse populations
 - Easier for outpatient research
5. Disadvantages of establishing off-site facilities –
 - Investigator inconvenience
 - Additional costs
 - Additional bureaucracy
 - Already have access to established off site facilities
6. Reasons (not ranked) cited for concerns about a centralized clinical research support program:
 - Self sufficient already
 - Too much bureaucracy
 - Concerns about diversion of resources
 - Lack confidence in quality
 - Research too individual to be supported by a centralized, comprehensive center
 - Perceive competitive or duplicative with GCRC or CTO
 - Lack of investigator control

C. Status of Information Technology (IT) Planning for Electronic Medical Record and Clinical Research

Lee Carmen, Director of UIHC IT provided the Task Force with an in-depth review of the current status of UIHC's IT capabilities and delineated the long term plan for improving IT. Clearly much has been accomplished and much remains to be done, with an estimated longitudinal time frame for this phase of fully implementing an electronic medical record and physician order entry system through the medical center extending out beyond 2010. Although there is recognition of the importance of incorporating unique IT capabilities to support clinical research, urgent needs in area of patient records and billing across the medical center has kept the staff highly focused in these areas thus far. Sophisticated bioinformatics capability which would include desktop access for investigators to the patient database for identification of potential study subjects was viewed as a very high priority. Although there are HIPAA issues associated with this type of patient identification, several examples of other centers with this capacity were mentioned. The Task Force invited consultants from Centers where a strong clinical research IT infrastructure is in place – e.g. Mayo Clinic, Vanderbilt, Mayo Jacksonville – and conducted site visits to places perceived as having moved forward aggressively along these lines. Although there are centers

where the IT is perceived to be of the level desired, there does not appear to be a system that can be purchased that easily links with existing state of the art hospital medical record systems. Rather, each center appears to have developed the specifications locally and then sought to build its own system.

Cost issues are central to discussion of an adequate IT infrastructure as current estimates to fully implement the current UIHC IT strategic plan are approximately \$60M and have not fully incorporated clinical research needs. There was a clear consensus to connect current IT implementation and planning with a strategic planning process focused on the IT needs for clinical research. An initial recommendation was that a few active clinical researchers be identified who would be willing to spend a defined amount of time (preferably reimbursed) with IT staff to clearly articulate the types of systems and capabilities that will be needed.

At this point, there is clear recognition of the critical importance of a high level IT system capable of fully supporting clinical research, but much needs to be done in terms of modifying the current plan and determining the funding levels and mechanism to achieve these goals. It is also recognized that this will, by necessity, be incremental as the current timeline illustrates.

D. External Assessment

Institutions Sampled:

Columbia University
UIHC Facility Planning Consultants
Washington University of St. Louis
UI Computer Consultants
University of North Carolina
Mayo Clinic

V. Infrastructure Elements for Clinical/Translational Research

A. Institutional Review Board(s) (IRB)

UI Institutional Review Boards & Human Subjects Office (HSO)

Background:

The required function of UI's IRBs is to protect the rights and welfare of human subjects in research. In doing so, an IRB must follow federal regulations as set forth in 45 CFR Part 46 and 21 CFR Parts 50 and 56 as well as guidelines from

federal agencies. UI has two IRBs (IRB-01, a biomedical IRB, and IRB-02, a behavioral and social science IRB) engaged in performing these reviews.

The Human Subjects Office provides staff and regulatory support for the IRBs. Staff perform a variety of tasks including: processing applications; initial review of applications for complete information; review of consent forms to assure that they contain all required elements and language consistent with template materials; scheduling and administrative support of meetings; initial review of adverse experience forms, modifications, and expedited review applications; and post-approval monitoring. The Human Subjects Office serves as UI's primary liaison with federal regulatory agencies, private accrediting bodies, and collaborating institutions including the Iowa City VAMC.

The Human Subjects Office serves an important coordinating function with other institutional committees involved in reviewing human subject research. This role has grown as there has been increasing pressure both nationally and internally to recognize that IRB review is only one component, albeit a pivotal component, of a larger Human Research Protections Program (HRPP). The HRPP includes the IRB in addition to other related, but independent, committees and units within the institution that address various facets of the protection of human subjects. At UI, these include the Medical Radiation Protection Committee, Institutional Biosafety Committee, Pharmacy & Therapeutics Committee, Conflict of Interest in Research Committee, Cancer Center Protocol Review and Monitoring Committee, and the General Clinical Research Center. The HSO and CTO share information in order to encourage investigators to submit IRB applications and sponsor contracts for parallel, rather than sequential, processing in order to facilitate more rapid initiation of studies. Although these committees are not components of the IRB, coordination is necessary and the HSO has accepted this role at the request of the other committees and UI administration. The HSO has also taken on the responsibility of reviewing research activities for compliance with the research components of HIPAA. This includes assuring appropriate patient disclosure authorizations when required under the Act as well as providing waivers of authorization when appropriate regulatory criteria are met.

Model Institutions:

There are two critical components to model institutions regarding IRB functions. First, and foremost, is compliance with regulations and the ethical principles embodied in those regulations. The importance of compliance has been in the national spotlight for the past 7 years as several premier institutions have gone through regulatory shutdowns and other penalties costing valuable time and millions of dollars to remedy. These actions continue at this time. In the area of regulatory compliance and the application of sound ethical principles to the review and conduct of human subject research, UI is a recognized national leader. As the first university in the nation to become fully accredited by the Association

for the Accreditation of Human Research Protection Programs (AAHRPP), UI receives a regular stream of questions from peer institutions around the country. Staff are frequently asked to speak at meetings and consult with other institutions attempting to establish a program that meets the same standard of compliance. Institutions to receive accreditation subsequent to UI include, for example, Washington University, Johns Hopkins, Massachusetts General Hospital, University of Minnesota, Indiana University, and Vanderbilt University. Informal surveys of other peer research institutions at national meetings indicate that nearly all are currently working toward the goal of accreditation.

The second component to achieving status as a model IRB program is adequate human and financial resources. This involves both a) staffing for the institution's human subjects administrative program and b) faculty membership on IRBs. In surveys of peer institutions, UI consistently ranks very low in staffing compared to the research workload. In fact, a recent comparison with other Big Ten institutions demonstrated that doubling the UI HSO staff would still place us near the bottom of this group.

UI's biomedical IRB (IRB-01) currently meets six times monthly. Two of these six meetings are devoted to continuing review, and four meetings focus on reviewing new applications. The number of meetings and the number of protocols reviewed at each meeting are limited by the number of faculty (primarily physicians) who are qualified to serve as primary reviewers of new applications and who are able to attend complete meetings. Even when a quorum (required by regulation) is met for a meeting, it often must end early because a quorum is lost due to other commitments by members. The HSO leadership has always worked to identify qualified alternates so that meetings and reviews can occur without unduly burdening any individual member. However, requirements that alternates also be appropriately trained and experienced to conduct in-depth reviews continues to present a membership challenge, as alternates face the same time pressures as primary members. Many comparable institutions have 4-6 biomedical IRBs each of which may meet as often as weekly.

A model institution which has approximately the same volume of active studies as UI is Vanderbilt University. The IRB/HSO budget at Vanderbilt is 3-4 times that currently spent at UI.

Issues for the IRB to Address:

The key issue to be addressed is how to accelerate the IRB review process while still maintaining the current level of compliance and ethics in the review process. The need for more staff and IRB members has been recognized for several years. The institution has dramatically increased staff over the past 8 years, but still falls

below the level of support seen at peer institutions and growth has not kept pace with the increasing regulatory burden imposed by federal agencies.

The Carver College of Medicine and the VP Research staff have recognized the challenge of adding and keeping faculty members on the IRB for several years. A variety of techniques, including providing compensation to departments, has been used to create incentives for service on the IRB. However, increasing pressures, particularly clinical pressures on physicians, continues to make IRB involvement a challenge.

An additional challenge regarding corporate-sponsored clinical trials has been a growing trend by pharmaceutical companies to attempt to turn the informed consent document into a contract between the company and the subject. This manifests itself in the form of companies dictating consent form wording, often in direct contrast to clear, written guidance from regulatory agencies requiring that the consent not contain any exculpatory language through which the subject relinquishes his/her rights. The implementation of HIPAA and requirements for HIPAA written authorizations has also compounded problems. This has increased HSO and CTO staff workload and often results in delays in initiating trials.

Progress and Ongoing Activities:

As referenced above, UI has been adding staff to the Human Subjects Office for the past several years. This includes 2 staff who have been hired over the past two years through an IRB-enhancement grant from the NIH. Subsequent years of support are the responsibility of the institution. Two additional staff have been hired this summer. The staff/volume ratio still places UI at the bottom of the Big Ten, but we are much closer to the “pack” than in the past.

In September 2004, the Human Subjects Office rolled-out a new electronic IRB system known as HawkIRB. This system moves all aspects of the IRB process into the electronic world. The system has been well-received by faculty, staff, and students. This has enabled the HSO to reassign staff from performing simple clerical tasks to assisting in more substantive reviews of application materials. Continuing review applications were added to the electronic process in June 2005.

The College of Medicine has recently made significant additional efforts to increase the number of physicians on the IRB. These efforts are succeeding. Beginning in November 2005, more physician members will be present at each IRB meeting which should enable the IRB to review more protocols at each meeting.

UI has signed an agreement with an external, AAHRPP-accredited commercial IRB (the Western IRB) for the review of industry-sponsored and -initiated multicenter clinical trials. Beginning November 1, 2005, new industry-sponsored studies go to the WIRB. The fees associated with this review will be charged to the sponsor. Also, one staff position has been added to the Human Subjects Office to coordinate submissions to the commercial IRB. This is necessary because pre-submission coordination and approval by any of the necessary ancillary committees listed above must occur prior to submission to the commercial IRB. The cost of this position will be recovered through a fee to be paid by the sponsor. It is anticipated that the out-sourcing of these IRB reviews to a commercial entity will have a substantial impact on IRB/HSO turnaround which will become more apparent as existing active studies close and all industry-sponsored and -initiated studies are handled through an outside IRB. While using a commercial IRB may address the problem we face regarding recruitment of UI faculty to serve on the IRB, it should not be viewed as a “model practice.” The great majority of leading research institutions still conduct all IRB reviews through internal IRBs.

UI also uses a central IRB (CIRB) for the review of Phase III NCI-sponsored clinical trials. The NCI established the CIRB in 2002 for purposes of reviewing their Phase III trials. UI was one of the first institutions in the nation to join this program. The program has had some difficulty since its inception, however, the NCI recently contracted with an AAHRPP-accredited commercial IRB to operate this program. We anticipate that this program will be more efficient and responsive as a result of this contract.

Recommendations:

An IRB program which is both in compliance and responsive to research timing is essential for a successful clinical research program. It should be a priority of the institution to continue developing and supporting mechanisms by which these goals are accomplished. Both financial and programmatic support is necessary from multiple academic and administrative units within UI for these efforts to succeed. Short-term resources have been identified to provide the added funding necessary to support the IRB/HSO enhancements recently implemented.

Specific Recommendations: In order to sustain these initiatives, a recurring commitment of approximately \$200,000 per year is needed to create and support an industry IRB and to provide increased staffing.

B. Subject and Minority Recruiting

Background:

- UI-based researchers are at a distinct disadvantage relative to independent clinical researchers and clinical trials groups in studies (especially those that rely on competitive enrollment) for a number of reasons:
 - Cost of infrastructure
 - Overhead expenditures, especially when come out of trial funds
 - UI-specific requirements (e.g. IRB) for trials
 - Delay in approval
 - Additional requirements for participation, consent, advertising, etc.
 - Ease of research subject participation
 - Location
 - Parking
- Enhanced subject recruitment is the best way to increase cost-efficiency of study (same fixed cost, progressively decreasing incremental costs)
- NIH and other federally-funded studies (whether multi-center or not) mandate inclusion of minorities as clinical research subjects:
 - <http://www.nihtraining.com/ohsrsite/info/sheet11.html>
 - See attached Guidelines
 - The National Institutes of Health (NIH) has established guidelines for research involving human subjects, including clinical trials, supported by the NIH. . . The guidelines define clinical research as any NIH-supported biomedical and behavioral research involving human subjects. . .
 - The guidelines are intended to ensure that all NIH-supported biomedical and behavioral research involving human subjects is carried out in a manner sufficient to elicit information about individuals of both genders and the diverse racial and ethnic groups and, in the case of clinical trials, to examine differential effects on such groups. . .
 - It is the policy of NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center (IC) director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. .
 - NIH funding components will not award any grant, cooperative agreement, or contract or support any intramural project that does not comply with this policy.

- The State of Iowa has relatively low racial/ethnic diversity
 - Iowa is one of the least diverse states (5th highest percentage of “White” in 2000 census).
 - There has been growth in minority populations over the past two decades.
 - In 1960, minorities constituted 1% of the population of Iowa
 - By 1990 minority percentage had grown to 3.4%
 - In 2000 minorities constituted over 8% of the population (2.1% African-American, 0.3% American Indian, 1.3% Asian/Pacific Islander, 1.3% other, and 1.1% two or more races; in addition, 2.8% identify themselves as Hispanic or Latino)
 - Regional variation is substantial: Quad Cities (9% African-American), Waterloo (13% African-American) and Muscatine County (12% Hispanic) have significant minority populations.
- Needs to interface with IT, especially in regards to recruitment of UIHC and Outreach patient populations
 - Blanket consent for all patients to agree to participate in research activities (at least for registry/recruitment, potentially biologic sample donation) unless specific “opt-out”.
- Clinical investigators need assistance in:
 - Identifying suitable populations for clinical research studies
 - Recruiting subjects rapidly, efficiently, and in a cost-effective manner
 - Advertising/marketing their studies to relevant research subject populations
 - Enhanced recruitment of minority subjects

General Recommendations:

- Help researchers with their subject recruitment
 - Within UIHC and outreach patient populations
 - Regionally
 - Nationally (in some specific cases)
- Lobby NIH to take into account demographics of specific research sites when mandating study populations
- Work towards blanket consent for UIHC and Outreach patients to participate in research activities (registry, database)

Specific Recommendations:

- Programmatic
 - Create office dedicated to clinical research subject recruitment
 - Available “recruiters” for patient interactions in clinics

- Infrastructure:
 - Outreach in regions with high minority populations
 - Identify appropriate media for advertising: newspapers, radio or television stations, etc.
 - Catchment area for clinical research generally under 100 miles
- Financing:
 - Should be substantially covered by overhead
 - Could have fee-for-service branch for industry-sponsored studies
- Governance issues:
 - Like Clinical Trials Office, could be under unified Clinical Research infrastructure

NIH Subject Recruitment

<http://www.nihtraining.com/ohsr/site/info/sheet11.html>

OHSR Information Sheets/Forms

[Back to OHSR Information Sheet Menu](#)

Sheet 11 INCLUSION OF WOMEN AND MINORITIES IN STUDY POPULATIONS GUIDANCE FOR IRBs AND PRINCIPAL INVESTIGATORS

The principle of Justice as outlined in the Belmont Report requires that research subjects be treated fairly. For example, subjects should be carefully and equitably chosen to insure that certain individuals, or classes of individuals are not systematically selected or excluded, unless there are scientifically or ethically valid reasons for doing so.

Consistent with this principle, the NIH Revitalization Act of 1993 legislated that special attention be given to the inclusion of women and minority groups in all clinical research conducted or supported by the NIH.

On March 9, 1994, the NIH issued Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research (copy available from OHSR). These Guidelines focus on the requirement for appropriate representation of women and minority groups in all NIH-supported or-conducted clinical research, particularly in Phase III clinical trials. On August 2, 2000, the NIH updated the Guidelines to reflect the requirement to include in the research plan of Phase III trials a description of how valid analyses will be conducted to detect significant differences in intervention effect among different populations. To review the update, see <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html>. Even though most Intramural Research Program (IRP) clinical research does not consist of Phase III clinical trials, the Guidelines nevertheless direct that all IRP clinical research projects should strive to recruit and enroll the most diverse study population consistent with the purpose of the project.

The Guidelines contain the following policy statements:

"It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute or Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances may be made by the Director, NIH, upon the recommendation of an Institute/Center Director based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. All NIH-supported biomedical and behavioral research involving human subjects is defined as clinical research. This policy applies to research subjects of all ages."

"The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. The research plan should describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection for such subjects. Such a plan should contain a description of the proposed outreach programs for recruiting women and minorities as participants."

NIH Intramural Research Program Principal Investigators (PIs) and Institutional Review Boards (IRBs) implement these Guidelines as follows:

1. Design of protocols: In their clinical research protocols, PIs must include in the protocol's headed section entitled Human Subject Protections:
 - a. the rationale for the research subject selection based on a review of the gender and population category(ies) at risk for the disease or condition being studied;
 - b. strategies and procedures for recruiting the subject population selected in (a) above, and
 - c. justification for exclusions, if any, of women and/or individuals from particular population categories.

<http://grants2.nih.gov/grants/policy/emprograms/overview/women-and-mi.htm>

INCLUSION OF WOMEN AND MINORITIES AS SUBJECTS IN CLINICAL RESEARCH - 96-04

The National Institutes of Health (NIH) has established guidelines on the inclusion of women and minorities and their subpopulations in research involving human subjects, including clinical trials, supported by the NIH, as required in the NIH Revitalization Act of 1993. The following are excerpts from the Notice of the "NIH Guidelines on the Inclusion of Women and Minorities as Subjects in

Clinical Research" that was published as a separate Part VIII in the Federal Register of March 28, 1994 (59 FR 14508- 14513).

The guidelines describe the requirement for the inclusion of women and members of minority groups and their subpopulations in clinical research, including clinical trials, supported by the National Institutes of Health (NIH). The guidelines define clinical research as any NIH-supported biomedical and behavioral research involving human subjects.

Since a primary aim of biomedical and behavioral research is to provide scientific evidence leading to a change in health policy or a standard of care, it is imperative to determine whether the intervention or therapy being studied affects women or men or members of minority groups and their subpopulations differently. To this end, the guidelines are intended to ensure that all NIH-supported biomedical and behavioral research involving human subjects is carried out in a manner sufficient to elicit information about individuals of both genders and the diverse racial and ethnic groups and, in the case of clinical trials, to examine differential effects on such groups. Increased attention, therefore, must be given to gender, race, and ethnicity in earlier stages of research so that informed design of Phase III clinical trials can occur.

Policy

A. Research Involving Human Subjects

It is the policy of NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center (IC) director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances may be made by the Director, NIH, upon the recommendation of an IC director based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. All NIH-supported biomedical and behavioral research involving human subjects is defined as clinical research. This policy applies to research subjects of all ages.

The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. The research plan should describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection of such subjects. The plan should contain a description of the proposed outreach programs for recruiting women and minorities as participants.

B. Clinical Trials

Under the statute, when a Phase III clinical trial is proposed, evidence must be reviewed to show whether or not clinically important gender or race/ ethnicity differences in the intervention effect are to be expected. This evidence may include, but is not limited to, data

derived from prior animal studies, clinical observations, metabolic studies, genetic studies, pharmacology studies, and observational, natural history, epidemiology, and other relevant studies.

As such, investigators must consider the following when planning a Phase III clinical trial for NIH support.

- If the data from prior studies strongly indicate the existence of significant differences of clinical or public health importance in intervention effect among subgroups (gender and/or racial/ethnic subgroups), the primary question(s) to be addressed by the proposed Phase III trial and the design of that trial must specifically accommodate this. For example, if men and women are thought to respond differently to an intervention, then the Phase III trial must be designed to answer two separate primary questions, one for men and the other for women, with adequate sample size for each.
- If the data from prior studies strongly support no significant differences of clinical or public health importance in intervention effect between subgroups, then gender or race/ethnicity will not be required as subject selection criteria. However, the inclusion of gender or racial/ethnic subgroups is still strongly encouraged.
- If the data from prior studies neither support strongly nor negate strongly the existence of significant differences of clinical or public health importance in intervention effect between subgroups, then the Phase III trial will be required to include sufficient and appropriate entry of gender and racial/ethnic subgroups, so that valid analysis of the intervention effect in subgroups can be performed. However, the trial will not be required to provide high statistical power for each subgroup.

Cost is not an acceptable reason for exclusion of women and minorities from clinical trials.

C. Funding

NIH funding components will not award any grant, cooperative agreement, or contract or support any intramural project that does not comply with this policy. For research awards that are covered by this policy, awardees will report annually on enrollment of women and men, and on the race and ethnicity of research participants.

Other References

To assist investigators and potential study participants, NIH staff have prepared two additional documents: (1) the "NIH Outreach Notebook On the Inclusion of Women and Minorities in Biomedical and Behavioral Research" and (2) "Questions and Answers Concerning the 1994 NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research." The notebook addresses both recruitment and retention of women and minorities in clinical studies, provides relevant references and case studies, and discusses ethical issues. It is not intended as a definitive text on this subject, but should assist investigators in their consideration of an appropriate plan for recruiting and retaining participants in clinical studies.

All investigators proposing research involving human subjects should read the NIH Guidelines, the Outreach Notebook, and the Questions and Answers documents. Investigators may obtain copies from the sources listed below or from NIH staff listed in announcements to which the policy applies.

C. Faculty Development

Education and Faculty Development in Clinical Research

Faculty, fellows, residents, and graduate students need to have an opportunity to develop knowledge and skills in clinical research. There are academic programs that provide an academic structure and credential to the training and prepare the trainee for the methodological basis for clinical research. This spectrum of educational opportunities is consistent with the NIH Roadmap program, Re-engineering the Clinical Research Enterprise. These programs are open to a broad range of clinical areas, including medicine, nursing, dentistry, pharmacy and other allied health professions and include a wide array of research areas, such as biostatistics, behavioral medicine, clinical trials, and epidemiology.

Educational Programs

The Graduate Program in Translational Biomedical Research

<http://www.medicine.uiowa.edu/gptbr/>

The Graduate Program in Translational Biomedical Research (GPTBR) is an interdisciplinary program leading to the training of clinician scientists in hypothesis-oriented patient-based research. Currently, most scientific training leads to an individual becoming skilled in a narrow research area. More programs are needed that instruct investigators on how to apply a basic scientific knowledge to patient-based research. This program is designed to meet this need. The GPTBR consists of one year of course work and two to three years of mentor-supervised patient-based research. Trainees in the program can earn either an MS or PhD. The GPTBR has considerable flexibility in both the background of the students accepted and the type of research these students select. All students take background courses in epidemiology, study design, and statistics. They will choose advanced courses in basic sciences that pertain to their individual plan of study and area of research. The intellectual environment of the program is enriched by a seminar series, courses in ethics, visiting speakers, and a yearly retreat. The student may choose to participate in research in any of the allied health sciences. Scholars in the program may earn a M.S. or Ph.D. degree. Research opportunities encompass the following areas: mechanisms of disease, new clinical insights into diagnosis, or natural history of disease, objective assessment and outcome of therapeutic intervention, medical informatics, development of new therapeutics, and gene based medicine.

Iowa Scholars in Clinical Investigation Program

<http://www.medicine.uiowa.edu/isci/>

The Iowa Scholars in Clinical Investigation (ISCI) Program is a two-year interdisciplinary program designed to prepare post-doctoral fellows and junior

faculty from the Colleges of Medicine, Nursing, Dentistry, and Pharmacy for careers in clinical research through the provision of a structured didactic curriculum in research methods and a mentored research experience. The program is supported by the Carver College of Medicine and a NIH K30 Clinical Research Curriculum Award. Scholars in the program may earn a MS or MPH degree, or a certificate in clinical investigation with the expectation that all scholars will become independent, funded investigators. An important component of the ISCI curriculum is a bi-weekly Seminar in Clinical Research that allows Scholars to deliver “works-in-progress” presentations of their ongoing projects. This seminar is designed to provide constructive feedback to the presenting Scholar and teach principles of critical review by senior faculty. The Seminar also includes several sessions that are devoted to methodological journals clubs reviewing important topics in clinical research and mock study sections. To date, the ISCI Program has enrolled a total of 42 Scholars in four cohorts (entering classes of 2001, 2002, 2003, and 2004), including 33 Scholars from Medicine and 9 from other health sciences colleges. This exemplifies UI’s success in recruiting scholars into this type of program.

Certificate In Clinical Investigation

The purpose of the certificate is to provide methodological training and applied patient-oriented research skills to clinicians to prepare them for a successful career in academic medicine. Clinicians who complete the one-year certificate program will receive a broad introduction to key aspects of clinical research methods, including basic study design, methodology, and analytic strategies in clinical research. They will also actively participate in clinical research projects of mentor(s), design and conduct a clinical research project, and prepare dissemination of research (manuscript and/or professional presentation).

Masters of Science Degree In Clinical Investigation

<http://www.medicine.uiowa.edu/isci/curriculum/MSin%20CI.htm>

This multidisciplinary program is coordinated by the Division of General Medicine of the department of Internal Medicine in the Carver College of Medicine (CCOM) and the Department of Epidemiology in the College of Public Health (COPH). The MS degree in Clinical Investigation provides proficiency in critical topics such as biostatistics, epidemiology, research ethics, and academic survival skills required of a successful clinical researcher. The degree allows the student to establish a core of methods and structured mentorship in three components:

- Patient-oriented research – investigation into therapeutic interventions, clinical trials, and testing of new technologies.
- Clinical epidemiology and behavioral research – investigation in patient populations defining risk and prognosis; classification and staging of disease; factors related to compliance and adherence to treatment; sociocultural determinants of health.

- Outcomes and health services research – investigation into the outcomes and cost of health care interventions; development of a comprehensive framework of measures, including health-related quality of life; evaluation of the organization and delivery of care by health systems and providers; and development and implementation of clinical guidelines to improve patient care and outcomes.

Masters in Clinical Investigation Focus

This degree, offered by the College of Public Health, is for those clinical professional students who desire to learn the fundamental concepts and methods of clinical investigation. The degree provides the methodological skills and knowledge and the practical experience associated with the clinical setting. The focus of the degree is to provide an overview of clinical research methods and examples. Scholars learn the methods of clinical trials and explore areas of diagnostic assessment, prognostic factor evaluation, cost-effectiveness analysis and outcomes research. Scholars choose methodological or clinical emphasis areas in which they will do a practicum. The program is designed to train health professionals to adapt clinical research methods into clinical practice.

Masters of Science Degree Program in Epidemiology

http://www.public-health.uiowa.edu/epi/prosp_students/ms_prog_desc.html

This program, the traditional educational training in epidemiology, is designed to prepare trainees for professional career opportunities in which specialized knowledge of epidemiologic methods and analytic techniques are useful. Scholars establish a foundation in epidemiological and statistical methods and develop an area of interest. While this program has a population-based research focus, scholars can also focus the program toward clinical epidemiology and outcomes research.

Other Masters of Public Health Degrees

<http://www.public-health.uiowa.edu/mph/>

The College of Public Health offers other MPH Programs that may be of interest to BIRCWH trainees. The MPH Combined Degree Programs include a DVM/MPH Combined Degree Program, a MD/MPH Combined Degree Program and a MSN/MPH Combined Degree Program. The MD/MPH Program is offered in conjunction with the Carver College of Medicine. This program provides graduates with expanded career opportunities and allows professionals to apply the principles of both medicine and public health in their practice. The student can pursue a MPH degree in a subtrack or focus area. The Focus areas offer students the opportunity to gain knowledge in important areas of public health that do not fit directly into the core areas of public health. Course work may be drawn exclusively from departments in the College of Public Health or from other

academic programs that provide public health training. These include General, Aging Studies, Clinical Investigation, Global Health, Maternal, Child, and Family Health, and Nutrition and Exercise. The BIRCWH trainee can also design their own focus in Women's Health.

Clinical Pharmaceutical Sciences

<http://www.pharmacy.uiowa.edu/CAP/pages/CPS/index.htm>

The Clinical Pharmaceutical Scientist Program offers Ph.D. training designed for students interested in clinical research. The goal of the program is to advance the science of human pharmacology and therapeutics and to improve the safe, effective and economical use of medications by patients.

The program emphasizes the integration of clinical and basic research. It involves advanced studies of clinical pharmacology, pharmacokinetics, pharmacodynamics, pharmacogenetics and the requirements for regulatory approval of new drugs. The graduate is well prepared to assume a tenure track academic position or career as a clinical research scientist.

Pharmaceutics

<http://www.pharmacy.uiowa.edu/pharmaceutics/>

The Division of Pharmaceutics provides a program of graduate education focused on research and coursework relating to the development, production and characterization of dosage forms, as well as the disposition and action of drugs in the body. Major areas of emphasis include physical and applied pharmaceutics, drug disposition and dynamics, and drug delivery and tissue engineering.

Pharmacology

<http://www.medicine.uiowa.edu/pharmacology/01geninfo.html>

The graduate program provides research opportunities for highly qualified, motivated students in cellular and molecular pharmacology, integrative cardiovascular and autonomic pharmacology, and cellular and integrative neuropharmacology. Research is conducted in laboratories of independent, creative and productive faculty members whose work is published in highly respected, peer-reviewed journals. Important complements to the graduate training program are the active seminar series which brings outstanding scientists from around the country to the department as well as weekly journal clubs, directed by members of the faculty, which meet to present and critique the latest results from the scientific literature in pharmacology.

Microbiology Ph.D. Bioinformatics Subtrack

<http://www.medicine.uiowa.edu/microbiology/educational/bioinformatics.htm>

The emerging field of bioinformatics has promoted a close working relationship between researchers in the life sciences and the computational sciences. The possible uses of bioinformatic technology in the microbiology field are immense.

At UI, many researchers in the Microbiology Department are now using bioinformatics to address questions such as how various microbes alter overall gene expression profiles in host cells, how microbes themselves alter their own gene expression in response to different stimuli and growth conditions, and how various pathogens affect expression of immune response pathways. It has become clear that the availability of more intense bioinformatic training is necessary for meeting the needs of microbiology students interested in bioinformatics. With the recently developed Center for Bioinformatics and Computational Biology at UI (<http://genome.uiowa.edu>), this has now become a possibility. We have therefore initiated a formal subtrack within the Microbiology Ph.D. program that will lead to a Ph.D. in Microbiology with a specialization in Bioinformatics. The goals of the Bioinformatics subtrack will be two-fold:

1. Offer a Microbiology Ph.D. training program involving coursework and Ph.D. thesis research opportunities in bioinformatics and microbiology for those incoming students who already have an interest in computational/computer sciences that would like to apply these interests and skills to microbiology-related topics.
2. Provide students with microbiology/life sciences backgrounds exposure and training in bioinformatics.

General Recommendations

- 1) The Health Sciences Colleges need to recruit new faculty interested in clinical research and clinical trials as a career, not just from participation but also as methodologists and scientists to development new methods, routes of intervention delivery, interventions and measures for outcome evaluation.
- 2) Promotion and retention of faculty interested in clinical research should be fostered by Deans and DEOs.
- 3) Provide an infrastructure to support the design, conduct, and analysis of clinical research.

Specific Recommendations

- 1) Hire faculty interested in biological interventions and statistical methods.
- 2) Support funding of pilot studies for the development and translation of new interventions.
- 3) Support resources and facilities to aid new investigators in the development and execution of clinical research.
- 4) Provide time for educational development in clinical research.
- 5) Provide adequate release time for the development, conduct, monitoring and evaluation of clinical studies.
- 6) Provide a mentoring network for young investigators in the design, conduct and evaluation of clinical research.
- 7) Provide rewards in terms of promotion consideration and monetary incentives for clinical research.

Budget Implications

- 1) Additional faculty positions.
- 2) Funding for release time.
- 3) Clinical science initiative pilot funds.
- 4) Infrastructure support of facilities and staff.
- 5) Grant funding of CTSA/K30/K12s and training grants.

D. Clinical Trials Unit, Including Facilities and Staff Support

Challenges

The current facilities for clinical research at the University of Iowa are outdated and inadequate. While the GCRC provides space for inpatient and outpatient encounters for investigators with peer-reviewed funding, there are significant limitations:

- Current GCRC layout is inefficient (based on a converted inpatient unit) and lacks sufficient rooms for patient interviews, counseling, infusions, blood sampling, EKGs, and phenotyping cores.
- The GCRC lacks space to serve the needs of investigators in terms of space for clinical research support staff, storage of supplies, computer workstations, filing of clinical trial paperwork, and secure storage of drugs. Research coordinators and other staff are often housed quite distant from where research subjects are encountered.
- The GCRC cannot provide full support for clinical trials initiated and funded by industry (of drugs or devices). This is due to lack of space and current NIH regulations.
- There is inadequate climate control, noise abatement and too much vibration for some instrumentation.

Opportunities

The NIH has recently requested applications from institutions under the Roadmap framework for 'Clinical and Translational Science Awards'. These awards will not provide funds for infrastructure, and the NIH has stated that success in an application will depend in part on institutional financial commitment to clinical and translational research. This provides

the UI with an opportunity to invest in clinical trials infrastructure to assist faculty performing clinical research, and also leverage substantial new NIH funding.

General Recommendations

- Clinical research infrastructure (for research subject interactions, phenotyping cores, office space for research coordinators, recruitment core, and storage space) should be centralized where possible to minimize inconvenience for research subjects and inefficiencies for staff.
- Construction of a dedicated facility for interactions with research subjects substantially larger than current GCRC (see specific recommendations below).
- Provision of dedicated office space for research coordinators, recruitment staff, outside monitoring staff, and storage (of clinical trial supplies, equipment, case record forms and drugs). This space should be near to or contiguous with the research subject facility.

Specific Recommendations

Research Subject Facility

- Total space?
- Inpatient rooms (isolation?)
- Interview rooms?
- Infusion Rooms?
- Blood sampling?
- Phenotyping Cores?
- Waiting area?
- Classrooms?
- Nutrition services?

Research Staff Facility

- Offices?
- Storage?
- Meeting/monitoring rooms?
- Recruitment?

E. Budgeting

Development and Research Billing Compliance

Human subjects research carries significant financial obligations for an academic institution. In order to preserve its tax-exempt status, the institution must document a (fair) budget development process that is consistently applied across studies, regardless of funding source. Also, there is tremendous liability involved in billing for clinical services associated with research. Thus, there are pre-award (budget development) and post-award (research billing) financial obligations.

In the results of the Clinical Research Survey (Appendix I) conducted by this Task Force, “finances” and “budget” were mentioned as follows:

- Reasons for declining studies – insufficient time to prepare paperwork (budget); budget too low from sponsor; unable to provide competitive costs for clinical procedures
- Discounts on clinical charges – ranked 10/15 in list of support services that would enhance ability to conduct studies
- Budget development – 63% respondents (researchers) do their own budgets
- Post-award budget management – 34% of respondents indicated “self” as responsible for this
- Budget preparation assistance – 72% of respondents who do not have assistance from their department indicated that they would like help with this
- Budget administration – 38% of respondents indicated that this should be included as a centralized clinical research support function

Pre-Award (Budget Development)

Study budgets should contain costs related to personnel, supplies, clinical tests and procedures, travel, and other expenses. NIH grant applications have budget and justification forms with detailed instructions, and typically, a department provides guidance to a researcher who is submitting a grant application. The information that is often the most difficult to obtain is the cost of various clinical tests and procedures.

For industry-sponsored clinical trials, companies usually propose a budget for the study, and the researcher or his/her support staff should determine all of the study-required expenses and compare them to the reimbursement offered by the sponsor. Unless this is done, the researcher does not really know if the study is financially feasible.

The key to a successful process for budget development is access to the technical and professional rates for tests and procedures and the associated research discount established by UIHC. The UIHC Business Office does provide a standard research discount for tests such as blood tests, routine x-rays, etc., but there is no uniform method for pricing and discounting more complex procedures which have a large professional component. This is especially challenging for an investigator whose study requires procedures and professional services from a department other than his/her own department. The UIHC and CCOM Faculty Practice Plan leadership should jointly pursue the establishment of a mechanism for pricing and discounting these complex procedures. There are multiple ways to accomplish this. For example, a standard discount rate could be applied or some form of revenue sharing implemented similar to the principles used in setting package rates for transplant procedures. Having a single contact point for investigators to obtain pricing could be achieved by utilizing a mechanism similar to the Joint Office for Managed Care.

Another way to assist investigators in budget development is to provide a web-based, password protected electronic tool similar to that used at the University of Pennsylvania. Penn's budget preparation tool is homegrown and available only to UPenn employees. The tool is linked to the institution's fee schedule, including technical and professional charges, for all clinical services, and the research rate (the discount) is provided for each service. This tool is especially useful for routine tests (blood tests, etc.). It automatically calculates F&A based upon the type of sponsor. The tool is used to determine the total cost for conducting a study (development of an internal budget). The categories of expenses include personnel, tests and procedures, subject reimbursement, supplies, equipment, and other expenses such as fees for IRB review, pharmacy services, advertising, etc. Use of such a budget tool requires an upfront determination of whether the procedures/tests are standard of care versus research only. Because such a tool is institution-specific, it has to be developed internally. Thus there would be a cost associated with its development. If the necessary funding for development of the tool were provided, the CTO could coordinate a collaborative effort among the clinical departments and UIHC offices involved in billing. After the tool had been developed, there would be an educational component to orient researchers and staff, and the CTO could provide the training.

Post-Award (Billing Compliance)

Academic medical centers need a well-defined process for research billing in order to:

- Ensure that neither the subject nor the third party insurers are billed for clinical services budgeted under the study

- Ensure that the previously negotiated discount research rate for clinical services are charged to the research account
- Protect the institution from unnecessary financial obligation and legal liability arising from research billing

Human subject research billing is very complex and detailed. Understanding the coverage rules of third party payers is a challenge, even for the most experienced billing personnel. Medicare rules are particularly complicated, and they preclude payment for services that are covered by another source of funding (such as from a research sponsor). Also, coverage of services related to investigational devices must be determined prior to submitting claims.

For these reasons, many academic medical centers have adopted a research billing compliance program. These are the essential components of such a program:

- Designated expert(s) in research billing (research biller) to communicate with Medicare/Medicaid for coverage determination before the study is launched, to pre-certify device implantation with insurance companies, to summarize billing charges after services performed, and to submit bills to designated third party payer or grant account
- Documentation of internal budget for all clinical research studies (to distinguish standard of care tests/procedures from those that are for “research purposes only”)
- Alignment of subject costs in the contract, the study budget, and informed consent document
- Mechanism for flagging patient registration as “research”

Currently at our institution, there is not a coordinated compliance program for research billing. The UI Internal Audit Department has completed an audit of a sample of billing records of subjects enrolled in research studies, and under the direction of Deb Thoman in the UIHC Compliance Office, a committee has been formed to formulate a research billing compliance program.

Summary

The following recommendations are made for enhancing budget development and research billing compliance:

Prior to study initiation

1. Require that all clinical research budgets have an analysis of costs (an internal budget) before the study budget is finalized. All budgets should clearly differentiate standard of care from research-only tests/procedures.
2. Develop an electronic budget tool to assist researchers.
3. Designate a UIHC contact person to establish prices for tests and procedures, especially those that are complex and intensive in their professional service.
4. Designate a billing clerk at the institutional level to pre-certify studies with Medicare and determine whether coverage will be available.

After study initiation

1. Develop system of designating patient registration as “research”.
2. Designate a research biller to process all charges for research subjects (review all clinical charges, identify and verify payers with research team or department administrator, and bill appropriate entity).

F. Clinical Research Coordinators: Training and Availability

The clinical research coordinator (CRC) is a specialized research professional working under the direction of the clinical investigator to conduct research activities in compliance with applicable federal regulations, including those of the Food and Drug Administration and the Office for Human Research Protections in the Department of Health and Human Services. Although the investigator is legally responsible for managing a clinical study, the CRC, who handles most of the day-to-day research activities, is critical to the success of a study. In fact, many industry sponsors will not place a clinical trial with an investigator who does not have an associated CRC.

Most, but certainly not all, CRCs have background training as in nursing, physician assisting, or other health sciences. Background clinical training provides many advantages for a CRC, such as familiarity with clinical settings, an understanding of medical language, and an ability to participate in the care of research subjects.

The CRC job is multi-faceted, with clinical, supervisory, regulatory, administrative, and financial duties. Typical responsibilities include the following:

- Evaluation of protocols for feasibility
- Meeting with sponsor representatives (attend investigator meeting)
- Completion of IRB application, modifications, and continuing reviews
- Development of study budgets (negotiating with sponsors)

- Screening, recruiting, and consenting research subjects
- Ensuring adherence to the protocol
- Maintaining and administering investigational products
- Providing care for research subjects
- Completing case report forms
- Tracking revenue and processing expenditures

At UI, there are nearly as many models of clinical research teams as there are investigators. For example, there are CRCs who work full-time with only one investigator, and that CRC might perform all of the duties listed above. Other CRCs have only clinical responsibilities related to studies, and the administrative and financial duties are done by other staff members in the department. Investigators who do not have access to a CRC often arrange for non-research personnel (such as a clinic nurse) to perform some of the functions of a CRC.

The UI has three job classifications specifically for CRCs: Research Assistant I, II, and III. However, there are many staff members assisting with clinical studies who are not classified in these categories (Staff Nurses, Advanced Practice Nurses, Program Assistants, etc.). The following table provides details about the Research Assistant positions at UI:

<i>Title</i>	<i>Pay Grade</i>	<i>Salary Range</i>	<i># UI staff</i>
RA I	4	\$25,875 - \$48,478	N/A*
RA II	6	\$30,302 - \$57,015	25
RA III	8	\$35,454 - \$66,436	22

*This classification includes laboratory assistants and clinical assistants;
There is no way to know how many are exclusively involved in clinical research.

All of these UI positions report to departments in the CCOM.

UI does not currently provide job training for CRCs, and this is a common complaint among new CRCs. In response to this complaint, the Clinical Trials Office has sponsored a two-day workshop (on three separate occasions) on research skills for CRCs. The workshops, which focused on introduction to industry-sponsored clinical trials, are taught by an instructor from a private educational firm. The attendance at each workshop is approximately 30 UI staff members. There is no cost to attendees.

The Association of Clinical Research Professionals (ACRP) has a national certification program for CRCs. The certification program is geared toward pharmaceutical or device studies, with an emphasis on FDA regulations.

Certification is achieved by having (a) at least two years of experience as a CRC and (b) successful completion of a written exam. The exam is offered twice a year, and the UI Clinical Trials Office has sponsored the preparation course (on three different occasions) for CRCs employed at UI or at other institutions. The CTO uses an independent trainer to conduct the course, and there is no cost for the attendees. Most of the attendees who later take the exam are successful in becoming certified. Currently, there are approximately 20-25 certified CRCs at UI.

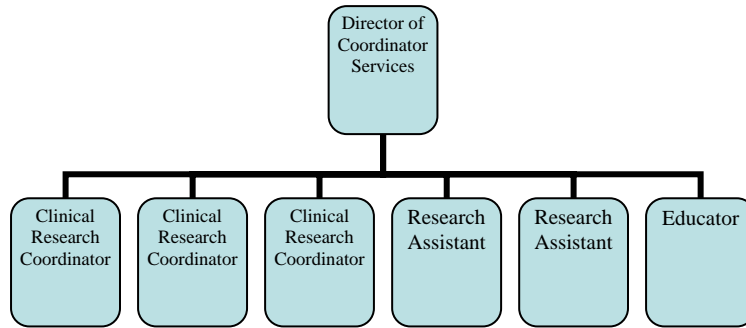
Neither of these two educational courses provides information about UI internal processes and policies related to human subjects research. The CTO has periodically offered short seminars on the following topics: how to work with the CTO to get a contract started; how to formulate a budget; how to complete a UI Routing Form; how to apply for research discounts through the UIHC Business Office; etc.

Recommendations

Although some clinical researchers have adequate administrative and clinical support staff to assist with studies, many do not. In addition, even researchers who have an experienced CRC on their research team have need for additional assistance if there are more studies than current staff can handle or if the CRC becomes unavailable. An approach that other institutions have taken is to offer centralized support services for investigators for study initiation, implementation of the protocol, and close-out of the study. An investigator could use any or all of the services for an hourly fee.

Two examples of institutions with centralized CRC services are the University of Maryland <https://medschool.umaryland.edu/cct/Investigators.asp> and Northwestern University <http://www.medschool.northwestern.edu/nccr/>. At both of these institutions, the CRC service is organizationally placed within a clinical research center in the school of medicine.

The following diagram provides one model for staffing the clinical operations portion of a research center. In addition to the CRCs, who are registered nurses (RA III positions), there should be positions for Research Assistants (at the RA I level) to perform nonprofessional functions such as data entry, phlebotomy, specimen processing, scheduling, etc.



The above model also shows a position for an Educator. The responsibilities for this position are as follows:

- Training new CRCs throughout UI (courses in Good Clinical Practices)
- Mentoring new CRCs (providing opportunity for “shadowing”)
- Providing continuing education for experienced CRCs
- Developing a practicum for nursing students
- Collaborating with local nursing programs to add content to curriculum

This model of centralized CRC services does not include clerical support, financial services (budget development; tracking revenue/expenditures, etc.), regulatory affairs (preparation of INDs; completion of FDA forms; registration of studies, etc.), or recruitment services. These additional services should be a part of a clinical research center and will hopefully be discussed in other sections of the Task Force report.

G. Biostatistics Support

Data Management and Statistical Resources

Department of Biostatistics

The Department of Biostatistics has faculty and staff offices in the General Hospital. The Clinical Trials Statistical and Data Management Center is housed in close proximity in the Westlawn Building, as is the Center for Public Health Statistics.

The Department of Biostatistics includes thirteen primary full-time faculty biostatisticians. Methodological expertise of the faculty includes: clinical trials, linear models, time series analysis, model selection criteria, Bayesian statistics, quality control, design of sample surveys, experiment design, survival analysis, nonparametric statistics, multivariate analysis, longitudinal data analysis, spatial statistics, missing data, health information systems, data mining, public health statistics and categorical data analysis.

Biostatistics Consulting Center

The Center currently provides expert short term statistical consulting and data management services to researchers across the UI, including those in the Colleges of Public Health, Medicine, Dentistry, Nursing, and Pharmacy. It is also involved in some longer term projects.

Clinical Trials Statistical and Data Management Center (CTSDMC)

The Center coordinates multi-center clinical trials and coordinates the statistical and data management. The Center has coordinated a number of studies in the past and is involved in a number of different studies currently. It is entirely supported by NIH grants and has an annual budget of \$3-4 million.

A large fraction of the current effort of the CTSDMC is devoted to the Consortium for Islet Cell Transplantation (CIT) a collaborative group of sites in the US, Canada and Scandinavia. CIT is currently in the process of implementing seven trials of islet cell transplantation in individuals with complications from Type I diabetes. One of the studies is a randomized comparison of islet cell transplantation to usual diabetic care in individuals who have received a kidney transplant. An ongoing study compares surgical to non-surgical treatment for carotid artery occlusion, another compares three language intervention programs on children with language impairment.

The CTSDMC has completed coordination of several studies including randomized trials in aneurysm surgery, stroke, Alzheimer's disease, and peripheral arterial disease. It has also coordinated an epidemiological study of health assessment of Persian Gulf War Veterans.

The CTSDMC is directed by Dr. William R. Clarke, Professor of Biostatistics and Deputy Head Department of Biostatistics, at UI. The CTSDMC involves other faculty in the Department of Biostatistics. Some of the trials coordinated by the CTSDMC have been collaborative projects with faculty in the UI CCOM, and others been in collaboration with clinical leadership from other institutions.

The Department of Biostatistics has identified its most pressing need as hiring a senior faculty member (full or associate professor) to be a Deputy Director

of the CTSMC who will be ready to take over leadership of the center on Dr. Clarke's retirement.

Center for Public Health Statistics

The Center for Public Health Statistics (CPHS) is a collegiate research and service center in the College of Public Health, under the direction of Dr. Jane Pendergast, a faculty member in Biostatistics. Research in the CPHS includes both within-Center projects and collaborative projects with researchers throughout the health sciences on a broad array of public health concerns and sponsored by a variety of national and state agencies. Examples include studies involving screening low-income women for several types of cancer and for cardiovascular disease risk factors in Iowa, studying spatial relationships in cancer screening, stage at diagnosis and survival in Iowa, studying patterns of care in lung cancer patients (national consortium), and evaluating economic issues related to the care of end-stage renal disease patients (national data). The members of the CPHS integrate these health-related research activities with the conduct of research on methodology in public health statistics, such as survey sampling, geospatial relationships, goodness-of-fit assessment and methods for analyzing longitudinal data.

Part of the service component of the mission of the Center is to provide statistical and data management expertise for researchers in the health sciences, as well as access to and advice on using large publicly-available national databases, such as those from the National Center for Health Statistics. The CPHS continues to develop liaisons to provide access to other important public health databases, including those held by the Iowa Department of Public Health and the administrative health insurance claims data from both Wellmark Blue Cross/Blue Shield of Iowa and the Iowa Medicaid Program. The Center maintains three secured data servers to hold protected health data, and maintains strict control over access to personal health information.

Holden Comprehensive Cancer Center

The Biostatistics Core provides statistical support for Cancer Center investigators in the design, analysis, and reporting of cancer research projects. Examples of services provided:

- Consultation on study design, selection of outcome variables and formulation of hypotheses
- Specification of appropriate methods of data analysis
- Sample size estimation
- Protocol development
- Generation of randomization schedules

- Support for the analysis of microarray data
- Data base design and implementation
- Data analysis
- Assistance in preparation of manuscripts
- Education and training

Department of Epidemiology

The Department of Epidemiology is an academic and public resource for assessment and improvement of human health. It strives to improve public and personal health by preparing students for careers that require specialized knowledge of epidemiologic theories, methods, and analytic techniques; by conducting innovative research in the magnitude, determinants, and prevention of disease and its consequences and in health promotion and evaluation; and by providing education, consultation and collaboration with public health and other programs.

The Department currently has 13 full-time faculty, 39 secondary and adjunct faculty, and four research scientists. The research activities support nearly 250 research staff and graduate research assistants. Space for the Department is available in the General Hospital for faculty and administrative staff. Research programs are located in the Westlawn Building, US Bank Building, and Oakdale Hall on campus as well as satellite clinics of the Preventive Intervention Center at the Towncrest Center in Iowa City and in Des Moines and Davenport

Prevention Intervention Center

The Preventive Intervention Center is an academic resource to facilitate studies that evaluate the effectiveness of new modalities designed to prevent occurrence and progression of disease. The Center includes the following activities: administration, epidemiology, biostatistics, behavioral medicine, nutrition, data management, recruiting, screening and evaluation, follow-up evaluation, compliance and protocol adherence, quality control and regulatory adherence. The Center provides support for on-line and scannable data entry, development and implementation of relational, interactive databases and analytic support for prevention clinical trials. The goals of the Center include to:

- Maintain a core methodological unit for design and conduct of intervention studies
- Develop new methods for testing and evaluating prevention strategies
- Educate students and practitioners in the evaluation and use of preventive intervention methods and programs

- Collaborate with practitioners, scientists and government officials in evaluating new prevention methods
- Evaluate prevention methodology, screening tests, and interventions in populations

Health Effectiveness Research Center

The Health Effectiveness Research Center of Iowa provides methodological expertise, training, mentoring, and databases for conduct of policy-relevant research on the costs and effectiveness of preventive and therapeutic interventions using cutting edge methods applied to large observational datasets, such as survey, healthcare claims, encounter, and discharge abstract databases, in order to enhance the quality of evidence provided by these data to inform sound policy and clinical decision-making.

College of Public Health Center for Statistical Genetics Research (CSGR)

The Center for Statistical Genetics Research (CSGR) is a joint College of Public Health and Carver College of Medicine initiative devoted to research on complex human inherited disease. Its missions are to support excellence in basic methodological work in statistical genetics, as well as to foster and promote interdisciplinary collaborative clinical research on genetic factors in human disease. Housed contiguously with the College of Public Health's Program in Public Health Genetics (PPHG), the CSGR provides a rich intellectual environment in which faculty, post-doctoral fellows, graduate students, technical staff, and clinical and molecular collaborators, can interact at the cutting-edge of human clinical genetics research. The CSGR houses core facilities in support of study design, database, and data analytic activities; as well as a simulation core facility for rapid, customized evaluation of both existing and novel statistical genetics methods. CSGR computing facilities include, in addition to a large suite of networked PCs and several UNIX workstations, a Linux cluster for high-performance implementation of computation-intensive statistical methods.

General Recommendations

- 1) Provide for the infrastructure in terms of space and personnel to facilitate design, implementation and analysis in a contemporary manner the data collection and analysis of clinical research
- 2) Recruit faculty and staff who have expertise in the design, conduct and analysis of clinical research including clinical measurement and analytical methods

- 3) Link data collection and informatics of clinical record data to facilitate the rapid and accurate collection and assessment of patient information

Specific Recommendations

- 1) Hire additional faculty and staff to support biostatistics and informatics for clinical research
- 2) Provide adequate support in terms of space, staff, computers and communication to facilitate collaboration
- 3) Commit adequate resources for linking data between the clinical information system and data management systems for clinical trials
- 4) Cost sharing of clinical design, execution and analysis, i.e., multiple PIs for UI initiated projects

Budget Implications

- 1) Faculty positions in biostatistics and informatics
- 2) Data warehouse of UIHC medical records
- 3) Data management staff for linking databases
- 4) Administrative costs for multiple accounts related to projects

H. Preclinical and Clinical Development of New Therapies and Diagnostics

A successful clinical research program at UI must be built around an infrastructure that promotes the translation of potential new therapies in clinically useful products or procedures. In addition to an extensive array of nationally recognized clinical research programs including, GCRG, PIC, CRIISP, Clinical Trials Office and a Cancer Clinical trials program, UI possess a series of unique expertise and facilities available to further develop drugs, diagnostics and vaccines for clinical evaluation. Among our existing strengths in this area include:

Pharmaceutical Services (PS) - <http://www.uiowa.edu/%7Epharmser>

The Division of Pharmaceutical Service at the UI College of Pharmacy is the most experienced university-affiliated drug manufacturing facility registered with the U.S. Food and Drug Administration. The division has been producing clinical supplies in compliance with Good Manufacturing Practices (cGMP) since 1974.

The facility is the only one of its kind to offer the range and scope of services needed by commercial clients. Its staff works closely with clients to produce virtually every type of pharmaceutical dosage form. A variety of large and small pharmaceutical firms, university investigators, and government entities from around the world use the manufacturing facility to produce supplies of new pharmaceutical agents for use in clinical trials.

The Center for Advanced Drug Development (CADD) –
<http://www.uiowa.edu/~cadd/>

CADD, also a service division within the College of Pharmacy, is an FDA registered laboratory, in full compliance with all federal standards for Good Manufacturing Practices, created in 1991 through the Iowa Department of Economic Development. CADD is also licensed by the US Drug Enforcement Agency to handle controlled substances Schedules 1 to 5. The Center has a wide range of assays to obtain data for pre-approved active pharmaceutical ingredients, new molecular entities, drug products and excipients. They also regularly perform long and short term stability studies in support of clinical products for industrial, government and university clients, often in support of manufacturing of contracts with PS.

The Center for Biocatalysis and Bioprocessing (CBB) –
<http://www.uiowa.edu/~biocat/>

The Center for Biocatalysis and Bioprocessing (CBB), stands at the center of a global revolution in biotechnology. At its inception 20 years ago, the CBB became the first and largest organization in the world to organize a multidisciplinary research group with a primary focus on the areas of biocatalysis and bioprocessing. The center reports to the Vice President of Research and comprises faculty in several colleges and many departments focuses on teaching and research in applied agricultural, chemical, nutritional and pharmaceutical research with a strong focus on technology transfer and works with university, industry and government clients world wide. Relative to human health and clinical development recently the State of Iowa awarded the CBB \$3 million dollars for construction of cGMP facilities to ferment and purify materials suitable for Phase I / Phase II clinical trials. This unique capability compliments existing CBB fermentation capabilities in research and links extremely well with PS and CADD to provide opportunities for the development and manufacture of clinical supplies of wide variety so new biologically derived therapeutics products and vaccines.

Research Expertise within the Colleges

Complete development of new human therapies requires a complex and costly series of steps being initiated by discovery and followed isolation, purification, scale up, extensive preclinical testing, toxicology, carcinogenicity, formulation, clinical development and the filing of an Investigational New Drug Application (IND, or other FDA preclinical approvals for devices and biologics). In combining the unique FDA registered facilities outlined above with faculty research expertise in the Colleges of Medicine, Pharmacy, Engineering, Dentistry, Nursing, Public Health and Liberal Arts and Sciences, UI has the potential to fully develop products from discovery and take them through clinical trials. The interdisciplinary and collegial culture of research at UI further supports this integration of expertise. Collectively these assets are unique among US research universities and positions us for not only developing important new therapies, but working with NIH in major new translational research initiatives as well industry partners. Commercializing new therapies also provides significant potential for UI's active participation in economic development within the State of Iowa.

An infrastructure to help Develop new Drugs, Devices, Vaccines and Diagnostics

Objective:

To develop a novel public/private research and development organization which can contract with clients both within UI and in the private sector to enhance new product development and promote IP transfer for the benefit of UI in the human health field. This will often require working initially between the company/inventor and the Food and Drug Administration (FDA) to agree on the scope of clinical testing that will be needed for approval.

Expected Outcomes:

- Interact with UI and industry scientists to identify new compounds which can benefit from further development through the array of services available within this platform.
- For each new compound work to create a contractual link between the technology owner and needed services from discovery, chemistry, scale up purification, formulation, pre clinical pharmacology, toxicology, manufacturing, IND development and all phases of clinical trials.
- Directly monitor the progress in each of the contractual areas and communicate back to the originator to create a virtual team to manage the progress.

- Interface with legal and other critically needed business development entities as the project moves along both within and outside of Iowa with an eye on attracting venture capital to support further development, licensing agreements that fit the product and attracting additional technical and managerial personnel to insure progress and ultimate success.
- Support academic drug discovery, development, translational research and experimental therapeutics and link to clinical trials.

Critical Gaps and Recommendations

Fully capitalizing on all of these strengths here will require identification key gaps which traditionally hinder the ability of investigators to work across departments in activities that require interface with the FDA. These include:

1. M.D./Pharm.D. with experience in IND development for drugs and diagnostics
2. B.S./M.S. technicians capable of formulating up new drugs and diagnostics for Phase I manufacturing
3. M.D./Ph.D. scientist with expertise in regulatory affairs and dedicated to the development of preclinical Pharmacology/Toxicology and ultimately the future clinical plan needed to fully develop a discovery into an IND.

I. Role and Dynamics of Current Clinical Research Leaders in a Governance Structure

The current UI clinical/translational research enterprise is led by many leaders that range from faculty with whose leadership role is part of their administrative duties (i.e., Deans, DEOs, Center Directors, Research Core Directors, etc.) to those for whom their role is that of an active and high-volume clinical investigator. For the latter group of individuals their role results from active use of support system that may be funded from their individual grants.

In order to establish a governance structure that is responsive to all clinical and translational investigators, regardless of their experience, type of research, varied sponsorship (government, private foundation, industry, etc.), and their specific role in the institution, many functions must be addressed. In order to support health sciences research, structure must allow for the coordination of trials that will include aiding development, initiation, recruitment, managing cost, contracts development, monitoring, and addressing regulatory issues. The structure must have a means for solving unique or common problems that individuals or groups

of individual investigators may encounter, have a critical role in strategic planning, for the future, and most immediately, to help support major clinical trial initiatives, such as the CTSA.

Proposal:

Establishment of a Council for Health Sciences Research

Principles:

- Integration of CTSA and Clinical Trials Institute into the scheme
- Need to involve those with a vested interest
- Representation from Colleges (RAC in College of Medicine), Centers, Grantees, Departments, Training Programs, and Investigators
- Interface with ongoing clinical (i.e., treatment) operations (UIHC for patient areas and FPP for faculty issues)
- Interface with the other clinical trials operations ongoing (HCCC, individual investigators, etc.)
- Led by a clinical investigator with adequate administrative support
- Broad authority, responsibility, and accountability
- Metrics for success need to be defined, timed, and prioritized
- Alignment with a Business Plan

Implementation:

- Council Leader needs to report and function at a high level within UI
- Administrative Authority (empowerment and resources)
- Membership will include some permanent and some rotating members (3 year terms) – approximately 8-12 members

~ Suggested composition:
???

Resources:

- FTE Faculty effort
- Administrative Support

J. Role of Smaller Units in Clinical and Translational Research

Translational research strives to understand the basic mechanisms of disease, and then apply that understanding to the design and development of real-life medical solutions. Translational research seeks cures that strike at the cause of the disease. Translational research rarely happens naturally or by accident. It must be designed into our work; it must be fostered and pushed.

The goals of our efforts to facilitate translational research should be to:

- Support an optimal setting for clinical research in normal adults and those with chronic diseases
- Support bi-directional interactions, or "translational research" among physicians and scientists involved in basic and clinical research
- Support an environment and the resources needed for developing future clinical scientists

Purpose:

- Interdisciplinary nature of smaller units provides expertise and access to special populations.
- Expertise to assist in observational and interventional studies associated with various disease states (e.g. cardiovascular).
- Access for medical investigators to niche expertise: drug development, pharmatherapeutics study expertise, compounding expertise, oral and salivary diagnostics, oral microbial/biofilm ecology, mucosal defensins; pain evaluation, impact on QOL, etc. (*functional status, behavior, mental status, cost efficiency*).
- Expanded involvement of allied faculty who are not aware of research opportunities: access to central data base of investigators, projects,

initiatives, grant discuss groups (think tanks); use of central grants management support systems.

- Broaden or add depth to the scope of research. In addition to providing expertise e.g, with respect to theory, content or measurement, additional original questions could be asked enhancing the importance and efficiency of research.

Location of allied activities:

- Maintenance of current niche activities within campus units such as College of Nursing, Pharmacy, Dentistry and Engineering.
- Outreach activities off campus coordinated with medical investigators as a means to increase access to special populations, etc.
- Access to and use of central databases of special populations (women at risk, head start children, native/first nation populations).
- Engineering – examples of medical imaging initiatives supported by the Imaging Institute
 - NETT (National Emphysema Treatment Trial - about 3,000 subjects) (Hoffman)
 - Mesa study (Multi-Ethnic Study of Atherosclerosis) (Hoffman)
 - Muscatine study - Arterial Endothelial Function -
 - An Epidemiologic Study, atherosclerotic risk factors, 900 subjects followed for over 40 years, with the entire cohort being close to 10,000, many risk factors are image-based, including coronary calcium from CT, carotid IMT from ultrasound, endothelial function from ultrasound, etc.)
 - Muscatine study - Epidemiology of Carotid Artery Atherosclerosis in Youth
 - 3-D and 4-D Coronary Hemodynamics and Local Atherosclerosis includes a study of 125 subjects undergoing coronary intervention and IVUS, goal is to predict coronary plaque development
 - Sonka's R01 HL071809 (2003-2007) Highly Automated Analysis of Cardiovascular MR Data includes a study of 90 subjects suffering from congenital heart disease plus cohort of normals
 - Ophthalmology - technology development for retinal screening
 - The IDRI project - the first private/public partnership entered into by the NCI - involving the foundation of the NIH and 11 major/minor imaging companies. All of these are multi-institutional
 - The NCI has 3 projects - the LIDC - establishing a publicly available image repository of lung nodules with associated ground truth
 - The RIDER project - establishing image based parameters for the early assessment of response to therapy in lung cancer

- The VENT study - industry supported evaluating for FDA approval the role of endobronchial valves in the therapy of emphysema. UI is the leading recruiter in the world for this study
- The National Lung Screening Trial - a \$200 million dollar, NIH supported study (8 year) evaluating the role of CT scans in early detection of lung cancer
- An NIH-supported project involving endoscopic image analysis and image fusion with CT - to quantitate endoscopic images for use in clinical outcomes in airway diseases in particular
- National Emphysema Treatment Trial, and the Severe Asthma Research Project (SARP)
- Engineering – Center for Bioinformatics and Computational Biology
 - Software systems to support a non-profit National Genetic Testing Laboratory. This includes strategies to improve the collection and refinement of phenotypic data to improve the definition of particular diseases. Currently, this is limited to ocular disorders and some limited cancer types.
 - A mature software system for mutation identification that CBCB is contracted with the NCI to make available as open-source software to all cancer centers (and anyone else). From this activity, CBCB has an active role in advising the NCI as to directions for developing bioinformatics to support translational research.
 - Resources and expertise to provide printed glass-slide oligo-arrays to complement the existing Affymetrix gene chips available in the DNA core -- for evaluating gene expression.

Challenges

- Facilitate access of smaller units (who may not be housed in UIHC) to hospital patients, possibly including a central mechanism for recruitment and streamlined access to patients when physician approval is required.
- Expanded access and communication between active investigators in health science fields that will produce synergy (e.g. computational bioinformatics; salivary gene therapy delivery; underserved populations, etc.).

K. IT System for Clinical and Translational Research

Informatics

Informatics at UI involves a multidisciplinary approach. Much of the clinical information system and databases have been developed and built at UI. Each was established to fulfill specific and separate needs. More recently the development of bioinformatics, computational biology, interactive data management, decision systems and digital measurement has emerged as not only an advancement in research and clinical measurement, but also a paradigm for merging disciplines into enhancement and progression of translational clinical research and patient care.

Clinical Informatics

UIHC maintains an interactive Clinical Information System (CIS). The current CIS includes the INFORMM Patient Record, a Nursing Documentation System, a Radiology Information System, an Operating Room System, Cerner Laboratory and Pharmacy System, an Electronic Medication Administration Record, and Clinical Outcomes and Regulatory Reporting System. The clinical systems interfaces with business systems for accounting, inventory, human resources, academics and research. Currently the staff is over 250 maintaining the CIS of 7 million transactions per day. Key issues are data security, user management and training and data storage and retrieval. In 2006 the current CIS will be upgraded using a commercial vendor. This system is necessary to keep up with the generational advancement in clinical information management and security and to progress to intelligent systems for user interface and to protect patient safety.

Registries or clinical information repositories exist at the institutional and departmental levels. Examples of specific registries include the Tumor Registry, the Trauma Registry, etc. In addition individual studies have included direct data collection for clinical trials. These require information obtained from the UIHC clinical information system and from direct observation and measurement. These records may be paper/notebooks or electronic and are kept for clinical review and copies are sent to sponsoring or monitoring agencies. If the clinical trial is under a FDA IND then records and data need to be available for FDA monitoring. The record storage is usually for 3 years post-study but can be up to 15 years. Project specific data management is done through centers or research programs such as the GCRC, HCCC, and the PIC. Individual research teams comprised of study coordinators, nurse clinicians, research assistants and data managers conduct study-specific data and manage the data for retrieval and analysis.

Population-Based Informatics

Data is collected and managed for large external populations. Examples of these include the Iowa Cancer Registry, the Iowa Registry for Congenital and Inherited Disorders, and the State Trauma Registry. Also data is obtained from the Iowa Hospital Association including hospital discharges, insurance claims data from Wellmark, Medicare and Medicaid data from the state and federal government. Collection and retrieval of this data is governed by state and national laws and must comply with HIPAA regulations for information retrieval and linkage.

Informatics Processing and Analysis

The Clinical Trials Statistical & Data Management Center (CTSDMC) was established in 1989 for the purpose of coordinating the statistical and data management functions for multicenter clinical trials. The CTSDMC is directed by William R. Clarke, Ph.D., professor of biostatistics. Collectively, the center is capable of providing the design, analysis and coordination expertise required for multi-center clinical trials. CTSDMC experience to date includes a variety of corporate and NIH-sponsored studies. The highly experienced professional staff includes project coordinators, programmers and statisticians, strongly supported by graduate student research assistants. The goals of the Center are to provide an infrastructure for the planning, conduct, and statistical analysis of clinical trials, to provide linkage to academic programs via student and faculty research opportunities and to provide an environment for development of new courses and preceptorship opportunities. Components of the CTSDMC include:

- Protocol Development
- Trial Design
- Biostatistical Analysis
- Safety Monitoring
- Report Preparation
- Case Report Form Design
- Distributed Computer Systems
- Relational Database Design
- Data Management
- Training and Certification
- Newsletter Design and Publication

The Center for Bioinformatics and Computational Biology (CBGB) aims to catalyze the development of new areas of study and expanded research opportunities in informatics areas related to the basic biological science, and applied medical research. Thomas L. Casavant, Ph.D., is the Director, with faculty and staff members of the Executive Committee from Microbiology,

Medicinal Natural Products, Biochemistry, Pediatrics, Biological Sciences, Electrical and Computer Engineering, Chemical and Biochemical Engineering, Biomedical Engineering, Computer Science, College of Nursing, Library and Information Science, Statistics and Actuarial Science, ITS-AT Research Services, and the DNA Facility. Center Support includes both overall support of the organization of the Center, plus support of research projects. The Center is supported by the College of Engineering and the CCOM and received external grants and contracts from NIH, United States Department of Agriculture (USDA), National Human Genome Research Institute (NHGRI), Alcon, Inc., Integrated DNA Technologies (IDT), W.M. Keck Foundation, **and the** National Science Foundation.

The Coordinated Laboratory for Computational Genomics (CLCG) conducts research in a variety of research topics in bioinformatics and computational biology. These include: gene and mutation discovery, expression analysis and functional genomics, genetic and physical mapping, genome-scale analyses, and information management. The CLCG is a charter member lab of the CBCB. Current projects include identification of microRNAs and their targets, full-length cDNAs, inter- and intra-species gene families, transcription factor binding sites, transcription start sites, alternative splice forms, alternative polyadenylation sites, and simple and complex repetitive elements. The Lab has also developed an integrated system for managing information relating to disease gene mutation identification. Similar database-centric systems have also been developed to manage clinical and genotyping data for disease linkage experiments, and to manage the information related to full-length cDNA sequencing. The full-length cDNA sequencing pipeline provides the ability to track the progress of individual cDNA libraries and clones, and to provide feedback into the system regarding the quality of the clones selected for full-length sequencing.

Informatics Education

Health Informatics education is a multidisciplinary program. Its goal is improving the utilization of health care data, information and knowledge to support health care education, research and practice. It requires and utilizes disciplines with interests in information management, processing and analysis. The program at Iowa began under the direction of Connie Delaney of the College of Nursing and Michael Kienzle in the CCOM. Dr. Delaney has accepted a position as Dean of the College of Nursing at the University of Minnesota.

Bioinformatics and Computational Biology (BCB) is an emerging discipline which is rapidly growing. It examines the creation of new methodology of advanced mathematics and computation for application to problems of biological and biomedical interest. These include utilization of information from areas such

as the human genome, evolution of plants and animals, and the relationships between micro-organisms and higher-order forms of life.

Academically the BCB is a multidisciplinary program of allied disciplines and areas involved in the measurement, collection, management and processing large amounts of data relevant to biological processes. Computer Engineering, Biomedical Engineering, Probability and Statistics, Computer Science, Biochemistry, Biology, Applied Mathematics, and Physics are some allied fields. At UI academic programs include:

- Computational Genetics Subtrack of the Genetics Ph.D. Program
- Ph.D. Program in Statistical Genetics
- Carver Center for Comparative Genomics
- Biotechnology Track in Biological Sciences
- Health Informatics
- Bioinformatics and Computational Biology Focus area in Biomedical Engineering
- Computational Subtrack in Microbiology

Integration

It is evident that further integration of the UIHC CIS, research centers and programs and the education of new researchers and health professionals are needed. The basic components are in existence but to transform and develop the clinical trial and research infrastructure requires further collaboration between administrators, faculty, staff and students. The concept of converting an idea into clinical measurement in concert with patient care into a comprehensive data portfolio of each research subject is needed. This is beyond the routine clinical data and requires information integration from such large data as genetics, radiology, and longitudinal records.

Recommendations

- 1) Interactive clinical interface with CIS
 - Characteristics
 - Database warehouse purely for research
 - Web based interfaces for data collection and monitoring
 - Integration of specific research clinical measures with CIS
 - Data storage and backup
 - Active interface with UIHC EMR
 - Accessible for design, collection and retrieval
 - Data coding conventions utility
 - Formatted compatible with analytical software
 - Integration with non-CIS data

- Integration with non-clinical research data
 - Patient information
 - Diagnoses
 - Demographics (address, age, gender, ethnicity)
 - Insurance, billing, vital signs
 - Medications
 - Labs
 - Imaging
 - Clinical physiological tests
 - Staffing and reporting
 - Establish information research advisory group
 - Engage UIHC (Lee Carmen Group)
 - Hiring of research data coordinator
 - Develop prospectus for data warehouse
 - Develop schematic for integrated use of CIS data from new vendors
- 2) Enhance and integrate education and research with clinical data
 - Encourage development of health informatics and train students and professional in health data domains
 - Link bioinformatics, computational biology, genomics, operational research, clinical data management, biostatistics, etc in clinical research
 - Develop a research infrastructure for investigators to facilitate the design, implementation and analysis of the integration of clinical data

L. Community

Engagement: Opportunities to Build Research Partners

Carver College of Medicine

Community Services is a community outreach division of OSCEP. It offers a number of ongoing programs and non-clinical services to Iowa communities and health care providers. For more than 25 years, University of Iowa relationships with community physicians and health care organizations have been enabled by the Community Services Division. Specific programs offered by the Community Services Division follow. The Rural Physician Support Program provides practice coverage, physician recruitment, placement, retention, and practice management consultation services to rural Iowa Communities under 30,000. The Iowa Practice Opportunities Program assists residents and relocating physicians who are searching for practice opportunities and collaborates with Iowa communities who are seeking physicians and non-physician providers. The

Community Relations Program serves all physicians and communities across Iowa with specific technical services including practice management consultations, substantive reviews of health care provider contracts, assistance in the formation of new medical practices, and conflict mediations. Health Care Market Research Services are offered to community hospitals and medical groups provide area wide surveys and community studies in regions throughout Iowa. These surveys assist in assessing the feasibility of proposed services, ascertain local opinions of area health services determine health care medical and hospital services used by area residents or provide data and direction of for marketing plans.

College of Nursing

The Rural Iowa Nursing Network builds a sustained partnership of faculty and students with Iowa rural nurse leaders and to begin to develop tools and resources geared to the needs of rural nurses. The Rural Iowa Nursing Network is unique in its focus on rural nursing practice. Iowa has the second highest number in the nation of Critical Access Hospitals (CAH), less than 25 beds, with 86 CAH (Kansas has 88). The partnership expands learning opportunities for students in rural nursing practice invigorating the practice environment. The expected outcomes of this project are: 1) strengthened relationships with Directors of Nursing (DON) and nursing staff of the Iowa CAH; 2) dialogue and identification of information about key issues facing CAH; 3) increased numbers of student experiences in CAH; 4) a website devoted to information and resources useful to rural nursing practice; 5) a partnership with the Iowa Department of Public Health, Bureau of Health Access to sustain continued dialogue; and 6) the development of proposals/grants for further research and demonstration projects.

College of Pharmacy

The College has full-time clinical faculty in each of 6 Family Residency Sites and clinics across the state, serving the teaching needs for Doctor of Pharmacy students and residents as well as Medical residents and faculty. In addition, each site has become a focus for multicenter clinical research coordinated by Dr. Barry Carter and funded by two NIH grants aimed at studying the control of hypertension in community elderly using a collaborative practice model. These sites and the faculty present there on a full-time basis allow for additional community-based Phase IV and V studies, which will be come central to the FDA process for drug approval and safety following the Vioxx episode.

A network of community pharmacies where very high levels of patient-centered care are practiced has been developed through the educational auspices of the College of Pharmacy and the Iowa Pharmacy Association. This group of nearly

150 pharmacists have been working with faculty in the Colleges of Pharmacy and Public Health to assess the outcomes of a DHS-funded Pharmaceutical Case Management Program in the high risk Medicaid population. This program is now in its third year and the platform on which is based will be used to initiate a much broader multistate Medication Therapy Management Pilot across our entire Medicare region in conjunction the new Medicare Modernization Act and the new Prescription Drug Benefit for Seniors. States involved in addition to Iowa include Nebraska, Minnesota, North and South Dakota, Montana and Wyoming.

College of Public Health

The Institute for Public Health Practice promotes the linkage between academic, service, and research with public health practitioners. Emphasis is on educational programs, practice site development, and supporting communities with technical assistance and research.

Community Research Resources

The Iowa Research Network (IRENE)

IRENE is a practice-based research network (PBRN) for family practice research especially in rural areas with a current membership of over 260 family physicians. IRENE is a collaboration between the Iowa Academy of Family Physicians (IAFP) and the UI Department of Family Medicine. The purpose of IRENE is to create new knowledge and improve clinical practice, especially in rural communities. It will accomplish its mission through the systematic evaluation of current practice and identification of the contributors to practice behaviors using the expertise of primary care providers and through its linkage to a research oriented academic health center. IRENE is particularly suited to studies that assess the generalizability of interventions to primary care practice and rural communities. Examples of research include: Computerized Interviews to Assist Secondary Prevention, Colorectal Cancer Screening Among Patients Attending Rural Family Physicians' Practices, An Evaluation of the WISE QI Program, Barriers to Adherence to Diabetic Guidelines, Osteoporosis Prevention, Unexplained Symptoms, and Depression Screening.

Nursing Research Centers

Center for Nursing Classification and Clinical Effectiveness, Gerontological Nursing Intervention Research Center (GNIRC) and Center for Nursing Informatics provide research expertise and knowledge as well as established relationships with the technology sector to successfully develop and test the tools and resources lacking in rural nursing practice.

The Institute for Quality Healthcare (IQH)

IQH is a regional consortium of healthcare organizations dedicated to the cooperative enhancement of the quality of patient care. Served by the UI Resource Center, IQH exists to provide services and support to healthcare providers that will enable and promote the advancement of healthcare.

Health Effectiveness Research Center (HERCe)

Healthcare effectiveness research assesses the degree to which preventive, diagnostic, and therapeutic healthcare interventions achieve their intended goals in clinical practice. Research has shown that health care providers sometimes vary widely in the preventive care and medical treatment they give to patients with similar health problems. This variation in practice can be examined to evaluate the effectiveness, cost and over- or under-use of specific health care interventions.

UI Center for Evaluation Research

The Center focuses on conducting evaluations of training, educational materials and procedures, workforce development, and community-based interventions and promotes training in program evaluation. It provides services in the design and conduct of evaluation procedures in ongoing UI and state public health projects and programs, conducts research on the design and application of program evaluation principles and methods in the field of public health, conducts research on data collection instruments and analysis procedures used in program evaluation and disseminate results, conducts training in program evaluation to public health project directors and staff members, and provides training opportunities in program evaluation to graduate students in public health and related disciplines. Projects include: Healthy and Ready to Work: Child Health Specialty Clinics, Evaluation of the Iowa Public Health Preparedness Center, Iowa Medical Home Initiative, Evaluation of the Upper Midwest Public Health Training Center, Heartland Center for Occupational Health and Safety, Pfizer Health Literacy Study, Annie E. Casey—Des Moines Making Connections, Evaluation of the Prairielands Addiction Technology Transfer Center (P-ATTC), Evaluation of the Practice Improvement Collaborative, Evaluation of the Palmer College of Chiropractic K30 Clinical Investigation Training Program, and the Linn County Project.

The Prevention Research Center (PRC)

The PRC is a part of the UI College of Public Health, Department of Community and Behavioral Health, and is funded by the Prevention Research Center Program of the Centers for Disease Control and Prevention (CDC). The PRC conducts community-based projects aimed at promoting the health and well-being of rural Iowans. The Center's mission is to improve community health by working toward the elimination of health disparities in rural Iowa and the Midwest through

research conducted by communities on issues of importance to them. Core research projects are:

Training of community-based organizations to promote physical activity and nutrition:

The main objectives of this project are to work with area schools to place a greater percentage of unsweetened beverages in school cafeterias and vending machines, to assist area restaurant owners in implementing and evaluating changes in business practices that will encourage healthy eating choices, and expand on existing shelf labeling activities at local grocery stores.

Building capacity to prevention underage drinking:

The purpose of this project is to increase the capacity of our partner organizations to engage in community-based participatory research in order to address the issue of underage drinking. In January, 2004, the partnership was instrumental in enacting the first county-wide keg registration ordinance in the state of Iowa. The goal of this project is to build the capacity of community-based organizations to prevent adolescent alcohol use.

Community Surveillance Project:

This project involves an ongoing cross-sectional survey designed to monitor and evaluate the effectiveness of health promotion activities in our partnership community. Study participants include 200 residents of our partnership community and 200 residents of our comparison community. Survey measures include physical measures such as body mass index, diet and exercise behaviors, and perceptions of community and empowerment. The hypothesis being tested is that the community with increased opportunity for program participation will experience positive physical, behavioral, and perception changes as quantified by these measures.

Evaluation of the MassHealth Essential Care Program:

The objective of this project is to determine the effectiveness of the MassHealth program through a qualitative analysis of case vignettes collected by MassHealth case managers. This research project will involve a process and outcome evaluation that will incorporate elements of participatory evaluation and is based on input from individuals representing key groups that have a stake in the overall success of the program.

Wellmark/Rockwell Collins Worksite Health:

This project is a partnership between the PRC, Wellmark and Rockwell

Collins to improve the health of employees through cost-effective strategies. A community-based participatory research approach will be used to identify potential interventions to address health issues of Rockwell Collins employees. Health risk appraisal data will be analyzed together with claims data from Wellmark to determine opportunities for primary, secondary, and tertiary prevention in addition to determining the cost-effectiveness of potential interventions.

Evaluation of the Paterson Minority Substance Abuse/HIV Prevention Initiative:

This project provides the research component to an effort aimed at developing and coordinating comprehensive community-based substance abuse and HIV prevention services targeting underserved racial and ethnic minority youth in Paterson, New Jersey. The initiative will focus on implementing the CSAP-endorsed CASASTART program to provide substance abuse prevention services to African American/Latino youth ages 8 to 13, as well as expanding Be Proud! Be Responsible! – a CDC-endorsed HIV prevention curriculum currently serving African American and Hispanic/Latino youth and young adults ages 13 to 24.

Preventive Intervention Center (PIC)

PIC is an academic resource to facilitate studies that evaluate the effectiveness of new modalities designed to prevent occurrence and progression of disease. The Preventive Intervention Center was established in 1992 to evaluate population-based prevention strategies including new screening methods and preventive interventions. The Center has participated in NIH sponsored and pharmaceutical company sponsored research of Phase II-IV studies. A major focus has been women's health research including the NIH Women's Health Initiative where the Center was one of the leading recruiting centers. The investigators include members of the CCOM, College of Public Health, College of Dentistry, College of Liberal Arts faculty as well as physicians in Davenport and Des Moines.

The Preventive Intervention Center has completed or is currently conducting over 20 studies. A description of the Center is included in Appendix A as well as recruitment results. The following is a description of similar studies:

The Fracture Intervention Trial (FIT) - This study was funded by Merck & Co., Inc. to evaluate the effect of Alendronate Sodium on the incidence of vertebral fractures and clinical fractures in postmenopausal osteopenic women. This study included women who were postmenopausal age 55 to

79 years of age. Qualification was through a bone density assessment using a Hologic 2000 of 0.68 gm/cm² in hip and stratification by spinal x-ray of vertebral fracture presence. Approximately 4,700 women had screening by telephone and then if qualified (2835) a clinic visit. A total of 611 women were randomized primarily from mass mailings which was 102% of the study goal. The local retention rate was 97%.

The Heart and Estrogen/Progestin Replacement Study - This study is funded by Wyeth-Ayerst Laboratories and coordinated by the University of California at San Francisco. The purpose of this study is to evaluate whether hormone replacement in women post-myocardial infarction will alter cardiovascular and overall outcome. Women were less than 80 years of age with an intact uterus and had evidence of existing clinical heart disease. Primary recruitment was through mailing which included driver's license records, clinic records and insurance records. Phone screens were conducted in 2,262. A total of 205 women in Iowa City were included in the study; 130% of the study goal. The retention rate for this 5-year study was 100%.

The Women's Health Initiative (WHI) - This is a nationwide study that enrolled postmenopausal women in either a clinical trial or an observational study. The clinical trial is evaluating the effect of hormone replacement therapy on heart disease and osteoporosis, dietary changes on heart disease and breast cancer, and calcium/vitamin D on osteoporosis and colorectal cancer. Women between 50 and 79 years of age, who were postmenopausal and were likely to reside in the area for at least 3 years, were recruited. Recruitment was done through mass media, posters, brochures in clinics and mass mailings using driver's license and HCFA lists. Clinic sites were initially located in Iowa City and Davenport and then a site in Davenport was added. The original goal was 3,500 participants. Locally, 5,542 women were enrolled in this 8-12 year study; (158% of the goal). The UI site had the leading number of participants in the hormone replacement therapy arm (1681) and ranked near the top in the observational study participants (3120). Recruitment took more than 4 years and while multiple strategies were used, the most effective method was mass mailings using the driver's license tapes. The overall retention rate is currently 98%.

FIT Long-Extension Study (FLEX) - This follow-up to FIT is examining the long-term safety and efficacy of Alendronate in postmenopausal women who previously took Alendronate as part of FIT. This study is funded by Merck & Co, Inc. This study evaluates the long-term use of alendronate and hence only approximately 300 women were eligible for

FLEX. We enrolled 128 subjects in Iowa City and Davenport. The retention rate is currently 100%.

Medical Therapy of Prostatic Symptoms (MTOPS) – This is a 5-year study funded by the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health. The purpose of the study was to determine the benefits and risks of pharmacotherapies (finasteride and doxazosin) in the clinical progression of benign prostatic hyperplasia (BPH). A total of 165 men, age 50 and older with low peak urinary flow and AUA Score of 8 to 30, were enrolled during an 18 month recruitment period (12/95-7/97).

FIT Genetic Study (see section C.2.1) -This study was locally funded and recruited 140 women who were ineligible for the Fracture Intervention Trial. Seventy cases with low BMD were identified and 70 women with high BMD were selected randomly as controls.

Raloxifene Studies - Two studies were funded by Eli Lilly & Co. The first study (GGHG) included 21 women and compared Raloxifene, Premarin, and Placebo for effects on the uterus. Retention was 95%. The second study (GGIJ) has 14 participants and is evaluating the process of switching from Premarin and Progesterone to Raloxifene and the effects on hot flashes. Retention for this study is 50% (the women stopped the study to go back on hormones because of hot flashes).

Alendronate Studies – Two similar studies are evaluating daily, bi-weekly and weekly doses of Alendronate on BMD in postmenopausal women. One is for osteoporotic women using doses for treating osteoporosis and the other is for osteopenic women using doses for preventing osteoporosis. A third study was conducted to examine the effectiveness of Alendronate in treating osteoporosis in postmenopausal elderly women living in residential treatment facilities. These multicenter studies are funded by Merck & Co, Inc., and involve 21, 18 and 20 women, respectively. The retention rates are 94% or higher for all three studies.

Ibandronate Study - This study is funded by Roche Global Development-Palo Alto and is currently recruiting a total of 48 postmenopausal women. It is evaluating the dose response and safety of an investigational medication or women who are either osteopenic or have normal bone density.

Lipid Research Clinic(LRC)

The LRC has been in operation for over 30 years. It opened in 1972 under the direction of Drs. Francois Abboud and William E. Connor. Funded by the National Institutes of Health (NIH), it was started with a \$12 million grant to mount a clinical trial to examine the beneficial effects of lowering blood cholesterol and a community prevalence study. The center was one of 12 in the nation to participate in the Coronary Primary Prevention Trial (CPPT), which involved 3,810 male subjects. The UI LRC successfully screened over 44,000 age eligible men to obtain 372 participants and became the second largest CPPT site. Dr. Helmut G. Schrott became director of the Coronary Primary Prevention Trial in 1973. The UI CPPT achieved high compliance from participants in taking medication, following diet and maintaining study visits. The study ended in 1984 with a five-year follow-up period lasting until 1989 and demonstrated conclusively that the risk of coronary heart disease can be reduced by lowering blood cholesterol.

Since 1986, the LRC has been conducting pharmaceutical industry sponsored research (Phases II - IV studies) on new or established drugs for the prevention of heart disease and risk factor interventions (e.g. lipids, diabetes, hypertension, menopause), offering coronary preventive strategies for the people of Iowa and surrounding states. To date, the center has been involved in more than 90 clinical trials ranging in duration from less than one month to more than five years. Trials have been conducted for over 25 different pharmaceutical companies and Contract Research Organizations (CROs). Since the end of the CPPT, the clinic has also participated in Nutrition Counseling Programs, the Lipid Disorders Training Workshop (funded by the American Heart Association), the Health Education and Research Trial (HEART - funded by the NIH), and Community Screening Programs.

Population-Based Studies

The Keokuk County Rural Health Study is a population-based, prospective study of health status and environmental exposures of a large stratified random sample of residents in one rural Iowa County. The study, conducted within UI's Great Plains Center for Agricultural Health, focuses on injury and respiratory disease. In addition, it monitors health care delivery, geriatric, reproductive, and mental health, and other health outcomes, as well as behavioral risk factors for disease and injury. Injury and disease prevalence is investigated in relation to occupational, agricultural, and other environmental exposures. The Keokuk County

Rural Health Study has enrolled 2,269 persons, representing 1,004 households. These 1,000+ farm, rural non-farm, and town households, representing men, women, and children, the elderly, farmers and non-farmers, will be studied for a period of 20 years. Although the sample is stratified by residence type (farm, rural non-farm, and town), the entire county is, by definition, rural, since the largest town, Sigourney, has fewer than 2,500 residents. Each participant over the age of eight receives medical screenings in our research facility in Sigourney, the county seat. Those 18 and over are interviewed at length about their health and behavioral risk factors for injury. In addition, they complete detailed occupational surveys. Adolescents (ages 12-17) are interviewed about behavioral risk factors for injury and parents are interviewed about the health of their children (newborn - 17). Each household receives an in-depth environmental assessment of their home and property.

Muscatine Heart Study, one of the largest and longest running studies in the history of cardiovascular research. Ronald M. Lauer, M.D., UI professor of pediatrics and epidemiology, initiated the project in 1970 to determine body size, blood pressure, and cholesterol norms in children. The Muscatine studies have generated a number of significant findings, including:

- Cardiovascular risk factors in childhood are related to risk factors in older adult life.
- Children with the highest levels of blood pressure are more likely to have hypertension as adults.
- Weight and blood pressure track in similar ways individually and, in combination, are very strong predictors for the development of cardiovascular risk factors in adults.
- Children in the upper levels of blood pressure, cholesterol, and body size relative to their peers are more likely to have a family history of cardiovascular morbidity or mortality.

People who participated in the study during the 1970s are now in their mid-30s to mid-40s. Thirty percent of these men and 16 percent of the women show evidence of calcifications in their coronary arteries. Obesity, high blood pressure, and high cholesterol levels in childhood are associated with the presence of calcifications in young adult life.

On going projects address the following: Blood Pressure and Cholesterol Levels in Childhood; Excess Body Weight; Carotid Arteries; and Coronary Artery Calcification. As with other portions of the Muscatine

Study, this research shows the importance of determining the heart disease risk of youngsters so that prevention can begin before symptoms appear.

Recommendations:

- 1) Expand practice networks into research collaborators
- 2) Maintain research resources in communities
- 3) Develop community partnerships with community leaders
- 4) Increase community-based participatory research
- 5) Faculty who participate in community research should be evaluated appropriately

VI. Interface With the Clinical and Translational Science Award (CTSA) Program

A. The Next Paradigm for Clinical/Translational Research

Overview of the new paradigm for c/t research

- Encompass the spectrum of clinical and health services research: physician-scientists pursuing fundamental human disease oriented research; clinical investigators; NIH and industry sponsored clinical trials; clinical epidemiology; and outcomes research.
- Institutional rather than departmental or collegiate infrastructure and orientation.
- Responsive and adaptable to NIH Roadmap.
- Infrastructure should include a readily identifiable and centralized home and advocate for clinical research, but include distinct, service oriented, interactive and facile units and programs.
- Recognition that Information Technology for Clinical Research linked to a Clinical Information System is a critical component of modern clinical research.
- Infrastructure should encompass facilities, core facilities and units, research information technology, training programs, and programs to promote faculty time for clinical research.
- Focus on quality in research and on opportunities to advance patient care and health in the State of Iowa.
- Programs and facilities to support the clinical investigator throughout their careers and not just as trainees and young faculty.
- Emphasize the importance of clinical research to all health science students and promote opportunities for early experiences and training.
- Focus on quality and human subject protection in clinical research.

- Capitalize on academic-industry interface to facilitate clinical and translational research even beyond multi-center clinical trials.
- Capitalize on opportunities for networking with community health care providers across the State.
- Elements of a financial and facilities plan.

B. Overall Summary of the CTSA Assessment

Significant reorganization of the clinical and translational research and training infrastructure is essential for the survival of UI as a premier Institution for Biomedical Research. The NIH Roadmap has mandated a new emphasis on bench to bedside research coupled with mechanisms to implement these studies into patient care in the community. It is expected that this research will be interdisciplinary and involve multiple Colleges within a research community. Therefore, it is mandatory that an Institute for Clinical and Translational Research is created which can bring multiple disciplines together to achieve these goals. This effort must be supported by significant institutional resources and space and be empowered to carry out the mission of the Institute to improve research and training related to clinical and translational research at UI.

Summary

- Much of the clinical and research infrastructure for clinical and translational research at UI either does not exist or is not well designed to facilitate clinical studies.
- There is no integration of training programs for clinical and translational research.
- There is little or no structure to facilitate development of faculty and trainees who wish to conduct clinical and translational research.
- There are no uniform policies that guide the design, budgeting, and implementation of industry supported trials. Nor is there space (inpatient or outpatient) that directly supports these studies.
- Bioinformatics, necessary to support clinical research, is lacking.
- There are few mechanisms to stimulate interdisciplinary and intercollegial research programs.
- There are few mechanisms to foster partnerships and build trust with community physicians and include them in our clinical research enterprise.
- There are few mechanisms that allow for follow-up health care when a clinical trial or treatment ends.
- Expectation should be set across the entire research community that study results and outcomes should be shared with research participants and the larger community promptly and consistently.

- The new NIH roadmap puts increased emphasis on clinical and translational research and training. The infrastructure for this research and training will be supported, in part, by a new NIH CTSA grant that will replace the current GCRC and NCRR K- and T- awards. This grant requires a home (Department, Center, or Institute) for clinical research and training. It also mandates significant institutional support and that the approach to research and training cross disciplinary and Collegiate lines and involve the community.

Recommendations

The mission of the Institute for Clinical and Translational Research should be broadly related to clinical and translational research and training and include community involvement. It will require significant institutional and state resources and space. The Institute for Clinical and Translational Research and must be empowered to create change necessary for the clinical and translational research mission of UI. To function in an optimal manner, the functions of the Institute will need to be broader than those proposed in the NIH CTSA grant. The mission of the Institute should include:

9. Serving as the home for the functions of the CTSA.
10. Integrating clinical and translational research training.
11. Integrating functions that support clinical and translational research, including regulatory support and drug development, essential research core support, pilot grants, and informational technology.
12. Providing an academic home and supportive environment for faculty across the university interested in clinical and translational research, including support for career development.
13. Serving as the engine to bridge basic and clinical research, and to bring these discoveries to Iowa communities.
14. Serving as the engine to develop multidisciplinary research and training programs.
15. Developing partnerships with industry for research.
Developing innovative programs to educate the community and to involve them in education and research programs focused on clinical and translational research.

APPENDICES

1. [Survey of Clinical Researchers](#)
2. [Discussion Matrix on Government](#)
3. [Task Force Members](#)
4. [Specific Recommendations—Resources For Personnel, Facilities, IT](#)