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Academic Health Center

RESEARCH SUPPORT SERVICE TASKFORCE

REPORT TO THE PROVOST

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1.0 EXECUTIVE SUMMARY

1.1 Introduction

The Provost for the Academic Health Center (AHC) assembled a Research Support Service Taskforce in September, 1996. The Taskforce was charged to develop a plan to help faculty by facilitating all of the processes involved in obtaining and performing corporate sponsored research. The fundamental objective is to improve and enhance the ability of faculty to market their research and service capabilities. A collateral goal is to do this while improving and assuring compliance with all federal, state and local regulations and guidelines so that individual faculty members and the institution are protected to the greatest degree possible, and so that the institution will stand behind faculty throughout.

Corporate sponsored research is one area for significant potential growth. Overall, in U.S. and global businesses, there is increased movement to outsourcing as a more efficient, more flexible mode of doing various aspects of business. This trend provides universities with a major opportunity, but one which they can take full advantage of only by delivering value to the corporate sponsor in a timely manner. Corporate sponsors want to deal with quality, responsive organizations and most importantly ones that they can count on. The planning and design phase of the Research Support Service Taskforce was completed over the months of September - December, 1996. The Taskforce report was completed February, 1997.

1.1.1 Objective

The objective of the Research Support Service Taskforce was to examine each and every step in the current process of applying for, receiving, monitoring and reporting on industry-sponsored research. Following the review of current processes and structures, our charge was to recommend changes, as needed, to develop a plan to improve and enhance the ability of faculty to market their research and service capabilities; to develop a plan to aid faculty in being more competitive in attracting corporate sponsored research; and to provide improved service to both sponsors and faculty research investigators through more responsive administrative, oversight, approval, and compliance services; and assure the seamless coordination of all institutional and regulatory policies, procedures, and approvals that affect corporate sponsored research.

1.1.2 Scope of the Review Process

The Research Support Service Taskforce met with a broad group of internal people involved in the management of corporate sponsored research. In general, these included the director and/or other designated senior person(s) of the unit such as representatives of the Institutional Review Board; Human Subjects Committee, the Department of Environmental Health and Safety, the Office of Research Technology Transfer Administration (both Sponsored Projects Administration and Patents and Technology Marketing), the General Clinical Research Center, the co-chief operating officers of the Fairview-University

Medical Center, and the University Vice President for Research, as well as with the AHC Provost and his council. The Research Support Service Taskforce also met with representatives from the Department of Surgery and the Department of Medicine of the Medical School as well as leaders of a number of other clinical departments in the Medical School and leaders involved with clinical trials in other AHC schools. Individuals from outside the AHC and University also met with the Research Support Service Taskforce, including representatives of local and multinational biomedical products corporations and a local medical research foundation that actually competes with us for sponsored research.

In the interest of protecting faculty and the institution, and avoiding some of the problems of the past, the Research Support Service Taskforce also collected and reviewed regulations and policies (federal and institutional) that govern the conduct of sponsored research. Much attention was paid to the institutional committees and processes currently in place designed to assure compliance with these regulations and policies. These regulations and policies are listed in the various appendices, the objective being to have, to the degree possible, all documents, policies and procedures pertaining to sponsored research in one place. This will serve as a resource for all faculty, staff and administration in the AHC or, for that matter, elsewhere in the institution.

This executive summary contains an overview of the Research Support Service Taskforce's principal findings and recommendations. An overriding theme that was seen was that there is no premium or reward for good performance nor consequences for gaps or delays in the overall process. We saw little evidence to show "consumer satisfaction" with any of the individual processes or the overall process.

The remaining sections of this document provide a detailed review of the current performance of research compliance monitoring and research support service functions, goals to improve performance where indicated, and a rationale for any changes recommended.

1.2 Principal Findings

The Taskforce's principal findings focus on opportunities the institution could take to provide more expeditious and improved service to faculty members and research sponsors. Overall, the Taskforce found that:

- there are no time performance demands placed on any area, committee or office involved in overall internal processes of grant submission and approval

- there is much "down" time, where a grant or contract may be in a particular office or with a committee and just "sits". The "action time" in a given committee or office might be very brief, e.g., on the order of 15-30 minutes, but for all intents and purposes the grant or contract may be interred within this office or committee for 30-60 days.

- each office or committee does its work, but there is little to no regard for how this effort could be improved to make the whole process more user-friendly for faculty and sponsors.

- there has been little or no discernible effort to look at how "parallel processing" could insure or improve quality of review, and, from a time perspective, do it in a dramatically enhanced manner. Multiple internal approvals should be acted on contemporaneously.

Recommendations for change made throughout this report are based on the following specific principal findings:

1.2.1 Conflict Review Committee

The Conflict Review Committee (CRC) has greatly expanded its authority significantly beyond that detailed in Regents' policy governing research. This expansion of authority includes, among other things, the review and approval of: (1) all industry-sponsored research whether there is evidence of conflict of interest or not; (2) budgets and research agreements related to industry-sponsored research; and (3) a myriad of other issues that have nothing to do with conflict of interest. We have been unable to find any authorization for extending this purview of review. The CRC currently requires that any potential conflict of interest be eliminated before a faculty member enters into an industry-sponsored research agreement. Federal regulations, Regents' Policy on Conflict of Interest and even the FDA, allow some categories of potential or even real conflict of interest to be managed through peer review or other mechanisms. Externally, the CRC has made the AHC more difficult for industry sponsors to access. It is a focus for scorn and derision often exemplifying how difficult the university is to deal with. Internally, the CRC has substantially delayed, duplicated, and confused the research application process through the expanded authority it has assumed.

1.2.2 Principal Investigator Responsibility

While much attention is paid to the role institutional committees play in the research process, ultimately it is the principal investigator upon whom all responsibility for the research and the associated process and regulation rests. Principal investigators (PIs) are expected to consider the proposed research in terms of: consistency with the mission and goals of the AHC, scientific merit, and feasibility (including financial, clinical and lab facilities, the pool of patients etc.). PIs are expected to define the research team and to assure the qualifications of associate investigators to perform the studies. PIs must insure that these and any other responsibilities are clearly understood by all parties when they delegate authority. It is the responsibility of the PI to develop and negotiate with the sponsor a budget that is adequate to pay for all costs of the study (including indirect cost recovery). PIs are required to identify subjects protection issues, environmental health and safety issues, potential conflict of interest issues, and to apply to the various review committees for approval of the same. PIs are required to be aware of and to comply with research regulations during the application phase and throughout the "life" of the research project. Financial management of the research account is often shared between PIs and department administrators. There is variability among investigators and across

departments in how well these research process responsibilities are met. PIs are often not aware of the scope of their responsibilities nor the consequences of failures to fully adhere to these responsibilities. Even if faculty are fully aware of all of these responsibilities and consequences, many PIs do not have time or trained staff to carry them out. Additional problems are unknowingly created when department administrative or other staff, to whom PIs delegate some responsibilities, are too far removed from the performance of the research project to achieve the desired or even adequate oversight.

1.2.3 Subjects Protection Programs - Human Subjects

For a variety of reasons, in all but a very few cases, the minimum length of time it takes the Institutional Review Board: Human Subjects Committee (IRB) to review and approve a study application is 45 days. It is not uncommon for months to elapse before a study is approved. Much of this "cycle" time is really down time during which not much active effort is being put toward the process. This time tends to represent time of mailing, response time of PIs, getting the study back into the queue for review, etc. The approval process is extended by the time it takes IRB staff to develop responses to initial applications and research investigators to develop responses to stipulations which must be addressed prior to getting approval. While there are a number of IRB panels, each panel meets only once per month. This meeting schedule, combined with drawn out cycle times involving communication between research investigators and the IRB, results in delays that are frustrating to faculty and increasingly unacceptable to research sponsors. The IRB process appears to be one in which much improvement could occur in time management with no compromise in quality of IRB decisions. There is also a concern on the part of faculty about the variability of review within and between IRB panels. Regulations and guidelines concerning the use of human subjects do not change frequently, but the application of these regulations and guidelines, and the definition of "local standards" varies between IRB committee panels.

1.2.4 ORTTA - Patents and Technology Marketing (PTM)

Patents and Technology Marketing for the AHC is under-resourced. There appears to be a shifting of royalty revenue from AHC PTM to support other activities not directly benefiting AHC faculty. This has long term adverse consequences for the AHC and, in fact, the University. As but one example, for a variety of reasons, Patents and Technology Marketing currently turns away 75 - 80% of the disclosures received each year. Patents are filed on the remaining 20 - 25% of disclosures. Decisions about filing patents are influenced, primarily, by the imputed value of royalties expected to be received for the technology. Therefore, among other things, budget constraints and the very reasonable desire to have "licensable technology" may hold down filings to the patent and trademark office. Greater than 90% of royalty income to the University comes from technology discovered by faculty in the AHC. This being the case, one wonders why resources are not redirected to support AHC PTM and/or cut back in other areas? It appears that PTM personnel also have their time divided by having to respond to distractions that compromise the overall time they have

available to aggressively market faculty technology. Some of these distractions involve getting into resolving perceived conflict of interest issues, including time spent responding to issues raised by the current CRC, and numerous other things that appear to encumber the time to do what may be their most important function - marketing technology and services and facilitating and promoting entrepreneurial activity of faculty.

While a cursory review of royalty income and licensing fees may provide one measure of the performance of ORTTA's patents and technology marketing function, there is considerable evidence in the U.S. and abroad that this may not be the best way to evaluate performance. In fact, it may even be misleading. A summary of reports dealing with this (available on various web sites) is excerpted as an appendix. A theme running through a number of these documents is that the greatest value of university technologies is not necessarily represented in the form of royalties and licensing but rather in generating entrepreneurial activities. It suggests there is greater value, or that it may be more relevant to examine the investment in enterprises or parts of businesses focused around a university faculty member's technology than simply waiting for and tallying royalty income. Most university-derived technology is very early stage and, as such, requires much time and money (generally many, many years) before any royalties might be realized, i.e., it might be 7 - 10 years.

It appears there is little to no activity on the part of PTM in promoting these entrepreneurial activities. In fact, because of PTM/ORTTA getting involved in various other areas such as the area of conflict of interest, the University may actually suppress these types of entrepreneurial activities. This is paradoxical as this may be the most important paradigm for promoting and deriving value from university faculty technology. The increase in entrepreneurial successes and the proliferation of numerous high technology companies with high paying jobs in the Palo Alto area and the greater Boston area speaks for itself. There have been few to no companies in recent (and even not so recent) years that have been started based on AHC faculty technology.

1.2.5 ORTTA - Sponsored Projects Administration

The performance of Sponsored Projects Administration (SPA) responsibilities appears to be compromised by a staff insufficient in number to manage the volume of projects, and by the variable quality (not from a scientific standpoint of view) of applications and supporting materials faculty send to SPA. The SPA proposal and award processes for industry-sponsored research take, in the best case, several weeks and, in the worst cases, several months. For many reasons, much of this is "down" time with little to no activity on any given grant proposal, sometimes because SPA may get a batch of grants at one time. SPA staff spend much of their time reviewing industry-sponsored project research agreements for intellectual property and publication rights. Once reviewed, changes to the research agreements must be renegotiated with the faculty member and the corporate sponsor. One of a number of circumstances exacerbating the problem is that SPA staff time is diverted to the review of confidentiality agreements and material transfer agreements while the backlog of proposals they must process often continues to grow. Indirect cost recovery (ICR) negotiation (while ICR is rarely, if ever, negotiable) is an added burden for

SPA staff managing industry-sponsored research. Frequently, for obvious reasons, corporate sponsors will attempt to downwardly negotiate this. In summary, there are many time consuming, sometimes complicated and competing demands on SPA staff which make their work difficult to prioritize. Also, because of other "unlinked" university processes, how and when SPA receives proposals causes problems in its own right in that they frequently get a large group of these at one time that have accumulated in the Conflict of Interest Committee.

1.2.6 Coordination of Clinical Trials Review Processes

There is no overall coordination of clinical trials in the institution. One area performing clinical trials is the General Clinical Research Center. Recently, the Cancer Center has established a protocol review committee. All other clinical trials falling outside of these areas are developed on an ad hoc basis. There is little opportunity to negotiate internally to aggregate any of the support services needed to perform these studies, so there is no discount on hospital beds, lab or other services. There is also great difficulty finding space for a patient where they may need to be in the institution for a few hours, e.g., 2 - 8 but not for a full day.

1.2.7 General Clinical Research Center

The General Clinical Research Center (GCRC) is an important component of the AHC. It is designed and funded by the NIH to assist faculty wishing to conduct clinical research in a very controlled setting. Unfortunately, the GCRC is used for no more than 5% of the clinical research in the AHC. The primary objective of the GCRC is to support investigator initiated, hypothesis driven clinical research. Because of this and the responsibility it has to fulfill this function for NIH, the GCRC appears to have ambivalent views on the desirability and the amount of corporate sponsored research it wishes to incur. The ambivalence is seemingly related to the fact that supporting corporate sponsored research is not the core mission of the NIH sponsored GCRC. On the other hand, corporate sponsored research trials are a source of revenue for the GCRC and fill up excess or unused capacity of the GCRC and its staff. Overall, however, the GCRC appears to function in a way to make it somewhat difficult for PIs wishing to do corporate sponsored research. One disadvantage to using the GCRC for industry-sponsored clinical trials is the daily charge of $725 for each hospital bed. This daily rate is not competitive with what corporate sponsors can get at other institutions. As a consequence, the AHC is losing industry-sponsored clinical research opportunities that involve the need for inpatient space. Another disadvantage is that the GCRC has its own review committee that passes judgment on whether a given study can be performed in the GCRC or not. Often the GCRC review committee will not accept FDA approved industry protocols. In cases in which the committee grants approval, the time necessary to obtain approval may span an average of 2 - 3 months. Other possible overarching disincentives to using the GCRC are its location on the 2nd floor of the Masonic Cancer Center, where it is out of the mainstream for most clinical staff, and the age and general condition of the facility.

1.2.8 Monitoring Compliance with Research Regulations

Monitoring compliance with research regulations at the University of Minnesota is limited almost exclusively to the approval phase of the proposed research. Compliance monitoring by institutional committees and university officials over the life of a research project is limited (in the case of the IRB) or non-existent. Principal investigators and the IRB staff are expected to become aware of and to comply with federal, (and state or local, if applicable) regulations and institutional policies related to sponsored research. Principal investigators are provided little, if any, training or support in developing a knowledge base about all regulations upon which investigator based compliance strategies can be formed. It is difficult to imagine that more than a very few principal investigators would be completely and thoroughly aware of the myriad of requirements expected of them or of the full consequences of not adhering to them.

1.3 Recommendations

One of the critical observations made by the Research Support Service Taskforce is a pervasive lack of performance criteria for almost each component of a research contract: submission, approval and execution of the research. We are struck by the fact there is little, and in some cases no, regard for the value of time.

Overall, the Taskforce recommends the following actions:

- Establish very rigorous performance criteria for each office, unit, or committee that is involved in initiation, approval, performance and closing of research projects sponsored by outside corporations. Assume that professionals in these offices have the authority they need and hold them accountable. Overall, there is a need to adopt more of a service mentality on the part of all staff.

- Establish a parallel review and approval process for all internal approvals and committee reviews. In negotiations, no 24 hour period should expire without the appropriate university official contacting both the corporation's representative and the university faculty member. It is the expressed goal of the-Research Support Service Taskforce to have the internal review and approval/denial process of all aspects of industry-sponsored research applications to be completed within 10 working days of application submission, without sacrificing the current high quality of the review.

- Establish a process in which an activity sheet will be placed on the front of each contract or grant that tracks time in and time out with a uniform office stamp. Professionals in the office would initial as things move along. In turn, this would establish a log of all actions and time taken to accomplish the work. Once this became routine it would not be very obtrusive. This is much the way other professionals such as lawyers and accountants work. Failing to institute such a tracking process would make it hopelessly

difficult to evaluate performance and timeliness through the various offices, committees, etc.

Detailed recommendations are provided throughout this document. The following specific recommendations address the improvements and changes that emerged from and correspond with the principal findings.

1.3.1 Disband the Conflict Review Committee

Establish a new, AHC wide committee to review conflict of interest issues (disband the current Medical School Conflict Review Committee immediately within an interim procedure developed). This committee should be named the Conflict Review and Management Committee (CRMC). The CRMC will include representatives from the AHC schools all of whom will have had research supported by corporate sponsors, representatives from either industry or government, and one non-voting representative from ORTTA. Other configurations of this committee might be as or more desirable. The CRMC should have a redefined role and much more restricted scope of responsibility than the Medical School Conflict Review Committee. The overall objective should be to manage any real or perceived potential conflicts of interest or commitment. The CRMC should develop management plans to assure scientific integrity to the highest degree possible when a conflict of interest may be determined to exist. These management plans should include review of study data by scientific advisory boards or peer review committees, and random reviews of research conducted by potentially "conflicted" investigators.

University policy should allow faculty to have recourse and department heads, directors, and deans to give authority for review of potential conflict of interest to a central research conflict management review and support group.

1.3.2 Establish a Research Support Service Office

The AHC should establish a Research Support Service Office with a director reporting into the provost's office. This office should provide research support to investigators who want assistance with industry-sponsored research processes from initial idea to final report. The Research Support Services Office staff's principal task is to facilitate and expedite research processes for faculty in grant application, committee approvals, budgeting, etc. The research support service office should share with principal investigators the responsibility for determining the financial viability, and assuring regulatory compliance of all research projects. The Research Support Service Managers will assist and partner with principal investigators in preparing and submitting proposals; reviewing clinical research protocols; preparing regulatory documents and applications for internal review committees; obtaining internal and external approvals and authorizations; developing, negotiating, reviewing and monitoring contracts and budgets; monitoring study progress; ensuring performance and compliance of the research team with the terms of the contract or grant; assuring compliance with internal policies and external regulations; directing FDA and sponsor audits; and performing all required study close-out functions. Faculty

support from knowledgeable Research Support Service Managers should enhance the quality of application materials submitted to institutional committees and provide information to faculty which they may draw upon during the performance of the project. Better preparation of applications, and particularly the supporting materials, should reduce the review time and ideally obviate the need for the recycling of proposals among institutional committees. Providing better information to faculty should improve compliance with research regulations before a process for spot checking or monitoring by the AHC is established.

The Research Support Service Office will also provide the business development services listed below.

1.3.3 Establish a Business Development Office

The AHC should better coordinate, promote, and serve faculty in their efforts to seek corporate sponsored research. The AHC should set goals consistent with its mission that complement research and discovery.

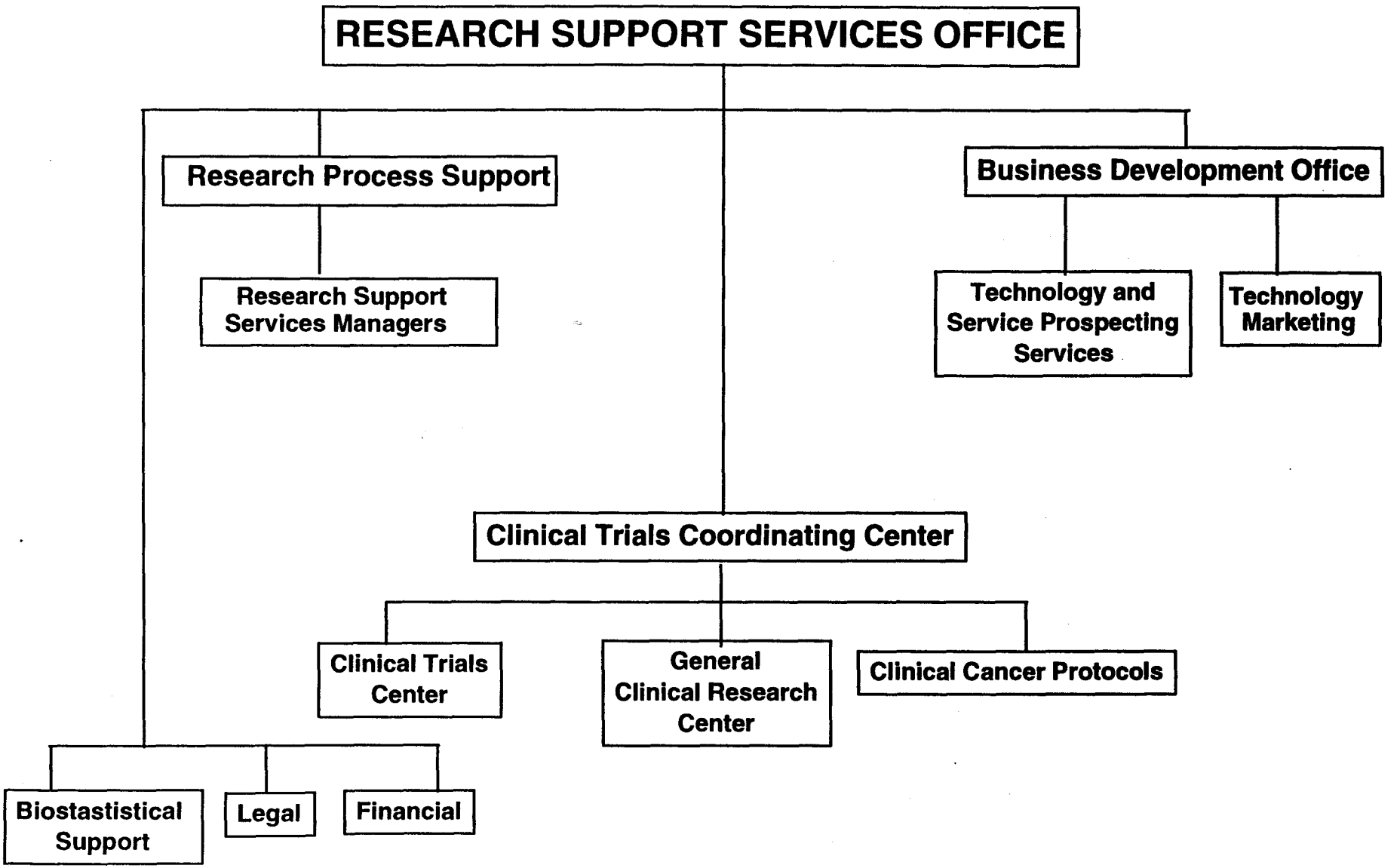
The Taskforce recommends developing a Business Development Office function within the Research Support Service Office. See Figure XYZ below depicting this on an organization/functions chart. An external advisory board will review and provide technical or market analysis of AHC technology and services. This would cover biomedical, biotechnology, bioengineering and other human and animal health related technologies, services and products.

A subsidiary function in the Business Development Office (BDO) would be a "prospecting" function. An individual, or individuals if so needed, would have responsibility for working with faculty, department heads, deans, and center or institute directors to identify technology and services that could be protected by patents or trademarks, if applicable, and then marketed. This person's job would be to develop relationships with faculty. His/her office would be a "clearinghouse" for faculty to go for advice and services in this area of intellectual property.

The Business Development Office would also have an individual or individuals whose exclusive responsibility would be marketing of AHC faculty technology and services on a local, national or global level. Technology marketing would include among other things: licensing, research & development agreements with companies and establishment of new ventures or joint ventures with university faculty as participants, to the degree they desire this.

The Taskforce recommends that licensing and royalty income (i.e, 33% that is institutional currently going to ORTTA) and other consideration derived from AHC technology and services should be allocated to the AHC. The 33% of royalty net income that is generated from AHC technologies could be used to supplement other resources to establish a Technology Investment Pool. This pool could be used to:

- invest in promising AHC technologies and services that may have commercial value,
- match funds for industry funded research and development within the AHC,


RESEARCH SUPPORT SERVICES OFFICE
Research Process Support
Research Support Services Managers
Business Development Office
Technology and Service Prospecting Services
Technology Marketing
Clinical Trials Coordinating Center
Clinical Trials Center
General Clinical Research Center
Clinical Cancer Protocols
Biostastistical Support
Legal
Financial

- provide incentives to investigators for disclosures that lead to licensure and facilitate an entrepreneurial research environment, and

- take equity positions in companies starting up with AHC technologies.

The primary goal of local AHC management of its corporate sponsored service and research program should be to enhance the overall success of faculty through a more expeditious and user-friendly process.

1.3.4 Enhance Performance of Subjects Protection Programs - Human Subjects Review Process

To achieve more thorough understanding and, as a result, better research applications, the University should provide sufficient staff to allow Subjects Protection Programs to actively and frequently train, consult, and provide information services to the University research community. This service to faculty needs to be provided on an ongoing basis not just on the front end, i.e., grant submission. Leaders to whom Subjects Protection Programs now report (the Vice President for Research and the Director of Research Ethics and Regulatory Compliance) assume performance responsibility for Subjects Protection Programs in terms of internal performance criteria (timeliness, quality, and consistency) as well as in terms of the external review requirements of Federal agencies.

One way to recognize the importance of services performed by members of the IRB is to have committee members be paid (or have salary offset) for their service. Given the pressure on all financial resources, it is not reasonable to expect faculty or other volunteers to be able to dramatically improve performance given all their competing demands. A small number of well-trained committee members could serve on one of two committee panels. Providing compensation or other consideration, training, and performance benchmarks to panel members should create more effective and responsive committees that could meet with much greater frequency of cycles for any one panel than is currently present. Reducing the number of panels and perhaps committee members, will increase the IRB's opportunity to be as consistent as possible in their review of research applications. Additionally, more executive level administrative staff are needed to support committee panels, manage the hoped for increased volume of research, and write the somewhat complex correspondence required.

Without compromising the quality of review the IRB review process could be made more efficient by allowing the committee panels and research investigators to interact via video-conference at the time of review of the proposal. In this way, the principal investigator could immediately address many of the questions a committee panel might have and thereby potentially remove the need for proposals cycling back and forth to the committee.

Another way to save time in the process would be for the IRB to take advantage of courier, e-mail, and fax services to get time-sensitive correspondence to and from PIs.

Setting up a web site where IRB results could be immediately posted would aid in this and could serve as an educational tool for faculty and staff to gain experience in the process from the experiences of others.

1.3.5 Improve and Expedite Contract Review and Negotiation

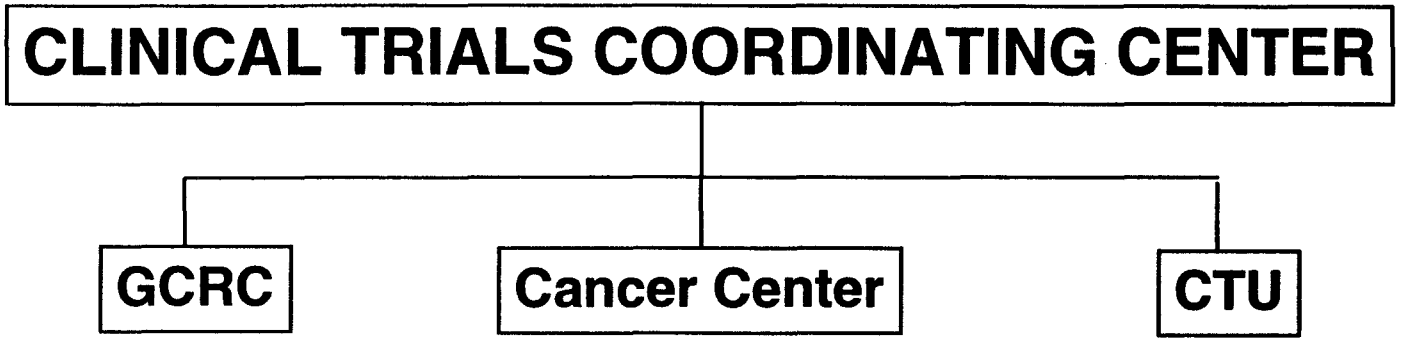
Sponsored Projects Administration (SPA) should identify the common problem areas in proposal and award processes. This information and instruction from SPA should be systematically distributed to the University research community, PI's, support staff, and be used to address these common problem areas. The process could be facilitated if the AHC had an on-site representative from SPA. This representative would have the authority to approve and sign contracts, establish CUFS accounts, and authorize purchases. In addition, SPA and the AHC should collaborate in developing (or revising) a standard research agreement (or if necessary set up agreements) for industry-sponsored research. Optional language for various sections should be developed and agreed upon internally as being acceptable to the University. This should aid in coming to acceptable terms with sponsors rather than starting from scratch with each agreement. There could be the development of an "expert system" that provides information to principal investigators and their staff to avoid these common pitfalls.

1.3.6 Establish a Clinical Trials Coordinating Center

It is recommended that a Clinical Trials Coordinating Center be established within the AHC. This would serve as a site for coordinating all clinical trials efforts in humans and animals. Figure XYZ shows a potential organizational chart of how this might work. For human trials, a clinical trials unit would be established. It would be "virtual", where patients could be integrated into the overall clinical operation of the new Fairview University Medical Center. Specialized research nursing and technical staff should be available to administer study protocols, perform minor procedures, manage specimens and data, and perform other trial or research related tasks. There is a need for overnight and also short stay or "day" clinical facilities. This clinical trials unit must be a service to investigators, welcome them, and assist them in the successful conduct of each study. It is believed that bundling all clinical trials together could aid in deriving the best prices for hospital beds and services. The aggregate cost of these services cannot exceed what the market will bear if the AHC is to compete for industry-sponsored clinical trials dollars.

The General Clinical Research Center and the Cancer Center each have a separate review process for clinical trials. Protocols for patients on cancer trials must be reviewed by an NCI mandated committee affiliated with the Cancer Center. All clinical trials, whether under the purview of the GCRC or the Cancer Center Protocol Review Committee or not, have many things in common. It seems reasonable that these separate review processes all be coordinated.

The GCRC could possibly function as a component of the Clinical Trials Unit and the Clinical Trials Coordinating Center. The GCRC has certain special needs that may make it difficult to function in a "virtual" manner. As the integration of UMHC and Fairview continues, where the GCRC is situated,



CTC = Clinical Trials Coordinating Center

GCRC = General Clinical Research Center

CTU = Clinical Trials Unit. Performs trials not in GCRC, or under the aegis of the Cancer Center Protocol Review

Cancer Center = Provides protocol review for patients with cancer involved in studies

whether it can be "virtual" and how the GCRC and other human trials units might function needs to be addressed.

1.3.7 Provide Support for Regulatory Compliance Monitoring

The AHC should develop an explicit plan to spot check or monitor and report compliance with all research regulations and policies. As is all too obvious from reading local and even national newspapers, failures to exactly adhere to regulatory guidelines, e.g., Food and Drug Administration, National Institutes of Health and others, can have disastrous and expensive consequences. Given the open, and thus vulnerable, nature of the university, it is surprising that more has not been done to remedy this situation.

Subjects Protection Programs and the Department of Environmental Health and Safety (DEHS) should implement compliance monitoring programs which span the duration of research projects. While not in the immediate purview of the Research Support Service Taskforce, for research involving humans, compliance monitoring of research not regulated by the Food and Drug Administration (FDA) should take priority over the need to monitor research that is more regulated and monitored such as industry-sponsored research by a major pharmaceutical company.

Departments, colleges/schools, and provostial units should assume greater local responsibility for protecting their interests and those of the institution in complying with the DEHS regulations. An individual in each college/school should be identified as the designated responsible party for DEHS compliance.

The AHC should provide coordinated regulation and policy update information in the form of educational training programs and by electronic means to assure that investigators are aware of regulations and changes to them.

The University should develop a reader friendly, electronic, Good Scientific Practices document to guide faculty, staff and students in their conduct of research. Clear instructions and guidance for faculty and staff is needed to inform all in how to deal with this very "charged" issue. There also needs to be better education of faculty and staff on issues surrounding scientific or academic misconduct. With respect to alleged or actual scientific/academic misconduct, the appropriate institutional authority should, at the appropriate time, without compromising the rights of complainants or respondents provide information to the institution's research community so that the experience can be shared.

1.4 Conclusion

Considerations that guided all discussions and reviews were: how can the AHC best provide service to faculty and sponsors; provide responsive administrative, management, and compliance services; and coordinate federal and institutional policies and procedures that affect sponsored research? The purpose of this review of current processes involved in corporate sponsored research was to identify barriers, bottlenecks, and weaknesses in these processes and structures, and to recommend changes, as needed, to promote industry-sponsored research in the AHC. The major objective is to promote industry-sponsored research for the faculty in the AHC.

Our principal findings show that institutional research committees and research support services must change, not to adversely impact the quality of their reviews but to streamline, prevent undue delays, and develop a "seamless" hands-off processing method so that much, if not all, of this can occur in parallel. These committees and support services play an important role in sponsored research; however, as these groups are quick to point out, the principal investigator has the ultimate responsibility to "know and do the right thing". This runs counter to the notion many principal investigators have, that research review committees and support services share their responsibilities and somehow offer protection in the event an error (of omission or commission) occurs. Failure to fully understand these circumstances creates a dissonance that has led to bad feelings, counterproductive actions and reactions, and bad press. Frequently, faculty do not have experienced staff upon which they can rely to assist them with the long lists of research responsibilities and compliance demands.

There is evidence from within the institution that improvement in our research processes, especially improved timeliness and responsiveness, is desired. There is evidence from outside the institution that improvement in our research processes is essential. In meetings with nearly all the groups about what performance change recommendations might be made, a desire and real commitment to maintaining quality and improving the functions was evident. There is also evidence that faculty could benefit from the assistance of knowledgeable support staff throughout various aspects of these research processes. PIs electing to use the Research Support Service Office will be able to assume, correctly, that their responsibilities are shared by experienced, informed, accountable staff.

2.0 IMPROVING EXISTING STRUCTURES AND PROCESSES

2.1 Introduction

The Research Support Services Taskforce was charged, among other things, to develop a plan to provide better, more expeditious and user friendly support and service to faculty investigators and research sponsors. As part of this plan, the committee was charged to assure that administrative, management, and compliance services are provided in a responsive, timely and accountable manner. By having high quality expedited processing of all aspects of grant approvals, etc. and a frustration free expedited submission of proposals, corporate sponsors would come to value this and likely increase their investment in and expenditures with University of Minnesota faculty.

In order to accomplish this we looked at each and every step of developing a proposal and budgets, submitting and getting approvals, setting up accounts and monitoring inflow and outflow of funds, filing of reports and complying with all appropriate regulatory requirements. An overriding objective is to help faculty get corporate sponsored research and to protect them and the institution from untoward actions of regulatory agencies.

The current performance of committees and institutional service groups involved with industry-sponsored research in the AHC has been reviewed. The findings of the Research Support Service Taskforce are included, as are the new performance goals and recommendations for change.

2.2 Conflict Review Committee (Board of Regents' Conflict of Interest Policy) and Board of Regents' Academic Misconduct Policy

The AHC is committed to developing relationships with industry that will benefit the public, the AHC and its faculty, and industrial research sponsors. The University can do this while following its education, research and outreach/service missions. While the AHC is committed to developing these relationships, it is also committed to promoting and maintaining public trust in the judgment and conduct of its researchers and clinicians. The way the University can maintain and enhance this public trust is by assuring that these activities are conducted in accordance with the highest standards of integrity and ethics.

Assuring scientific integrity at the University of Minnesota is directed by the Board of Regents' Conflict of Interest Policy and the Board of Regents' Academic Misconduct Policy. The AHC will apply these policies in the firm belief that its researchers are honest, committed to protecting the public interest and their own integrity, and will adhere to the highest ethical standards in the conduct of their research.

The Academic Misconduct Policy provides the mechanism for dealing with cases of alleged scientific/academic misconduct. Procedures for reporting and managing allegations of research misconduct including: scientific misappropriation, interference, or misrepresentation; obstruction of investigations of research misconduct, and noncompliance with research regulations have been discussed at Responsible Conduct of Research workshops. These workshops have been run as of 1996 and will continue to be held.

Since 1994, the Medical School Conflict Review Committee (CRC) has reviewed all industry-sponsored research proposals with budgets exceeding $10,000. The CRC has served as the advisory group to the Dean of the Medical School on conflict of interest issues for medical school investigators proposing to conduct industry-sponsored research. To our knowledge, no other school in the AHC has such a committee. It appears that the CRC functions to eliminate all real or perceived conflict of interest.

2.2.1 Current Performance - Conflict Review Committee

The CRC has expanded its authority well beyond that detailed in Regents' policy to include review and approval of various things that have nothing to do with conflict of interest. The CRC currently requires that any potential conflict of interest must be eliminated before an investigator enters into an industry-sponsored research agreement. Federal regulation and Regents' Policy on Conflict of Interest allow some categories of potential conflict of interest to be managed through peer review or other mechanisms.

The average length from application to CRC approval is approximately one month. However, there are numerous applications that remain tabled or that go unresolved for many months - sometimes indefinitely.

It is a common occurrence, weekly or more often in meetings in the community, that business leaders or government officials disparage the University and the AHC because of difficulty in dealing with us. They commonly cite the Conflict Review Committee as needing substantial remediation and fault University leadership for not addressing this.

2.2.2 Current Performance - Application of Academic Misconduct Policy

Information regarding the application of Regents' Policy on Academic Misconduct is not available beyond the guidelines evident in the policy. The Office of the Vice President for Academic Affairs is responsible for the application of this policy and is the main point of contact.

2.2.3 Goals and Recommendations for Conflict Review Committee

We recommend that the current CRC be disbanded and a new Conflict of Interest Review and Management Committee (CRMC) be formed. (See the Executive Summary for the proposed new committee membership.) This new committee should acknowledge its more circumscribed role and restrict this to managing real or perceived conflicts. Many issues the old CRC has dealt with come under the purview of various other offices at the University such as ORTTA. For example, Sponsored Projects Administration has a major role to play in the overall grant process regarding budgets. If this and various other aspects of the grant process are respected, it will limit the scope of CRMC proposal review to nothing other than conflict of interest policy issues and with a directive or mandate to provide solutions that still permit the faculty to perform the corporate sponsored research except in the most unusual circumstances.

The CRMC should thoughtfully consider and, if necessary, actively assist faculty in preparing processes and plans to properly manage situations in which potential conflicts of interest may seem, to critical observers, to have the potential to bias research results. Some examples of ways for the organization to deal with this potential or with the perception for the biasing of research owing to financial gain include: putting any equity, stock options or warrants in escrow until completion of multi-center trials and having the data file submitted or "locked" at the FDA; holding consulting money in escrow until a like occurrence; appointing an ad hoc peer review group to meet quarterly to review the research; and various other means.

Only in cases in which a potential conflict of interest is determined to exist, should applications be reviewed by the CRMC. The Committee should meet as often as necessary (no less often than bi-weekly) to review applications which might be referred to it.

The CRMC review process should be limited to addressing the issue of investigators' (or immediate family) external financial relationships and review and approval of the proposed plan to manage the perceived potential conflict. The Committee will review applications in less than 10 working days and may recommend approving or denying the plan for managing the potential conflict. It should be the preponderant outcome that a plan for management of the situation, not denial of the proposal, occurs.

The final decision authority should rest with the AHC, e.g., Vice Provost for Research or deans who may seek the recommendation of the Public Private Partnerships Committee at the University level for advice and recommendation if necessary.

The rationale for proposed management options is to protect the institution and its faculty and staff from real or perceived impropriety. The rationale is to restrict any realization of economic gains until the work has been corroborated or reviewed by others than the PI who will no longer be able to influence the results after the sponsor database is locked or after the final independently audited or peer reviewed report is issued to the sponsor. It should be noted that other management options could be developed, but they must unambiguously pass the "sniff test" for propriety in the public's opinion.

Income exceeding $10,000 per year received for consulting relationships or board appointments, and familial financial relationships which may introduce the potential for conflict of interest are all proposed to be managed in a manner similar to that described for the management of stock/equity or options.

Assistance should be provided to faculty in reviewing the policy and his/her external relationships, and in choosing the best management plan for assuring scientific integrity whenever a potential conflict of interest may appear that could potentially bias the outcome of the research. Department heads/directors and deans should be allowed to delegate authority for review of potential conflict of interest to the Research Support Service Office. If they elect to retain this authority and the responsibilities associated with it, the same performance relative to determining a management plan, and timeliness is expected.

Options for Managing Potential Conflicts of Interest

Potential conflicts of interest may be created by, but are not restricted to, the following relationships between the faculty member, their staff or immediate faculty and the proposed industry sponsor: owning equity, warrants, or rights to stock options, consulting agreements, and serving on advisory or other board appointments where some consideration is provided.

The conflict management plan for all potential conflicts of interest could include, among other things:

- A detailed description of the conflict management plan signed and submitted by the faculty member prior to the initiation of the project.
- Formation of an ad hoc scientific peer review committee that will:
  - review the proposed study protocol, identify areas where there is concern about the potential to introduce bias, and review the management plan designed by the Research Support Service Manager and the faculty member to mitigate this, and,
  - audit the study as it proceeds and upon completion (including the collection and analysis of data). If the industry sponsor is monitoring the regulatory compliance and clinical practice of the investigator, the AHC will not, in general, duplicate this review. If this review is not provided for by other objective means a system providing for spot checks will be instituted.
- A detailed post-contract completion report documenting the management process for the potential conflict of interest.

Ownership of stock/equity options or warrants exceeding $10,000 or more than 5% ownership interest of the entity (present market value) are proposed to be managed as follows:

- Human Clinical Trials: The stock/equity will be put in trust until such time the clinical trial database is "locked" by the sponsor. At this point in a study there has been data collected from single or multi-center trials and there is no longer an ability for the PI to influence this data.
- Animal Trials: The stock/equity options, etc., will be put in trust until the final quality assurance audit report is issued to the sponsor. This final audit is typically performed by an outside company/or service.
- "Bench"/Basic Research: The stock/equity options, etc., will be put in escrow or trust until peer review or independent audit of the final report to the sponsor is completed.

2.2.4 Goals and Recommendations Regarding Application of the Academic Misconduct Policy

The Vice President for Academic Affairs, as the responsible institutional authority for the Academic Misconduct Policy, should commission the faculty and staff to develop a Good Scientific Practices document to guide the conduct of research at the University of Minnesota.

2.2.5 Rationale

It is unlikely that the current CRC (established for the Medical School) would voluntarily relinquish much, if any, of the expanded authority it has assumed. The current committee does not represent all, or a majority of AHC schools as the newly constituted CRMC surely must. Requiring CRMC committee members to have had prior experience with industry/academic institution research relationships will protect the integrity of research (and thereby the public and the AHC) without compromising the ability of the AHC to cultivate research relationships with business and industry. It may be reasonable to provide some consideration for compensation or salary offsets for faculty serving on this committee, depending on how extensive the time commitment is.

The Research Support Service Office will provide support to faculty in reviewing the proposal and protocol, the PI's external relationships, the identification of any potential conflict of interest, and a plan to manage the potential conflict, should one exist. The Research Support Service Office will also provide biostatistical assistance to the PI to assure that the sample size and statistical design are adequate to answer the research question. Overall, the best way to assure scientific integrity is to begin with a well conceived and well-designed study.

Department heads, institute directors and deans are currently responsible for determining whether an industry-sponsored research application should be sent to the CRC. Because deans are overburdened with a myriad of responsibilities the Research Support Service Office will perform this review, develop a management plan for any potential conflicts of interest, forward the disclosure and management plan to the CRMC, and provide information to the Department head and/or Dean for their information.

2.2.6 For More Information

Board of Regents' Policy: Conflict of Interest	http://www.fdp.finop.umn.edu
Office of Research Integrity Advisory Document: Model Policy and Procedures for Responding to Allegations of Scientific Misconduct - April 1995	http://www.os.dhhs.gov/phs/ori/policy/policy.html
University of Minnesota Board of Regents' Policy: Academic Misconduct	http://www.ortta.umn.edu/policy/respolcy.htm
Integrity and Misconduct in Research (Report of the Commission on Research Integrity)	http://law.house.gov/7.htm

2.3 Subjects Protection Programs (Human and Animal Subjects) Human Subjects[1]

The Institutional Review Board: Human Subjects Committee (IRB) is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the University of Minnesota. The IRB has authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction as specified by both the federal regulations and Regents' Policy.

The IRB carries out its responsibilities through review and approval of research, through continuing reviews of approved research, and through collecting and determining the significance of adverse events experienced during clinical research. PIs are required to report to the IRB any changes made to the research plan during the conduct of the study, and the incidence of serious or unexpected events.

The IRB is required to follow two sets of federal regulations: Department of Health and Human Services (DHHS) Regulations and Policies, and Food and Drug Administration (FDA) Regulations and Policies. The FDA regulates but does not usually support or conduct research. While the FDA is a DHHS agency, its regulatory mandate differs substantially from other DHHS agencies that conduct and support a significant amount of research.

The University of Minnesota IRB includes approximately 75 members that form six committee panels: 4 medical, 1 social sciences, and an executive panel. Each of the 4 medical panels and the social sciences panel meets once each month. Agendas for each medical and social sciences committee meeting may include as many as 30 different projects to review.

2.3.1 Current Performance - Human Subjects Protection Programs

Many faculty research investigators are not fully aware of all of the regulations, guidelines, and community standards by which their research applications will be judged. The application may be confusing and consent forms investigators submit for IRB review may reflect the research investigators' lack of familiarity with regulations, guidelines, and local standards.

In all but a very few cases, the minimum length of time it takes the IRB to review and approve a study application is 45 days. It is not uncommon for 60 days or more to elapse before final notification of approval of a clinical study is received by the PI

In the review process of an application submitted to the IRB there are a number of processes in which time management could be improved. For example, the approval process is delayed when IRB staff must request additional information from the PI or changes prior to approval being granted. If improved information had been provided at the original submission, this recycling could be obviated. There may be considerable time delays when the proposal is back in the hands of the faculty member for his/her response to the IRB's questions and comments and there is additional time taken with the subsequent recycling through the process. These communications back and forth between the PI and IRB staff sometimes may be very simple but are often complex and can be time

consuming to prepare. Responses are often further delayed by sending them through the mail.

The committee may approve the PI's response to stipulations or may add more stipulations, in which case the process is repeated. Overall, the "cycle" times can amount to a significant number of months when all is said and done.

PIs are frequently frustrated by the variable review between and within IRB committee panels. What may be approved by one committee panel may not be approved for a similar project reviewed by a different panel. While the regulations and guidelines do not change frequently, the application of these regulations and guidelines by individual IRB committees and, more commonly, the "local" standard, varies between committee panels, sometimes significantly.

After the proposed research is approved by the IRB and the PI is notified, the PI is thereafter responsible for complying with federal human subjects regulations and guidelines as the research is conducted. To assist faculty in meeting their responsibility, the IRB provides information to the research community in a subjects protection programs column that appears each month in the ORTTA publication - *Research Review*. The Subjects Protection Programs office collates these columns approximately annually, and provides the document to research investigators as a local guide to subjects protection. A member of the IRB administrative staff or a member of one of the committee panels participates in the annual Responsible Conduct of Research workshop to provide human subjects-related training to the University of Minnesota research community.

2.3.2 Goals and Recommendations - Human Subjects Protection Program

It is the expressed goal of the Research Support Service Taskforce to have the IRB review and approval/denial process for industry-sponsored research applications to be completed within 10 working days of application submission, without sacrificing the current high quality of the review.

The institution has an obligation and is committed to achieving the highest standard of compliance with all pertinent regulations. The institution, in consultation with and under the guidance of the IRB, could better protect the rights and welfare of human subjects in research by supporting and training its members and the research community.

The IRB should consider the possibility of assuring: (1) increased compliance with human subjects regulations as studies are in progress, (2) better quality of the pertinent information submitted to the IRB in research applications, and (3) greater efficiency of the overall IRB process through providing training, service, support, and information to faculty and staff; and (4) overall, more expeditious processing/or approval of proposals by decreasing or to the degree possible eliminating "cycle times." This could be accomplished by a variety of means, for example through a positive, visible IRB presence in frequent training sessions and consultation with PIs; and by continuing to provide information in the publication *Research Review*. Routine AHC e-mails and a web page dealing with a broad scope of human subjects protection issues are some of a number of things that would be helpful.

The IRB could develop a primer of local standards to aid faculty and staff in understanding the conduct of human subjects research. Developing local

standards to guide investigators would address ongoing training, education and information needs and help to "raise the institutional consciousness" about the IRB's role and the important issues it deals with. Development of this primer of local standards would also increase the likelihood of consistent reviews of applications between and within committee panels.

The University should provide staff adequate in number to allow Subjects Protection Programs to actively and frequently train, consult, and provide information to the University research community not just at the time of protocol approvals. It appears that more executive level administrative staff are needed to support committee panels, manage the expected increased volume of research, and communicate to various members of the organization these very complex issues.

In order to appropriately value the important contribution to the institution and the time this requires, IRB committee members should be paid for their service in the form of salary offsets or other compensation. In addition, funds should be available to the IRB to enlist the advice of consultants when expert advice is required. If there were a small number of highly-trained committee members who worked a significant percentage of time and if they were compensated, we might need only one or two IRB committee panels. Providing compensation, training, and performance expectations for panel members would serve to create more efficient and responsive committees. Given the competing demands on faculty it's amazing we are able to get anybody to serve on current IRB panels. At the same time, consolidating the number of panels and committee members would increase the IRB's opportunity to provide a more even or consistent review of research applications. While it is recognized that this is an area of frustration for PIs, dealing with this phenomenon is a challenge even for NIH in their peer review system.

The IRB review process could be made more efficient by enabling the committee panels and investigators to interact via video-conference at the time of review of the proposal. In this way, the faculty member could address immediately on a "real time" basis many of the questions a committee panel might have. Additional time could be saved in the process by the faculty and IRB taking advantage of courier, e-mail, and fax services to get time-sensitive correspondence to and from faculty to make their life easier and provide for a more timely resolution to any issues.

2.3.3 Rationale

The University of Minnesota will be best protected from human subjects research regulation violations when the faculty and overall research community is well-informed, provided with high quality and timely staff support and by having studies randomly monitored. Understandably, the chief concern of the IRB is protecting human subjects; however, overall the institution directs little attention or staff time toward providing training, consultation, and support for faculty and research study colleagues. This is of deep concern, given the number of clinical trials ongoing at this institution (numbering in the thousands). The institutional authorities to whom the IRB staff report should be provided with resources that they could direct towards an increased commitment to serving the faculty on the

part of the IRB office, in essence, extending their compliance function through education and providing information.

Providing appropriate assistance to faculty through the Research Support Service Office will improve the quality of research plans, human subjects research applications, and consent forms. The IRB has said that the most frequent reasons for delays in the review and approval process are deficiencies in information provided by PIs in applications and consent forms. This may occur for various reasons, including prior inexperience of the PI, who might be unfamiliar with the process and without sufficient time to take the care which must be taken to fill out the forms.

A major bottleneck in the IRB review and approval process of initial applications is at the level of the executive assistants. There are currently only two. These two staff members have a huge responsibility and must write all the response letters to PIs following IRB committee meetings. As many as 30 letters communicating the recommendations and actions may be required after any single meeting. Among a number of other things, many of these letters are complex and time consuming to write. In the current system, additional executive assistant staff would decrease the volume of letters to be developed by any one staff member and thereby increase the speed with which responses could be provided to faculty. It is imperative that additional executive staff be recruited.

Allowing PIs to appear before the IRB committee panel (via video conferencing) to answer questions and review their research should be seriously considered. The committee could ask questions and receive responses within minutes that, in the current process, could take a month or more to communicate and get reviewed. It has been suggested that approximately 75% of stipulations and deferrals could be managed immediately by allowing the committee and the investigator to communicate in real time. PIs will not be required to appear before the committee, but will be notified of the opportunity when a committee panel is meeting so that the PI could answer any questions and concerns about the proposed research. We envision a conference room where the faculty could go within a given time frame to link on line with an IRB review group.

Finally, faculty would be greatly assisted by receiving notice of the committee's decision as quickly as possible after it is made, ideally electronically with a paper copy to follow.

2.4 Subjects Protection Programs (Human and Animal Subjects) - Animal Subjects[2]

Every institution that falls under authority of the Animal Welfare Act and/or receives Public Health Service support for research and teaching involving laboratory animals must operate a program with clear lines of authority and responsibility for all matters surrounding animal use. Among other things this includes: establishing a properly functioning Institutional Animal Care Committee (IACUC), having procedures for self-monitoring, the provision of adequate veterinary care, having a program of occupational health to assure sound animal husbandry practices, and assuring quality maintenance of facilities for housing animals.

The IACUC must have at least five members. Membership must include: a veterinarian with program responsibilities, a scientist experienced in laboratory

animal research, a non-scientist and an individual who has no other affiliation with the Institution besides membership in the IACUC. The IACUC has authority to approve studies/proposals, require modifications before approval, or withhold approval of proposals submitted to it for review. No research activity involving animals can begin unless it is first approved by the IACUC.

The IACUC is required to follow two sets of federal regulations: Public Health Service (PHS) Regulations and Policies, and United States Department of Agriculture (USDA) Regulations and Policies.

Federally mandated IACUC functions are to :

- Review, at least once every 6 months, the research facility's program for the care, use and housing of animals, using the USDA Regulations or Guide as a basis.
- Inspect, at least once every 6 months, all of the animal facilities, including animal study areas/satellite facilities, using USDA Regulations or Guide as a basis.
- Prepare reports of IACUC evaluations and submit the reports to the Institutional Official.
- Review and investigate legitimate concerns involving the care and use of animals at the research facility resulting from public complaints and from reports of non-compliance received from facility personnel or employees.
- Make recommendations to the Institutional Official overseeing animal care regarding any aspect of the research facility's animal program, facilities or personnel training.
- Review and approve, require modifications in order to secure approval, or withhold approval of those components of the proposed research activities related to the care and use of animals.
- Review and approve, require modifications in order to secure approval, or withhold approval of proposed significant changes regarding the care and use of animals in ongoing activities.
- Suspend an activity involving animals when necessary; take corrective action, and report this to the funding agency and USDA.

The University of Minnesota IACUC includes members that form one committee panel and an executive panel. The review panel meets once each month. Agendas for each committee meeting may include as many as 30 to 40 different projects to review. The executive committee of the IACUC meets less frequently.

2.4.1 Current Performance - Animal Subjects Protection Program

Over the past few years, considerable effort has been devoted to enhancing the awareness and improving the knowledge of faculty in the use of animals in their research. Internal and external regulations governing the use of animals in research, education and display have been presented to the faculty using a variety of methods. These efforts have resulted in distinctly improved submissions to the IACUC which has directly improved the quality and speed of the review process. Currently, the average length of time from application to the

IACUC to approval is approximately 30 days. Since the IACUC consists of one committee panel, the review process is fairly consistent from project to project. Having a single committee also facilitates the efficiency of the review/approval cycle.

After the proposed research is approved by the IACUC and the PI is notified, the PI assumes responsibility for knowing and applying federal regulations and guidelines as the research is conducted. To assist PIs in meeting their responsibility, the IACUC provides information to the research community in a subjects protection programs column that appears each month in the ORTTA publication - *Research Review.* The Subjects Protection Programs office collates these columns approximately annually, and provides the document to researchers as a local guide to subjects protection. A member of the Subjects Protection administrative staff or a member of the committee participates in the annual Responsible Conduct of Research workshops to provide animal subjects related education and training to the University of Minnesota research community.

2.4.2 Goals and Recommendations - Animal Subjects Protection Program

Recently, administrative responsibility for the IACUC was assumed by a reorganized Office for the Protection of Research Subjects. This action directly addressed some of the problems or deficiencies. Among some of the issues that needed attention were the responsiveness of the staff to PI concerns, the quality of the written correspondence between the IACUC and faculty, and the organization of committee files. Notwithstanding these changes, as stated above, the review cycle remains at an average of 30 days.

It is the expressed goal of the Research Support Service Office to have the review and approval/denial process of industry-sponsored research applications to be completed within 10 working days of application, without sacrificing the current high quality of the review. Therefore some changes would be necessary.

Adequate staff numbers to allow the IACUC to continue to train, consult, and provide information to the University research community should be provided. There are many ways that the efficiency of the overall IACUC review process could be improved for example by having the IACUC: hand-deliver or courier the review materials to committee members; add executive personnel to help write stipulations, deferral, and approval letters; consider having executive personnel dictate letters or implement voice recognition transcription technology; consider having the person who develops the response letter also enter it in the database, and increase the number of student staff to assist with compiling application responses.

Recommendations in the human subjects protection section regarding providing the opportunity for investigators to meet with the committee panel via video conferencing, and communicating correspondence electronically in advance of the formal letter, apply to the animal subjects review process as well.

2.4.3 Rationale

The appropriate and considerate use of animals must be a guiding principal for science. The University of Minnesota will be best protected from animal subjects research regulation violations when the research community is well-informed and supported by the institution and randomly monitored for compliance. Understandably, the chief concern of the IACUC is protecting animal subjects; however, overall in the area of use of animals the institution probably does not direct sufficient attention or staff time toward providing training, consultation, and support for faculty and research study investigators. This is of deep concern given the amount of animal research ongoing at this institution, and the emotional and political sensitivity of the public regarding the appropriate care and use of animals in scientific experimentation. The institutional authorities to whom the IACUC staff report could direct resources to, and encourage an increased commitment to service on the part of, the IACUC office, in essence extending their compliance overview function.

Providing assistance to faculty and their staff through the Research Support Service Office should improve the quality of research plans as they pertain research applications involving animal subjects. The most frequent reasons given for delays in the review and approval process are lack of clarity or other deficiencies in information provided in the applications. This may be for various reasons, including prior inexperience of the PI, who might be unfamiliar with the process and the time or care that must be taken to fill out the forms, etc. In addition to increasing quality of the information provided to the oversight committees in the applications, the Research Support Service Office can assume much of the pre-review functions the IACUC must now perform thereby facilitating their function and allowing them to focus their time on decision making based on the most complete information.

Allowing faculty to appear before the IACUC committee panel (via video conferencing) to answer questions and review their research would allow the committee to ask questions and receive responses within minutes that could, in the current process, take a month or more to communicate and get reviewed. As with the IRB, it has been suggested that approximately 75% of stipulations and deferrals could be managed immediately by allowing the committee and the investigator, to communicate in "real time". PIs will not be required to appear before the committee but will be notified of the opportunity to respond immediately when the committee has questions and concerns about the proposed research. We envision a conference room where the investigators could go within a given time frame to link on line with an IACUC review group.

Finally, PIs would be greatly assisted by receiving notice of the committee's decision as quickly as possible after it is made via e-mail, fax, or a web page/data base.

2.4.4 For More Information

Food and Drug Administration Information Sheets	http://www.fda.gov/oc/oha/toc.html
FDA Code of Federal Regulations (21 CFR Parts 50, 56)	http://law.house.gov/cfr.htm

OPRR Protecting Human Research Subjects Guidebook http://www.nih.gov/grants/oprr/oprr.htm

University of Minnesota Subjects Protection Programs Homepage

University of Minnesota IRB: Human Subjects Committee: A Series of Articles Collected from the *Research Review*, September, 1995

IRB: Human Subjects Committee Application Form and Information Packet - Health and Biological Sciences

IRB: Human Subjects Committee Continuing Review of Approved Research Form

University of Minnesota IRB Membership List

OPRR Institutional Animal Care and Use Guidebook

[1]OPRR Protecting Human Research Subjects: Institutional Review Board Guidebook

[2]OPRR Institutional Animal Care and Use Guidebook

2.5 Office of Research Technology Transfer Administration (ORTTA)

Responsibilities of the Office of Research Technology Transfer Administration are divided into two primary areas: Patents and Technology Marketing (PTM) and Sponsored Projects Administration (SPA). The mission of Patents and Technology Marketing[1] is the identification, protection, and transfer of technologies from the University of Minnesota for commercial development in the public interest and with fair consideration for the transfer. Sponsored Projects Administration performs roles in managing grants and contracts including: grant application review, approval, and post-award grant administration functions. A "roles and responsibilities" document for sponsored research program management is now available. This document is expected to improve the management of sponsored research programs by defining responsibilities and clarifying roles for investigators, departments, units, and ORTTA.

From 1992-1996, the Academic Health Center (AHC) averaged 79 technology disclosures per year. This represents 48% of the University of Minnesota total for that time period. In fiscal year '95-'96, the AHC faculty generated nearly $6 million dollars in royalty income. This represents 92.8% of the total University of Minnesota royalty income for that year.

From 1992-1995, the AHC averaged per annum $139,700,000 in sponsored research expenditures. Of this total, $11,175,000 per annum was sponsored by business and industry. By comparison over this same time frame the Institute of Technology had an average of $57,920,000 in sponsored research expenditures, $4,750,000 of which were sponsored by business and industry; and the College of Biological Sciences had an average of $11,380,000 in sponsored research expenditures of which $625,000 was sponsored by business and industry.

ORTTA defines and assumes current specific responsibilities in terms of the following categories regarding grants and contracts: providing institutional oversight, notifying, expediting, approving, initiating, and providing local oversight.[2]

2.5.1. Current Performance - Patents and Technology Marketing (PTM)

Patents and technology marketing staff are notified via faculty members when an invention is to be disclosed. A form provided by ORTTA is filled out by faculty members (on paper) describing the nature of the technology being disclosed. PTM then makes a judgment as to whether to file a patent. If the decision to file is affirmative, the PTM representative typically might identify a law firm and lawyer they have a relationship with who has expertise in the given area. The disclosure is sent to them, and the PI is requested to send any supporting papers or documents or data that might be useful in developing the patent application. Generally, there will be discussion between the inventors and the drafting lawyer facilitated by PTM.

University policy stipulates that ORTTA will respond to a patent disclosure within 30 days. PTM for the AHC, says they try to respond within 10 working days. If PTM decides not to file a patent (which they do in about 75-80% of the cases), a final release is sent to the inventors. At that point, the inventors are

free to file a patent at their own expense and have all rights to this invention to pursue as they wish. If this occurs, the University has neither financial obligation to nor benefits financially from anything that ensues.

PTM has an advisory group of investors, experts in technology, or technology-based companies that they, on occasion, use to help evaluate the potential market and general wisdom of going forward with the expense of the patent filing and prosecution.

A significant concern in this whole process is cost. Currently, PTM estimates that it might take on average $20,000 to fully prosecute a U.S. patent with the Patent and Trade Mark Office. Foreign filings incur considerably more expense given the need for country-based counsel and costs of translation into various languages. The current University Patents and Technology Marketing office policy is, in general, that unless some corporate agreement or similar vehicle is in place or imminent at the time that actions are needed to be taken to continue to prosecute the foreign filings, these will be dropped.

In meeting with Dr. Severson he discussed the dilemma PTM faces: on one hand PTM solicits technology disclosures from faculty, and on the other hand PTM is in the position for a series of what are understandable circumstances to be able to pursue only ~20 - 25% to U.S. applications.

The next step after this process is final notification of the relevant department heads and deans regarding the filing of a patent by one of their faulty members. Subsequent to this, the next challenge going forward is licensing, in which a development agreement, option and/or outright sale or license is developed and negotiated.

In discussions with PTM it was described that they would ideally like to devote about 30% of their time to "marketing." Marketing is described as researching data bases, finding companies that have interests in a given technology, and ultimately contacting these companies and negotiating an agreement. It doesn't appear that responsibility for marketing faculty services is under the purview of ORTTA.

Contacts for outlicensing technology to companies are made via a host of methods including the Licensing Executive Society (LES). LES is comprised of licensing personnel from academic institutions, representatives of business and industry, and patent attorneys.[3]

It appears that PTM gets involved in all sorts of things that compromise the time they have available to aggressively market University faculty technologies. This includes getting drawn into conflict of interest matters and the issues raised by the Medical School's Conflict Review Committee. Many other internal issues (some directly and others perhaps not directly) in the purview of PTM distract the time PTM staff has to really actively and aggressively go out and market AHC/University of Minnesota technologies.

In addition, the Research Support Service Taskforce was left with the clear impression that some reorganization and redefinition of responsibilities of ORTTA and PTM needs to occur. This reorganization would need to cover a broad range of activities from the whole process of filing of patents and the protecting of intellectual property, to marketing the technology and executing licensing deals or new business start ups. Associated with this, it was the Research Support Service Taskforce's view that some enhanced level of staffing to meet these

responsibilities needs to be achieved in order to maximize the return derived from innovation and discovery capabilities of faculty in the AHC.

The current performance of PTM is determined by the guiding premise that quality is more important than quantity. Decisions about filing patents are influenced, primarily, by the expected or imputed value of royalties to be received for the technology. This is a very difficult task to undertake as it is a very imperfect process that we all use to predict the future value of some technology. Venture capitalists who do this for a living might not be "right" more than two out of ten times.

2.5.2 Current Performance - Sponsored Projects Administration (SPA)

Proposal Process: The budget and related materials for proposed research are generally prepared by the PI and his or her staff in concert with the sponsoring organization. SPA is notified of any subcontracts, and generally via the BA 23 (though this requires full and accurate information) of any regulatory requirements which may govern the conduct of the research including human and animal subjects protection, environmental health and safety oversight, and conflict of interest review. SPA is also notified as to whether there may be any confidential or proprietary information in the proposed research. During the proposal development phase, SPA also provides institutional oversight for cost sharing. In processing the proposal, SPA staff make attempts to respond to the sponsor's and/or University's deadlines.

Grant or Contract Award Process: During the award process, SPA is responsible for the approval of the project budget, the terms and conditions defined in the grant or contract, and for the review and approval of the research agreement and its execution. Establishing the account to be used by the faculty member for grant expenditures is initiated by SPA staff. If pre-award arrangements between the sponsor and the University are required, these are reviewed and approved by SPA staff. Institutional oversight by SPA is required in order for the PI to accept and initiate work on all new awards.

Sponsored Project Management: SPA staff expedite and approve subcontract agreements and approve materials transfer agreements. Institutional oversight is provided to determine whether purchases of materials and services are allowable, reasonable, and in accordance with the project budget. Institutional oversight is provided by SPA when mandatory cost sharing or matching must be documented. SPA approval is required when any rebudgeting of a project is requested or costs are to be transferred. SPA expedites payment of subcontractor invoices and records program income (including unexpected income). Institutional oversight and responsibility for assuring compliance with the effort certification reporting policy also rests with SPA.

Project Closure: SPA is notified of the final technical report submission and retains institutional oversight for the same. SPA staff initiate and approve the writing and submission of all project close-out reporting except financial.

In evaluating the performance of current SPA responsibilities in terms of response time, it appears performance is compromised by a staff inadequate in number to manage the volume of projects, and by the variable quality of supporting materials in applications sent to SPA. The proposal and award

processes for industry-sponsored research managed by SPA in the best case will generally take several weeks and in the worst cases several months.[4]

SPA staff spend much of their time reviewing industry-sponsored research agreements for intellectual property and publication rights. Once reviewed, changes to the research agreements must be negotiated with the faculty member and the sponsor. This may take numerous discussions back and forth and a considerable amount of time (phone tag, etc.). Staff time is also diverted to the review of confidentiality agreements, another responsibility SPA must bear. Indirect cost recovery (ICR) negotiation (while ICR is rarely, if ever, negotiable) is an added burden for SPA staff managing industry-sponsored research. That is, companies understandably may attempt to downwardly negotiate ICR. Overall it appears that there are many competing demands that must be dealt with by SPA that are time consuming, sometimes complicated, and difficult to prioritize under the current circumstances.

2.5.3 Goals and Recommendations - Patents and Technology Marketing

The AHC is uniquely positioned to dramatically alter the current paradigm for corporate sponsored research. The University of Minnesota is searching for innovative ways to serve our constituents, bring more research dollars to faculty, and create value. Untapped synergies exist within the University that could stimulate innovative approaches for health care products and services. Industry is looking for innovative partners willing to share their vision, risks, and goals and be responsive to the inexorable pressure to move technology to the market.

To accomplish this new way of doing business, we recommend the formation of a Business Development Office as a discrete functional unit within the Research Support Service Office . The Business Development Office would coordinate, promote and serve the AHC corporate sponsored research program. This office will report to the Research Support Service Office director, and in turn to the AHC Vice Provost for Research or to whomever may have senior responsibility for research in the AHC.

An entire section devoted to discussion of the proposed function of the Business Development Office can be found elsewhere in this document.

The AHC is not deriving its fair benefit of the royalty streams currently managed centrally. The patents and technology marketing function for the AHC is undercapitalized.

Estimating the value of a patent at its filing is very difficult, if not impossible to do. Therefore, the more patents that are filed, the more likely it is a big winner will be realized. To put this in perspective, the drug Prozac had sales in 1996 of $2.8 billion comprising some 1/3 of all of Eli Lilly's revenue. Major pharmaceutical companies don't want to develop a drug with less than $500 million in annual projected sales.

That being the case, the AHC/University should file more patents on meritorious technology. The AHC filed about 20 patents last year. To add five more per year would only cost approximately $100,000.

2.5.4 Goals and Recommendations - Sponsored Projects Administration

SPA continues to observe and meet the proposal deadlines of research sponsors that impose submission deadlines, although research sponsored by business and industry is typically not deadline driven in the same manner as that sponsored by government agencies. SPA should assure that the proposal and submission processes for industry-sponsored research are completed within 10 working days of receiving the BA 23.

SPA should identify the areas of common problems in proposals and award processes and develop guidelines, information and an appropriate information plan and management plan to attempt to obviate these problems. This information should be provided to the AHC faculty and the Research Support Service Office. SPA should provide an on-site grant administrator to the AHC Research Support Service Office (with authority to approve and sign contracts, establish CUFS accounts, and authorize purchases).

By establishing a Research Support Service Office, the AHC will support faculty in developing budgets and assuring the degree possible compliance with all regulatory requirements that may apply to their research projects. The Research Support Service Office would also provide support for faculty as a liaison with SPA through preliminary contract review and negotiation of the areas in which most problems occur: intellectual property rights, publication rights or terms and conditions, indirect cost charges, etc.

Sponsored Projects Administration and the AHC should collaborate in revising/developing a standard research agreement for industry; and language for optional sections predetermined to be acceptable to the institution from which the Research Support Service Office can choose and use as contracts are negotiated.

2.5.5 Rationale

The AHC is committed to increasing research relationships with industry in order to aid faculty in their scholarly endeavors. Increasing the number of these relationships will further burden a system currently unable to respond in the 10 working day time frame, the Research Support Service Taskforce goal for the internal proposal review and award process. Providing assistance to faculty in all aspects of the "grant process", using a standard contract (or other "pre-approved" language), and/or otherwise reviewing and pre-negotiating the contract will significantly reduce SPA review and approval time. A close relationship between faculty and the Research Support Service Office (in both proximity and understanding of shared goals and objectives) will reduce errors and the overall time needed to negotiate contract changes. A Research Support Service Office-based SPA grant administrator with authority to approve contracts and establish CUFS accounts will assure that the proposal and award associated processes occur within the stated desired performance goal of no more than 10 working days.

2.5.6 For More Information

ORTTA Home Page http://www.ortta.umn.edu

[1]See Business Development section for a thorough discussion of PTM.

[2]Roles and Responsibilities Document for Sponsored Research Program Management - 11/15/96.

[3]RSSO Meeting minutes 11/11/96.

[4]RSSO Meeting minutes 11/21/96.

2.6 Department of Environmental Health and Safety[1]

The Department of Environmental Health and Safety (DEHS) provides programs to protect the health and safety of all people on University campuses and works to assure compliance with applicable federal, state and local codes and regulations. DEHS is comprised of nearly 70 professional, technical, service, and student employees providing service to support University activities statewide. The Director of DEHS reports to the Assistant Vice President for Campus Health and Safety.

The overall application of regulatory authority regarding environmental health and safety has increased in general in society and also in academic settings. Some granting agencies require certification of compliance with environmental health and safety regulations at the time of application. Occasionally, depending on the nature of the research work, environmental permits for research may be required prior to award. Fines and criminal penalties assessed against research institutions found to have been out of compliance with environmental health and safety regulations have ranged as high as $1,000,000. There has been greater and greater enforcement and consequences for breaching environmental regulations and we can only anticipate this growing will be growing in the future.

Some of the federal, state, and local regulatory agencies involved with environmental health and safety are: the Occupational Safety and Health Administration (OSHA), Minnesota Occupational Safety and Health Administration (MnOSHA), Environmental Protection Agency (EPA), Minnesota Pollution Control Agency (MPCA), Nuclear Regulatory Commission (NRC), Department of Transportation (DOT), Minnesota Department of Transportation (MnDOT), and metropolitan counties.

The general regulatory requirements of each agency include documented training of personnel, records retention, labeling, and incident reporting. Specific regulatory requirements exist for hazards often present in academic research settings including among other things: chemical, radioactive, biological, and physical.

2.6.1. Current Performance[2]

DEHS staff members assist academic units by establishing standards, interpreting regulations, reporting on compliance, providing technical services, recommending corrective actions and providing training resources. With respect to research, the goal of DEHS is to assure that research is carried out in a way that protects everyone within the University community; prevents accidents and minimizes exposure to hazardous agents and conditions; prevents degradation of the environment through responsible waste management and active waste reduction; conserves resources and minimizes losses; and achieves regulatory compliance.

Research involving recombinant DNA or other biological hazards; ionizing or nonionizing radiation; highly toxic, flammable or reactive chemicals; or known or suspected carcinogens must be reported on the Application for External Research, Training or Public Service Support (University of Minnesota BA 23 form).

Research applications that involve the use of recombinant DNA or other biological hazards (infectious agents and toxins) are reviewed by the Institutional Biosafety Committee (IBC). Investigators are required to file an application and description of the proposed research with the Biosafety Officer. Most applications can be reviewed and approved by the Biosafety Officer, but in cases in which he/she cannot, the IBC reviews all applications for which the Biosafety Officer requests recommendation from the full committee. The Vice President for Research is the institutional authority for implementing the Regents' Policy on the Use of Recombinant DNA and other Biological Hazards.

The Radiation Protection Division of DEHS is responsible for assuring certification of research laboratories in which radioactive materials are used. Approximately 400 University laboratories (>200 in the AHC) are certified. A Radiation Protection Division database assists in record keeping of certification, isotope inventory, and waste management. The Radiation Protection Division review committee is appointed by the University President.

The management of hazardous chemical use or of known carcinogens in research is not reviewed by any institutional oversight committee. Research investigators are often not aware of regulations related to the use and management of hazardous chemicals. Departments using hazardous chemicals are supposed to have developed and implemented a "chemical hygiene plan". Anecdotal experience would suggest that this may be performed at a variable level throughout the institution. Departments found to be out of compliance with the regulations regarding the management of hazardous chemicals are required to pay any fines assessed. Given the financial circumstances of various units, there may be little ability of a department to pay these fines. Thus, the charges or perhaps other penalties for mishandling of hazardous chemicals would revert to a college, or higher level. Therefore, there is considerable liability for the institution and individuals in administrative positions.

2.6.2 Goals and Recommendations

The Department of Environmental Health and Safety embodies the University's commitment to provide a safe and healthful environment for all students, faculty, staff, patients, and visitors. The DEHS commitment to service, and to the idea that assuring compliance with a vast array of complex regulations is best achieved through providing service, support and assistance, is evident and could serve as a model for other parts of the University.

The Research Support Service Office will assist DEHS faculty and research investigators in identifying hazards for which specific approval must be applied. To best perform their function, the Research Support Service Managers should enroll in all of the training courses provided by DEHS so as to be alert to these issues.

The AHC should develop a network of contacts between DEHS, the AHC, departments, lab safety officers, and lab techs to assure safety and compliance information is widely distributed. Information should travel both directions in this network that is back and forth between EHS and the research community.

The AHC should develop a PI, laboratory and laboratory staff certification program and database. BA 23s for research involving any of the regulated hazards should not be signed without evidence of laboratory and PI certification.

Likewise, the AHC should require DEHS training for new faculty, staff, and students who plan to conduct or participate in laboratory research; and have some mechanism for updating and on some routine basis (i.e., yearly) do an inventory of all employees and students to pick up any who may have "fallen through the cracks."

The AHC should require and monitor the development, implementation, and compliance with a Chemical Hygiene Plan in all AHC schools.

2.6.3 Rationale

The Research Support Service Office can assist faculty research investigators and the DEHS by identifying research involving hazards regulated by DEHS. By identifying these hazards as early as possible in the project application process, the principal and associate investigators and DEHS will have time to prepare for management of the research hazard without delay. Since Research Support Service Managers will be dealing with these issues on a daily basis, it is likely that they will be better prepared to identify hazards and assist with DEHS applications after taking DEHS training courses.

The rationale for development of Chemical Hygiene Plans, research certification courses, and communication networks is that the protection of faculty, staff, and students, and overall institutional compliance can best be achieved through support and training.

2.6.4 For More Information

BA 23 - Application for External Research, Training or Public Service Support

University of Minnesota Regents' Policy on Research Involving Recombinant DNA and Hazardous Biological Materials

University of Minnesota Institutional Biosafety Committee Applications:
- Artificial Gene Transfer and Recombinant DNA Form
- Biological Toxin Usage Form
- Infectious Agent Usage Form

University of Minnesota Radiation Protection Division
- Application for the Possession and Use of Radioactive Materials Guide

[1]Environmental Health and Safety Brochure (6/96)

[2]RSSO Meeting Minutes 11/1/96

2.7 General Clinical Research Center

The General Clinical Research Center (GCRC) is supported by NIH funding in the amount of approximately $2.6 million yearly. The GCRC operates out of the Medical School Dean's Office with the Associate Dean for Research Dr. James White as the PI on this grant. Dr. Paul Robertson is the Director of the GCRC. This grant supports salaries of the GCRC staff, which includes a portion of the director's salary; the associate director's salary, nursing staff, administrative staff, dietitians, space, cooks, and professional support (see organizational chart). Among the personnel and facilities located in the GCRC are: dietary kitchen/staff, a statistician, an administrative core, nurses, and laboratories that are open 24 hours, 7 days each week. The GCRC is funded by the NIH grant for 7-8 beds daily but has 14 beds and 2 outpatient rooms assigned by the hospital.

2.7.1 Current Performance

The process for a faculty member submitting and gaining approval for a clinical trial submitted to use the GCRC is generally more or less as follows:

- The Director of GCRC typically gets contacted by the research investigator interested in using the GCRC.
- The Director of GCRC has the faculty member call Patrice Schaus, Director of the administrative core to get an application for submission, which is generally furnished via mail.
- After forms are completed by the faculty member/investigator they are copied (original + 25 copies) and delivered to the scientific advisory committee of the GCRC.
- The GCRC biostatistician reviews the proposals before the scientific advisory committee meets (the fourth Monday of every month) and gives suggestions and comments to the committee. (There may be times that not much time or any time is provided for this review by a biostatistician.)
- At the committee meeting the proposal is either approved or tabled.
- If the submission is tabled by the committee it is usually returned to the clinical investigator. The most common reasons for a proposal to be tabled are: because the GCRC form was not completed correctly, or the GCRC biostatistician was not consulted and there may need to be some design changes. Generally, a letter is sent to the clinical investigator requesting more information. The faculty member's response may satisfy the committee's stipulations, in which case the study can be approved by the director without full committee review. If there are more complex issues involved, at the director's discretion, the committee may need to meet to review responses.
- The average time it takes for approval of a protocol or study is 2 - 3 months; however, it may range beyond this.

The Director of the GCRC, Dr. Robertson, is concerned that the GCRC is not being used like it should. In meeting with the Research Support Service Office Taskforce, Dr. Robertson expressed the following concerns:

- The GCRC doesn't see more than 5% of the clinical research proposals or protocols of the institution since the committee reviews only 4-5 proposals/month.
- Many faculty are not well aware of what the GCRC can do for them and need to be better informed. Dr. Robertson does visit with Deans and some Department heads annually to "market" the GCRC and inform them of the GCRC capabilities but numerous heads and other senior clinical researchers are pretty much in the dark about the GCRC.
- It is increasingly difficult for University investigators to find funding for the types of clinical investigations the GCRC is intended to serve.
- That research investigators submitting studies should use the GCRC biostatistician before the proposal submission to optimize study design and thereby improve the likelihood of obtaining quick approval.
- The location of the GCRC and even physical condition are suboptimal.
- The cost to use GCRC for a trial might be high.

There are various economic base charges for patient care in the GCRC. The current cost categories for using beds in the GCRC are as follows: (per Dr. Robertson):

- Basic Research Day ("A" rate) - This GCRC patient stay is gratis to investigator and patient for routine studies.
- Medical Care Day ("B" rate) - This rate is for non-research related stays where any diagnostic procedure or treatment is done. The patient's insurance coverage must pay for this GCRC stay, i.e., "daily hospital rate".
- The "C" rate is charged for patients boarded in the GCRC because the hospital is overloaded.
- The "D" rate is designated for pharmaceutical, company sponsored Research - not investigator initiated research. These charges are paid by the investigator and the sponsor of the study.

A disadvantage for faculty clinical investigators involved with industry-sponsored research is the daily rate for D days ($725). The rate is not competitive with other Drug Evaluation Units or Clinical Trial Units; therefore, most industry sponsors are not willing to pay this rate. Dr. Robertson stated that if the Medical School can retain the second floor of Masonic Hospital then perhaps the GCRC can fix rates much lower than the hospital fixed rate of $725. (However, in order to assure this, it would need to be cost accounted out.) On the surface, it seems as a free standing unit from Fairview University Medical Center that costs would be higher not lower.

In relation to compliance, the GCRC offers regulatory compliance service on each project. Suzanne Ganzhorn-Kotula, GCRC Nurse Manager, stated that the nurse involves the PI in the consent signing process with the patient. Additional attention to compliance matters is evident in that if a protocol deviation occurs, Dr. Robertson will contact the PI and make sure the proper changes are made both internally at the GCRC and that the IRB is informed. It is important to note that a major focus of the GCRC is patient protection .

Other than the obvious, there seem to be incentives for clinical investigators to use the GCRC:

- Nurse staff to assist and provide research support for the PI,
- Nurses to educate patients and form a partnership with the PI,
- Biostatistics support.

Dr. Robertson stated that he believed there were also disincentives to using the GCRC including, among others:

- Location (2nd floor Masonic Cancer Center),
- Older building and equipment
- Distance for the PI to travel from their normal or routine locale

2.7.2 Goals and Recommendations

Dr. Robertson and the Research Support Service Office committee discussed what has occurred at other institutions with respect to clinical trials coordinating centers and units and the potential for corporate sponsored research. A number of very superior and capable institutions have actively developed and marketed their clinical trials capabilities. Some examples include Duke, Massachusetts General, and Alabama, to name a few.

The Research Support Service Office work group raised the possibility of a clinical trials coordinating center, a "virtual" clinical trials unit and a "virtual" clinical research unit that wasn't necessarily fixed in one location, but was more a multifunctional group of health professionals who could deliver a desired outcome at various clinical settings. This appeared all the more important given the merger of University and Fairview hospitals and the multiple clinical sites within the Fairview System.

The potential benefits of integrating the GCRC with a Clinical Trials Unit (CTU) and Clinical Trials Coordinating Center were discussed. Some of these potential benefits are:

- The structure of the nursing staff for clinical trials and the GCRC under this concept could continue if the staff was unified and reported to one Director,
- Better facilities would be available and they would be part of the overall clinical services of the medical complex,
- Leveraging of personnel and capabilities across the organization could occur,
- A more aggressive and comprehensive marketing plan of our capabilities could be pursued,
- Nurse skills needed in a clinical trials unit are scientifically and detail oriented and could be applied in the optimal fashion,
- The clinical trials coordinating center could develop clinical trial coordinators who do non-patient care so that nurses have more time to work on clinical research and patient care.

These clinical trials coordinators would work with the PI and could provide non-patient care assistance to faculty involved in trials anywhere in the institution e.g., GCRC, the Cancer Center, or for other clinical trials and work on among other things:

- The paperwork/case report forms for trials,
- Compliance matters, and
- Data management.

The potential disadvantages of integrating the GCRC with a clinical trials unit discussed were:

- There might be financial pressures that would change the environment of or the current GCRC mentality to one of "money driven science"; however, the Research Support Service Taskforce felt that most research relies on money and that while the sanctimony of the GCRC's mission should be respected the fiscal realities and opportunities of doing corporate sponsored research should be recognized.
- There is some possibility of destroying the nature of the General Clinical Research Center, but it's difficult to see how this might occur.
- Dr. Robertson raised the point that NIH dollars would have to remain separate. Therefore, a separate administrative staff would be necessary for the two units. The Research Support Service Taskforce is not certain of this and believes there should be a way to do keep the funds flow and accounting separate without a major problem.
- There is no space currently assigned for a corporate sponsor's data auditors, and this would have to be found if a clinical trials unit/GCRC were formed.

A functional depiction of how a clinical trials coordinating center and clinical trials unit would work with other units doing clinical trials is shown in the figure below.

The potential utility of an overarching coordination of clinical trials in the AHC was suggested in considering the potential relationship of the GCRC and the Cancer Center with a clinical trials unit. As do trials in the GCRC, the Cancer Center must now also have a protocol review function in addition to the review processes of all clinical trials that don't fall under the purview of either group.

This suggests the need for a Clinical Trials Coordinating Center to oversee and provide a coordinating function for all review processes.

The clinical trials coordinating center would:

- provide administrative support in consolidating review processes
- assist with compliance
- assist in marketing of clinical trials capability of faculty
- support biostatistics
- negotiate the most favorable arrangements for hospital beds and services

The GCRC would:

- provide a group of highly trained research nurses
- provide a host or other care/study functions such as dietary, etc.
- review study protocols for "fit" with the GCRC mission

The Cancer Center would:

- provide this advice and input to guide clinical trials on patients with cancer

2.7.3 Rationale

It would be very helpful to clinical investigators to have as much assistance as possible in proposing securing funds for performing clinical trials. This would also assist sponsors. This would enhance and facilitate the ability of faculty to perform their scholarly work, and train residents, fellows and students thereby benefiting their academic performance; and would facilitate, enhance, and promote faculty abilities to obtain external support for such studies.

The facilities would include research rooms and beds, perhaps anywhere in the institution, for comfortably taking care of subjects during clinical trials. Specialized research nursing and technical staff would be available to administer study protocols, perform minor procedures (blood pressure, blood drawing), subject specimen and data handling, and other research related tasks.

A clinical trials unit must be a service to faculty investigators, in all ways needed to assist in the successful conduct of each study. The cost of this service, in conjunction with the direct costs to cover the expenses of each study, must not exceed market pricing overall .

There are other advantages of the Research Support Services Office working with a clinical trials unit and clinical trials coordinating center:

- The Research Support Service Office would promote these capabilities outside of the institution and market this organization.
- The Research Support Service Office would help develop a survey of faculty to determine their needs and determine their satisfaction with these activities.
- In an overarching clinical trials Unit, clinical services and lab functions could be bundled, consolidated and negotiated internally to obtain the best price, or outsourced to obtain the best price and the best service to make us more competitive and/or more profitable.

2.8 Ongoing Compliance with Research Regulations

Institutional oversight committees are responsible for assuring compliance with federal, state, and local regulations, guidelines, and standards that govern the conduct of sponsored research. These committees include: the Institutional Review Board: Human Subjects Committee (IRB); the Institutional Animal Care and Use Committee (IACUC); the Department of Environmental Health and Safety (DEHS); and the Conflict Review Committee (CRC)[1]. Additional review and compliance committees are in place to review research protocols to be conducted in the National Institutes of Health sponsored research facilities in the AHC including: the General Clinical Research Center (GCRC) and the Cancer Center.

Each of these institutional committees has review and approval authority independent of the other institutional committees. As research proposals and applications are prepared, and after projects are approved, each clinical investigator is expected to be fully aware of and to comply with the myriad of regulations that guide the conduct of research. They are expected to do so when there are changes in their research, research protocols, or if there are other changes that affect these broad areas of compliance.

The federal and local agencies that govern the use of human and animal subjects, environmental health and safety issues, and the review of conflict of interest are provided in the appendices to this document.

Locally, the Vice President for Research and Dean of the Graduate School (VPRDGS) is the responsible authority for promoting research ethics and assuring regulatory compliance. A Director of Research Ethics and Regulatory Compliance position in the office of the VPRDGS has recently been created. The IRB and IACUC (which comprise the Subjects Protection Programs office) report to this office. The VPRDGS also bears institutional responsibility for assuring compliance with the conflict of interest policy, and biological safety policy on the use of recombinant DNA. The Department of Environmental Health and Safety otherwise reports to the Assistant Vice President for Campus Health and Safety.

Policies regarding scientific integrity and misconduct in research (academic misconduct) have been developed at the federal level by the Office of Research Integrity and have been adopted locally by the VPRDGS. It is not evident that the University of Minnesota has a committee review and approval process nor quality assurance monitoring program in place with respect to scientific integrity and misconduct in research; if it does it is not widely known. However, the University of Minnesota Board of Regents' Policy on Academic Misconduct does delineate the procedures for responding to allegations of scientific misconduct.

2.8.1. Current Performance of Compliance Functions

Monitoring compliance with most regulations governing research is currently limited to that provided in the review processes of University of Minnesota regulatory committees prior to approval of a research study.

2.8.11 Subjects Protection Programs : Human Subjects (IRB) and Institutional Animal Care and Use Committee (IACUC)

Protection of subjects compliance monitoring activities are currently limited to collection of information regarding the proposed research in the application process, review of this information by local committees, and annual review of human subjects research by the IRB. Review committees must apply federal regulations, guidelines, and community standards before any research project involving human or animal subjects, regardless of funding source, is approved. Many investigators are relatively unaware of the regulations, guidelines, and community standards by which their proposed research will be judged. Except in a very few cases, the minimum length of time it takes to receive IRB approval is about 45 days; often times it can take considerably more time. IACUC approval can usually be obtained in approximately 30 days.

If the proposed research is approved by either of these committees, researchers must independently become aware of and then apply federal regulations and guidelines as the research is conducted. The only local mechanism for providing ongoing information on human subjects use or use of animals, is through a subjects protection programs column that appears each month in the ORTTA publication - *Research Review.* The Subjects Protection Programs office collates these columns approximately annually, and provides the document to investigators as a local guide to subjects protection programs.

2.8.12 Department of Environmental Health and Safety (DEHS)

The DEHS is committed to providing a service to researchers within their overall responsibility for protecting health and safety on an institution-wide basis This department provides assistance, training, and support to all researchers within the institution. Faculty and their research colleagues are often not fully aware of the additional compliance measures they may be required to take if their proposed research includes activity regulated by DEHS. This lack of awareness can result in delays in processing a grant and frustrations for the PI that could be avoided by early actions in the process to assist the investigator. Principal investigators are expected to know, and to comply with, DEHS regulations as the research project is conducted and to continue to do so if there are changes in research work.

2.8.13 Conflict Review Committee (CRC)

The CRC has expanded its authority in assuring compliance with National Institutes of Health and National Science Foundation regulation regarding Objectivity in Research and Investigatory Financial Disclosure Policy. The CRC has also evolved its own oftentimes unduly restrictive notion of the propriety of and conditions for corporate sponsored research. The expanded authority assumed by the CRC is beyond anything it was intended to do and was not instituted via any directive. Among other things, this expanded scope includes: review and approval of budgets, determination of whether sufficient resources are available, how a potential research services organization might function and

a host of things that have nothing to do with true conflict of interest resolution. The institution has placed responsibility for review and approval of budgets and research agreements with SPA in ORTTA[2], not with the CRC.

The CRC currently requires that any potential conflict of interest be eliminated before a faculty member enters into an industry-sponsored research agreement. This requirement has made the AHC extremely difficult to deal with and is a source for derision of the Medical School by the local business community. In numerous venues locally, the University is vilified for its occasionally obstructive actions in dealing with industry sponsors. Federal regulation and Regents' Policy on Conflict of Interest allow some categories of potential conflict of interest to be managed. It should also be noted that the FDA expressly allows for conflicts of interest to exist as long as they are disclosed. The FDA even recognizes that there will be situations in which an individual may have stock in or a consulting relationship with a company for which that the individual is doing a trial. It does not seem reasonable to require that all potential conflicts of interest be eliminated.

It is the unequivocal conclusion of the Research Support Service Office Taskforce that the CRC has unnecessarily delayed, duplicated, and confused the research application process through the excessively expanded authority it has assumed.

The average length of time it takes to receive CRC approval is approximately one month. That is because most grants are processed without any real conflict of interest concerns. However, in cases where there is some perceived conflict it may take many months and numerous meetings and conversations. In more than a few cases, proposals may be tabled indefinitely.

Compliance monitoring of conflict of interest issues post-CRC approval is conducted by the faculty member's department head.

2.8.14 Scientific and Scholarly Advisory Board

This board functions on an institution-wide basis. Allegations of scientific misconduct at the University of Minnesota, if they occur, are not made widely known. No information is available by which to judge the adequacy of local management of policies and procedures for responding to these allegations.

2.8.15 The General Clinical Research Center (GCRC)

The GCRC reviews, primarily for scientific merit, protocols for all research conducted in this inpatient and outpatient research facility regardless of funding source. The GCRC views industry-sponsored research in a less positive way than it does other sponsored research, in part, because the GCRC has obligations to fulfill in order to maintain its NIH funding. It is often difficult for clinical research investigators to obtain approval for industry-sponsored research protocols from the GCRC review committee.

The GCRC review committee often requires changes in protocols that have already been approved by the Food and Drug Administration (FDA) through application by the industry sponsor. This usually means that the research cannot be conducted at the GCRC. Corporate sponsors will seldom if ever agree to making protocol amendments at the request of individual centers, particularly in

the case of a product that has proceeded to multi-center trials. Any protocol amendments that might be requested or needed result in long delays because of the need to apply for and receive FDA approval for such changes. The average length of time it takes to receive approval from the GCRC is 2 - 3 months. As stated in the GCRC section of this document, the Director of the GCRC monitors investigator compliance with the protocol and with regulations regarding the use of human subjects.[3] However, it was uncertain as to precisely how this is done.

2.8.16 Cancer Center

The Cancer Center's Protocol Review Committee (CPRC) reviews all cancer related clinical research protocols proposed to be conducted in the AHC. Approval by this committee is required before the application may be sent to the IRB. This has been recently formed and met to review protocols for the first time December 3, 1996. The expected length of time required to obtain approval from the CPRC is 30 - 45 days. No other information about the ongoing compliance function of this committee is available at this time. Coordination of the CPRC with the Research Support Service Office and Clinical Trials Coordinating Center, and the need to have 10 day turnaround, will present a challenge.

2.8.2 Goals and Recommendations

In general, but not always (e.g., IRB) many of the oversight functions of the various compliance committees are largely at the "front end," when a grant or contract is being submitted to seek approval. Often there is little to no ongoing monitoring. This is an unacceptable situation. In many cases there may be changes in circumstances that require compliance review. Because of this and the exposure of the institution, provision of monitors who could spot check ongoing compliance would benefit the institution.

The AHC should continue to provide support and information in the form of educational programs for investigators, in conjunction with electronic or other updates, to assure to the best degree possible that they are aware of the regulations. The AHC should also develop an explicit plan to monitor compliance with all regulations and policies.

The Vice President for Academic Affairs, has a policy on how public or confidential alleged scientific misconduct should be handled. A Good Scientific Practices document should be written and adopted to guide the conduct of research for faculty, staff, and students.

The desired performance with respect to management and scope of research review and approval processes is outlined in the sections of this document devoted to each committee.

2.8.21 Subjects Protection Programs

Research investigator compliance with regulations governing the use of human and animal subjects in research must be assured. The Subjects Protection Programs office must play a role in the development of an ongoing compliance review/quality assurance program to protect human subjects, investigators, and the institution. This compliance function is especially critical in

research activities not regulated by the FDA. FDA regulated clinical trials are monitored frequently by sponsors to assure compliance with human subjects regulations. The institution should also monitor compliance with human subjects regulations, in order to protect itself, PIs and other employees, particularly for research not otherwise monitored by pharmaceutical companies or contract research organizations. This is the case with most NIH or department-sponsored clinical research.

2.8.22 Department of Environmental Health and Safety (DEHS)

DEHS should continue their service oriented approach to assuring compliance in the research project review and approval processes. DEHS should continue to provide and facilitate training for local (departmental, collegiate, or provostial unit) faculty, students and staff to assure the consistent application of and good compliance with research-related DEHS regulations institution-wide.

Departments, colleges/schools, and provostial units (or whatever might take their place) should assume greater local responsibility for protecting their interests and those of the institution in complying with DEHS regulations. An individual in each college/school should be identified as the designated responsible party for DEHS compliance. They probably should be paid for doing this.

2.8.23 Conflict Review Committee (CRC)

The Conflict Review Committee is not charged to perform ongoing compliance functions. Changes in PI's business relationships during the course of a study may necessitate further review by the CRC but this is not well understood by faculty.

2.8.24 Scientific and Scholarly Advisory Board

The institution has an obligation to protect the rights of the complainant and the respondent in cases of alleged scientific/academic misconduct. The institution also has a responsibility to educate, train, and encourage faculty, staff, and students to consider the rights and privileges with which they have been entrusted, the consequences for breaching that trust, and the processes for determining whether actual misconduct has occurred. Information sufficient to increase awareness of the institutional community should be provided to everybody on an ongoing basis. When cases of scientific/academic misconduct are alleged or found to have occurred, locally and nationally the circumstances involved in these might be used as "case studies" to increase the knowledge base of faculty and staff.

2.8.25 GCRC

The Director and staff of the GCRC should continue to monitor investigator compliance with research regulations for human subjects admitted to this facility.

To do this effectively, however, they must coordinate this activity with Subjects Protection Programs.

2.8.26 Cancer Center

Ongoing compliance monitoring may not be a part of the Cancer Center Protocol Review Committee responsibilities, therefore this should be provided for by other means.

2.8.3. Rationale

Potential non-compliance with protection of subjects regulations places the institution and its employees at significant risk, but most importantly, the humans or animals involved. A plan for achieving and monitoring compliance needs to be developed and, once clearly defined, adopted. Random review or audits by compliance review staff would increase the attention to these regulations institution-wide.

Assistance to faculty and other research investigators during the protocol review and approval processes will bring specific compliance issues to their attention before the project begins. By virtue of the Research Service Office's actions, the quality of applications, research plans, and compliance will be improved and will benefit science, patients, PIs and the institution.

Requiring each college/school to assure compliance with DEHS regulations should improve awareness of the need for compliance and assist DEHS. Assistance to faculty and other research investigators in identifying areas of their research to which DEHS regulations apply early in the proposal review and approval process will avoid delays which may have occurred in the past if such a review had been postponed. As with subjects protection programs regulations, if a plan for compliance with DEHS regulations is developed and clearly explained, it is much more likely to be followed and therefore the level of compliance in the overall institution will be raised and improved. This is increasingly important as local and federal agencies have become more aggressive in prosecuting DEHS breaches imposing significant fines and sometimes even criminal sentences.

When an investigator is alleged to have erred, or found to have engaged in scientific/academic misconduct, the institution suffers. Raising the level of awareness of these matters to the University would underscore the importance. The institution should develop a readable, engaging Good Scientific Practices document to guide faculty, staff, and students in the responsible conduct of research. Cases of breaches of scientific integrity, whether here or elsewhere, could be used as case studies for faculty, staff and students.

The GCRC and IRB should cooperate in developing a compliance review program for the GCRC. The GCRC Director and staff should have all details of the IRB approved research plan to perform the most meaningful compliance reviews. This same type of thing would likely have to occur with patients entered under the Cancer Center protocol reviews.

2.8.4 For More Information

Food and Drug Administration Information Sheets http://www.fda.gov/oc/oha/toc.html

FDA Code of Federal Regulations http://law.house.gov/cfr.htm
(21 CFR Parts 50, 56, 312,361, 511,514, 571, 812, 813)

Federal Register http://lay.house.gov/7.htm
Docket No. 93N-0445
Objectivity in Research (Volume 60, Number 132)
Investigator Financial Disclosure Policy (Volume 60, Number 132)
Financial Disclosure by Clinical Investigators (Volume 61, No. 44)
Frequently Asked Questions.....(Volume 61, Number 129)
Protection of Subjects (Volume 61, Number 192)

Board of Regents' Policy: Conflict of Interest http://www.fdp.finop.umn.edu

Office of Research Integrity http://www.os.dhhs.gov/phs/ori/policy/policy.html
Advisory Document: Model Policy and Procedures
for Responding to Allegations of
Scientific Misconduct - April 1995

University of Minnesota http://www.ortta.umn.edu/policy/respolcy.htm
Board of Regents' Policy: Academic Misconduct

OPRR Protecting Human http://www.nih.gov/grants/oprr/oprr.htm

Research Subjects Guidebook http://www.nih.gov/grants/oprr/oprr.htm

OPRR Animal Care Guidebook http://www/nih.gov:80/grants/oprr/library_animal.htm

NIH Policy for GCRCs

NCI Policy for Cancer Centers

Integrity and Misconduct in Research http://law.house.gov/7.htm
(Report of the Commission on Research Integrity)

University of Minnesota Subjects
Protection Programs Homepage

[1]See sections Subjects Protection Programs, Assuring Scientific Integrity, Biohazards and Other Health and Safety, and Clinical Research Center.

[2]Roles and Responsibilities Document for Sponsored Research Program Management - Draft 11/15/96.

[3]RSSO Meeting Minutes - 11/11/96.

3.0 PROVIDING SUPPORT TO AHC INVESTIGATORS: RESEARCH SUPPORT SERVICE OFFICE

3.1 Introduction

It is clear that PIs in the AHC bear primary responsibility for all aspects of performing and managing industry-sponsored research. It is also clear that knowing the myriad of research regulations and policies PIs are required to be aware of and to comply with exceeds the time limitations of, in many cases, already overburdened faculty investigators.

We recommend the AHC provide a Research Support Services Office for its faculty and associate investigators involved with industry-sponsored research. This would be a service available to faculty on a voluntary basis. The principal goals are to:

- Aid faculty as much as possible regarding supporting materials and filling out of forms for all the internal approvals.
- Provide biostatistics support in developing the research plan.
- Aid in developing budgets.
- Provide help to faculty and staff to assure compliance with all federal and state and local regulations.
- Expedite and make "seamless" the whole process.
- More effectively market faculty technology and services to outside companies and organizations.
- Be able to submit grants to sponsors within 10 days of their internal submission.
- Assure that all steps in the internal approval process proceed contemporaneously - parallel processing.
- Assist faculty in meeting their responsibilities under the grant or contract.
- Produce more complete and consistent supporting application materials for internal review committees.
- Encourage and promote faculty entrepreneurial activities and technology and licensing to companies that may involve AHC faculty.
- Adopt a new operating principal for how the AHC works: by parallel process to provide concurrent, timely approvals for grants and contracts .

The Research Support Services Office Taskforce has divided and reviewed all of the processes involved in getting a proposal submitted and approved and broken these into their component parts. The order in which these process steps appear is intended to suggest the order in which these activities typically occur. It should be noted, however, that several of the approval processes do, and will continue to, occur simultaneously if we follow the process for concurrent, timely approvals for grants and contracts to the greatest degree possible.

In this introduction, background information gathered by the Research Support Service Office committee is provided regarding the current performance of each research process step.. Some of the individual steps are directly related to the function of institutional committees. These functions are discussed more

completely in the sections of this document devoted specifically to each group. Goals and recommendations for change are also included in this introduction.

3.1.1 Current Performance

3.1.11 Proposal/Protocol Review of Industry Sponsored Trials

Most commonly a PI receives an industry-sponsored research protocol. Before the study can be started, approval must be obtained from the PI's department head and dean. These approvals may require a department peer review of scientific merit and appropriateness to that department's discipline(s).

Before the department head and dean will approve a study, a review of the budget by a departmental financial administrator is usually required to assure salary/effort budgeting for the faculty member is included and fringe benefit rates are calculated correctly. The department head, center or institute director/dean must sign a BA 23 form, Subjects Protection Programs application form, and a letter to the Conflict Review Committee all indicating approval of the research.

The PI must apply to Subjects Protection Programs for approval if the protocol requires the use of human or animal subjects in the research. This review for approval is discussed elsewhere in this document.

In studies that require the use of the General Clinical Research Center (GCRC) for "maintaining" the patients and for data collection, the protocol must be reviewed and approved by the GCRC's scientific advisory committee (Dr. Paul Robertson, chair).

As is now required by the National Cancer Institute, the Cancer Center has recently created a scientific review and protocol coordinating committee (Dr. Phil McGlave, chair). Research studies that involve the study of cancer or patients with cancer must be reviewed and approved by this scientific advisory committee.

With respect to determining the feasibility of the proposed research, general experience suggests that many researchers often overestimate the number of potential subjects that might be available for a study. This tendency to overestimate is created by the PI's recall or impression of how many patients have been admitted, or might be available, with a specific disease state. It is not easy to fully recognize the limitations most study protocols place on the study subjects (inclusion and exclusion criteria) when determining the available subject population. In addition, simple over-enthusiasm, or the desire of the PI to use a new drug or device which may have the potential for additional research or clinical funding that aids the investigator's scholarly career, can sometimes bias the PI's judgment regarding the feasibility of enrolling a given number of patients.

In general, the General Clinical Research Center and hospital have not facilitated many investigators interested in industry-sponsored research. This is understandable since this is not their primary function. The GCRC protocol review process sometimes or often requires responses to stipulations that have already been defined and approved by the sponsor, investigator, and Food and Drug Administration, and usually cannot be changed, at least not without considerable difficulty.

Laboratory, clinic, and hospital services are frequently difficult to obtain or coordinate. There is no place to call to get comprehensive information or one

place or person to negotiate with. Rates for these services are hard to determine and personnel frequently are not very service-oriented when dealing with PIs. It is often difficult for PIs to find nursing services to assist in protocol administration without having to hire their own staff - which they often do out of necessity. There is an overall lack of trust in the efficiency, ease of use, responsiveness and cost competitiveness of the system.

There is a wide range in the comprehension and understanding by PIs of federal and University research study requirements. For example, PIs are often not aware that "clinical judgment" (except in life-threatening circumstances) is preempted by the need for strict "protocol compliance." This can create potentially serious compliance problems. In addition, PIs have often not fully considered or realized the time required to perform the duties they have agreed to by signing the study contract. Also, there are circumstances where PIs have not determined in advance which study tasks will be delegated, what the oversight mechanism for the study team will be, or that it is in place to assure successful completion of the research.

Some PIs are not aware that industry-sponsored clinical trials require that anyone treating subjects, assisting with research procedures and making assessments, or administering the study drug to subjects must have reported their credentials to the FDA. The FDA Form 1572 is often not updated as medical professionals are added to, or leave the study team.

3.1.12 Conflict of Interest and Academic Misconduct

Assuring scientific integrity at the University of Minnesota is directed by the Board of Regents' Conflict of Interest Policy and the Board of Regents' Academic Misconduct Policy. The AHC will apply these policies in the firm belief its researchers are honest, and committed to protecting the public interest and their own integrity by adhering to the highest ethical standards in the conduct of their research. Little or no ongoing support is provided to the faculty and other research investigators to aid in their understanding of or compliance with these policies.

3.1.13 Budget Preparation and Negotiation

Currently, there are no University guidelines for creating a budget for industry-sponsored research. Preparation of budgets is done on an individual basis by the PI with support staff from his/her department. We are aware of no training or guidelines that are available for budget preparation and negotiation. PIs developing budgets have little or no help and oftentimes lack experience estimating the actual costs of a study.

There are many reasons why this may be the case. Many factors make it difficult, if not virtually impossible, to accurately predict costs and then manage budgets and finances. While there is an intent to do this as best is possible, often there is no penalty for doing a poor job and in many cases organizational dysfunction precludes this.

After the direct costs are finalized, the indirect cost rate is applied to the budget. For industry-sponsored research, 20% of direct costs is the fixed rate.

We have heard from anecdotal industrial feedback that for many, the concept of indirect cost is an anomaly to them. They are much more used to and comfortable with the concept of fully allocated or fully burdened costs and might accept this more easily.

Commonly, the PI will negotiate budgets with the sponsor - and may accept the per patient reimbursement offered without precisely knowing whether that amount will cover the cost of doing the project at the University or not. For whatever reason, if the precise actual costs were not developed before creating the budget, there is a distinct possibility of negotiating a contract below cost. There are a number of examples of shortfalls on contracts. Department staff often do not get involved until the BA 23 is reviewed at the department level even though ultimately the department must take responsibility for the consequences of over expenditures relative to the budget. For industry-sponsored fixed price contracts - "the bottom line" has often already been established once it reaches the department level and there is a need to assure that this adequately covers costs.

3.1.14 Contract Review and Negotiation

In the current system, contracts from industry sponsors are sent directly to PIs. Faculty may review these contracts and/or elect to have a department administrator review them. After all internal approvals are obtained SPA staff review the contract, negotiate with the sponsor and PI any changes requested, and sign on behalf of the University of Minnesota.

It may take SPA anywhere from several weeks to several months to accomplish the review, negotiation and acceptance of a contract from an industry sponsor. This leads to extreme frustration on the part of sponsors and PIs who are often left in limbo with corporations; it leaves corporate sponsors, the business community and government with the feeling that we just don't care and that we have no appreciation for their position nor how valuable time is to them.

3.1.15 Subjects Protection Programs

Many investigators are not fully aware of all the regulations, guidelines, and community standards by which their research will be judged, and with which they must comply throughout the project. The applications and consent forms research investigators submit for IRB review often reflect their lack of familiarity with regulations, guidelines, and local standards.

Little ongoing support or education is currently provided to faculty on an ongoing basis in understanding and complying with human subjects research regulations.

3.1.16 BA 23 and Account Assignment

The Application for External Research, Training or Public Service Support (BA 23) is used to provide the approvals necessary to submit an application for external research or training support. In addition, it provides information for the institutional databases on grants and contracts.

The BA 23 form must be completed and submitted with all applications for new projects, continuations, renewals and supplements, and must also accompany agreements for the transfer of proprietary research materials (MTA's - Materials Transfer Agreements). The BA 23 form is not required by ORTTA for preliminary proposals and revised budgets.

The application must be submitted to the department head or unit director for review and signature. As centers and institutes proliferate around the University these may become the administrative "home" for grants, i.e., where authority and accountability rests. There may need to be some policy to make this clear. The application must then be processed in the same manner through the appropriate collegiate office. Again, centers and institutes may cause alterations in this procedure. Once these approvals are obtained, the application is submitted to ORTTA for final review, execution, and submission to the agency/sponsor.

After the agency/sponsor and ORTTA have reviewed and signed the research agreement or contract, a CUFS number is assigned to the project. The PI may begin charging expenses related to the project to the account as soon as it is established.

PIs may request that a preaward account be established when there is sufficient certainty the grant will be received and work on the project cannot be delayed. The PI's department, institute or center must guarantee payment of any charges to preaward accounts not covered by grant funds.

The BA 23 form is initiated by the PI who signs it and passes it on to the PI's department head and dean who are required to review and sign the BA 23. Approval signatures by the department head and dean indicate the following role or responsibility[2]:

- **Department head**: approval authority for on and off campus space, prorating department credit, the academic and management qualifications of the PI, the adequacy and correctness of the budget, equipment requests, cost sharing arrangements, and conflict of interest review.

- **Dean**: approval authority for on and off campus space and requests for indirect cost waivers. Local oversight authority for prorating department credit, affirming PI qualifications, determining the adequacy and correctness of the budget, appropriateness of equipment requests, cost sharing arrangements, and whether there has been approval of the conflict of interest review; these are all attested by the dean's signature.

- **PI:** signature indicates that the information provided is correct and that the equipment budgeted in the application is not otherwise available for use on the project from existing departmental or collegiate inventories. The PI indicates his/her agreement to abide by all applicable institutional and sponsoring agency policies and procedures (including the Patent and Technology transfer Policy of the University of Minnesota) and to follow commonly accepted scientific practices in recording and maintaining records of their research.

Experience would suggest that the quality of research applications, supporting materials and forms and the amount of time devoted to quality review of research applications by department heads and deans is variable. Many department heads and deans have delegated their review authority to the PI or to a department administrator. Department head and dean signatures, in many cases, indicate their trust in the PI and/or administrator rather than their meticulous review, knowledge, and approval of the research project. It is common, in the rush to meet agency/sponsor deadlines, for signatures to be provided without much or any local review of the proposed research except for budgets.

CUFS numbers to establish the specific accounts are assigned by SPA upon final acceptance of the contract, research agreement or award statement. An SPA grant administrator expedites assignment of the account number. SPA attempts to provide a CUFS number to the PI and his/her department within 48 hours after the contract or research agreement is approved by the University.[3] If SPA were able to achieve this it would be tremendous; however, it is not uncommon for months to elapse from the time the BA 23 is delivered to SPA to the time a CUFS number is assigned to the project.

3.1.17 Managing Project Changes

Changes to approved research projects may require additional review and approval when the changes involve: (1) a change in the faculty member's external relationship with the research sponsor, (2) a change in the budget or contract, (3) a change in the proposed conduct of human or animal subjects research, or (4) any change in the use of hazardous materials.

The principal and associate investigators are responsible for knowing that proposed changes in the research plan cannot be implemented without approval of local oversight committees or offices. Making application for approval of any proposed changes to the research plan is the responsibility of the research investigator and their collaborators.

3.1.18 Managing Research Funds

The responsibility for management of grant funds is shared between the PI, the department or unit administrator and the department head or institute or center director as follows:

- **PI:** initiates or approves the project budget and purchases in accordance with the budget, initiates documentation of mandatory cost sharing or matching, rebudgeting, cost transfers, and resolution of overdrafts. The PI is responsible for assuring he/she is in compliance with the effort reporting policy and that it is accurate. The PI is also responsible for approving payment of subcontractor invoices.

- **Department/Institute/Center Administrator:** administers the project budget and purchases in accordance with the budget, initiates documentation of mandatory cost sharing or matching, rebudgeting, cost

transfers, and resolution of overdrafts. Department administrators are also responsible for developing the effort reporting.

- **Department Head/Institute/Center Director:** provides local oversight in project budget management, approval of cost transfers, overdraft resolution, and rebudgeting.

Responsibilities for management of research funds are shared differently across departments, institutes, centers and between investigators within departments and these other units.

There is variability across departments in how well sponsored research accounts are managed. In some cases it is outstanding, in other cases the department administrators given responsibility are too far removed from the activity of the project to be able to participate effectively in the management of the funds. Perfunctory financial review may occur, but the reviewer (perhaps a department administrator) may have difficulty and cannot accurately judge whether a charge is appropriate, a payment due, etc. While a misappropriation of funds may occur infrequently, we have many examples locally of this problem and the consequences can be rather severe.

Currently, PIs must request approval from their ORTTA grant administrator (who often knows even less about the project than does the local department administrator) to spend grant funds beyond a single purchase dollar threshold.

Monitoring contract benchmarks and payment schedules is performed by the PI's own support staff or department administrator or their designees. The same is the case for monitoring charges by internal service providers.

Currently, PIs are very compromised by the University due to the difficulty of accurately gathering and having financial information presented to them in a way that makes sense. Compliance with effort certification continues to be problematic and in some cases questionable. Effort reporting is often less of an accurate reflection of effort extended than it is a financial juggling act to avoid over-commitment.

3.1.19 Closing the Project

PIs and department heads, center or institute directors are responsible for various activities required to close a sponsored project. These include, but are not limited to, review of regulatory documents, final reports, review of final account status and contract terms and closing the budget account at the University.

Current performance surrounding project closing responsibilities varies with the experience level of the PI and department administrator. In some cases financial closing of a project can be as difficult for a department administrator as was the management of the contract or grant funds. One of the factors contributing to this is the "distance" between the project activity and the responsible manager or administrator.

3.1.2 Goals and Recommendations

3.1.21 Proposal/Protocol Review of Industry-Sponsored Trials

The Academic Health Center should develop a check list that defines what each investigator (and Research Support Service Manager working with the PI) must consider before agreeing to an industry-sponsored (or any) research proposal or protocol. This statement or policy should be in sufficient detail such that the PI, Research Support Service Manager, and Research Support Service Office, are fully informed of their responsibilities when making a decision on whether or not to accept the proposal/study protocol.

This statement or policy should start with the mission statement: "The mission of the Academic Health Center is to be a leader in the ethical, innovative, and efficient discovery and dissemination of knowledge to enhance the health and well-being of Minnesota, the nation, and the world." It should include clear statements of what it is to be a scientist, responsibilities to the University and society, etc.

To assist with feasibility review, the Research Support Service Office will provide detailed demographic data on the patients in the University-Fairview health care system. Data on inpatient and outpatient admissions such as medical problem lists, treatments received, etc. would be used to estimate the potential subjects available and at what sites.

In order to meet the need for research facilities, the AHC must develop a cost-based, affordable inpatient and outpatient "facility" for clinical research. This facility doesn't have to be a specific hospital unit (though it can be), but must provide a detailed list of services (lab, radiology, clinical) and their costs, how to gain access, etc., in the form of "one stop" shopping. In addition, the AHC needs to develop the ability to purchase these services outside the University if they cannot be provided at a cost competitive rate.

Existing services such as the General Clinical Research Center, may have difficulty servicing a broader group of clinical investigators. Therefore, establishing a clinical trials unit or a "virtual" clinical trials unit would be highly desirable. The Research Support Service Office will need to employ a staff of experienced research nurses who can function in a "virtual" clinical trials unit. The research nurses will be assigned to PIs for each study. Since the working relationship between the Research Support Service Manager, Research Nurse and PI is critical to the success of each study, compatibility and consistency must be considered when forming these research teams. The research nurses will need to have flexible working hours, be able to cover for other nurses, and be willing to see and be involved with various types of research subjects.

The Research Support Service Manager will explain the study team requirements to the PI and assure all the federal and University compliance checks have been satisfied. A database of faculty expertise will be created to assist the Research Process Manager with locating potential sub-investigators.

3.1.22 Conflict of Interest and Academic Misconduct

Complete details of recommendations for the Conflict Review Committee can be found elsewhere in this document. With respect to the services which could be provided by the Research Support Service Office, we recommend that the AHC provide assistance to PIs in reviewing the PI's specific situation regarding the conflict of interest policy, his/her external relationships, and in choosing the best management plan for assuring scientific integrity when a potential conflict of interest may appear that could potentially bias or be perceived to have potential to bias the outcomes of the research. The Research Support Service Taskforce also recommends that the institution allow Department heads/Directors and Deans to delegate authority for review of potential conflict of interest to the Research Support Service Office. If this were to occur the Research Support Service Office, Research Support Service Office director, Vice Provost for Research or senior administrator or director of research in the AHC, would then be the arbitrators.

The Research Support Service Office will assist investigators in writing soundly designed studies. Importantly, this would include assuring that the statistical analysis used in reporting results is consistent with the planned analysis used to design the study. The AHC should provide random reviews of research conducted by potentially "conflicted" investigators where the integrity of the research data may be called into question.

3.1.23 Budget Preparation and Negotiation

It is highly desirable to develop a centralized function within the AHC to aid researchers, to the greatest degree possible, to ensure that research projects are budgeted correctly relative to what the real costs are expected to be. It is also desirable to create a centralized audit function for PIs who voluntarily want to ensure that they have budgeted for actual costs and have charged the account appropriately once the project has started.

The Research Support Service Manager will work with the PI to take responsibility for determining "actual costs" of the project and creating a budget. The Research Support Service Manager will use a data base developed to identify the median costs for performing a given study. The Research Support Service Manager will work with the PI to determine, as closely as possible, the actual costs of the project. Every effort will be made to estimate actual hours required to perform the study - and the likelihood that the work will be completed on budget. In no case, except with the concurrence of the faculty member, will a budget be used by the Research Support Service Office for its services in an amount greater than that agreed upon with the PI and reflected in the prospective budget.

As they now do, departments will continue to be able to participate in this process to the degree they wish - within the guidelines of 1) the research must pay for itself and 2) expenses cannot exceed allocated dollars. The Research Support Service Office will work with departments (who will still assume ultimate responsibility for the accounts in their areas) to provide faculty and departments

with well-researched and well-written industry-sponsored research budgets, and all the accompanying forms and information they require.

The anticipation is that via a database, having more accurate costing information, and by including staff most intimately aware of the project, the faculty member will be properly supported in developing the budget based on truly actual costs plus a stated amount of indirect costs.

Because expediency will be at a premium (with no compromise in quality), and the investigator will have participated in developing the budget, departments will have one working day, ~8 hours, to review proposed budgets and respond to the Research Support Service Manager with any requests for changes.

Upon initiation of the studies, and given an accounting system that works, the Research Support Service Managers should monitor expenditures on a monthly basis and report any unanticipated expenses over budget to the PI, department administration and the Research Support Service Office finance director/Research Support Service Office director.

3.1.24 Contract Review and Negotiation

The AHC should provide assistance and support to faculty and research investigators and be a liaison/support to SPA through preliminary contract review and negotiation in the areas in which most problems occur: intellectual property rights, publication rights, etc. SPA should identify the areas of common problems in proposals and award processes and develop an appropriate management plan in an attempt to remedy these problems before they start. This information should be provided to the Research Support Service Office. This could be in the form of standardized positions or terms that might represent a range of terms that are acceptable to the institution. More recommendations regarding the role of SPA can be found in the ORTTA section of this document.

3.1.25 Subjects Protection Programs

The quality of research plans, applications, and consent forms submitted to the IRB and IACUC should be improved by providing assistance to faculty and associate investigators as applications are prepared and research plans developed. More recommendations about Subjects Protection Programs can be found in the section so named elsewhere in this document.

3.1.26 BA 23 and Account Number Assignment

PIs should receive assistance from the Research Support Service Office to complete research applications, including the BA 23. The department head, institute or center director and dean approval authority, if continued to be required, could indicate delegation of review authority to the Research Support Service Office for the academic and management qualifications of the PI, the adequacy and correctness of the budget, and the conflict of interest review. It is clearly uncertain what importance, if any, the perfunctory "sign-offs" by deans and department heads accomplishes. It seems that the powers that be within the institution could agree that one person who was responsible and accountable could adequately do this for everybody currently involved in the chain of

signatures, i.e., department head, dean, ORTTA. For the time being, space, department credit, equipment, and cost sharing issues will continue to be reviewed and approved by an institutional authority outside the Research Support Service Office.

ORTTA should provide a CUFS number to the investigator and his/her department within 24 hours of signing the research agreement or contract from the corporate sponsor.

The rationale for these recommendations is that providing assistance and support to PIs will increase the quality of the supporting material in research applications and budgets. With respect to the current meaning of review signatures, department heads and deans, in many cases, have already informally delegated review authority to the PI or department administrators. It is known that there is great variability among PIs and department staff with respect to their knowledge of research regulations and policies. The Research Support Service Office will be staffed with individuals with sufficient skills to whom department heads and deans might more reasonably delegate review and approval authority for PI eligibility, budgets, and conflict of interest review. Research Support Service Office staff can also assist department heads and deans by identifying space, appropriate credit, equipment, and cost-sharing issues department heads and deans should consider.

Abbreviating the contract negotiation process should make the time from BA 23 submission to CUFS number assignment significantly shorter. Requiring ORTTA to provide a CUFS number within 24 hours of signing the contract or research agreement will allow PIs to proceed with the project as quickly as possible.

3.1.27 Managing Project Changes

PIs should be assisted by the Research Support Service Office in assuring that all proposed changes to approved research are approved by the appropriate local oversight committee or office. Compliance with regulations will be increased by Research Support Service Managers assisting research investigators in notifying local oversight committees and offices of proposed changes to research plans. When proposed changes must be approved by a local oversight committee or office, the Research Support Service Manager will assist the PI by completing the application and tracking it through the system as was done during the initial review and approval phase. The same aforementioned timeliness of approvals within 10 working days will be expected.

3.1.28 Managing Research Funds

The Research Support Service Office should provide grant management support to the PI and department or unit administrator. The Research Support Service Manager responsible for working with the PI in developing the budget and negotiating the contract should also be responsible for working with the PI to manage the grant funds within the current or any new grants management system.

Research Support Service Managers should review requests to spend grant funds and make approval recommendations to ORTTA. In conjunction with

the PI, the Research Support Service Manager will be responsible for monitoring progress on the study and assuring that the sponsor is following the payment schedule in the contract.

The Research Support Service Manager should be responsible for preparing and distributing a monthly financial report to the PI and his/her or local grants management unit, i.e., department, institute or center. The Research Support Service Manager will also assist the PI to assure compliance with the effort certification policy.

Centralizing these grant fund management responsibilities in the Research Support Service Office will assure that staff knowledgeable of not just policies and regulations, but also the project, budget, and contract are managing the funds. This should remove the "disconnect" which so often appears to interfere with the provision of adequate grant funds management information to faculty, and especially in providing this on a timely basis.

3.1.29 Closing the Project

The Research Support Service Office should assume responsibility for review of any regulatory documents, final reports, review of final account status and contract terms, and closing the account. The Research Support Service Manager will assist the PI in completing the end of study requirements and will provide information to the PI and to the PI's department, center or wherever the grant is administratively housed.

Centralizing the end of the project management responsibilities in the Research Support Service Office will increase the probability of assuring compliance with regulations. In addition to this, the institution is interested in developing or monitoring long term relationships with corporate sponsors. Therefore providing the sponsor and regulatory bodies with the appropriate information in a timely manner is important so that corporate sponsors believe that they have invested their money wisely. Also, the Research Support Service Manager will assure that all payments from the sponsor have been received, bills paid, and that any approved cost overruns are billed to the sponsor.

The following sections describe the services we recommend the project service division of the Research Support Service Office should provide. These services expand on the recommendations listed in this introduction.

3.2 Research Support Services

3.2.1. Proposal/Protocol Review

One of the Research Support Service Office responsibilities is to serve as an administrative advocate for the PI within and outside of the institution. The Research Support Service Manager will review the study protocol overall, including but not limited to: reviewing the project for scientific merit, for consistency with the mission and goals of the AHC, for feasibility (such as subject population, resources), and for determining the composition of the research team. In conjunction with the PI the Research Support Service Manager will work to complete a series of steps toward documenting the consideration given these issues. The intended purpose of this is to provide a process in which the PI can consider the merit of the research, the likelihood the project can be successfully performed, and to determine the staff and services support the project will require.

The Research Support Service Manager has the authority to complete all approvals in the protocol review process. The project will be forwarded beyond the Research Support Service Manager only in the event there is a question that cannot be resolved by the Research Support Service Manager and the PI. It is not anticipated that this would occur with any frequency but when it does, the Vice Provost for Research, Dean for Research, or most senior official dealing with research in the AHC would arbitrate this.

3.2.11 Review for Scientific Merit and Consistency with Mission and Goals of the AHC

The research proposal/protocol will be reviewed by the Research Support Service Manager and the PI. The PI will be responsible for helping the Research Support Service Manager provide information and answers to basic questions upon which the scientific merit of the proposed research will be defended. The questions or information collected will be:

- A brief description of the drug or device,
- The proposed subject population,
- The hypothesis being tested,
- Study endpoints,
- Statistical plan,
- A brief statement of the principal investigator's time commitment to the project.

The Research Support Service Manager will use the information provided in this preliminary step to complete other internal or external regulatory committee forms and applications. To assess scientific merit, these are examples and questions that will be discussed and documented:

- Is this new drug or device just starting clinical testing, or is it a study to allow the PI to gain experience with the drug or device?

- Does the study involve a vulnerable population? Has the investigator thought about how to justify the use of this population?
- Is there a hypothesis being tested?
- Will the endpoints answer the research question?
- Is there a statistical plan that would provide a definitive answer?
- After considering these issues, why do this study?

This general review for scientific merit will be forwarded to the department or unit at the time all study materials are delivered for their files. In the rare case in which the PI and Research Support Service Manager cannot come to agreement regarding the scientific merit of a study, a statement will be forwarded to the Research Support Service Office Director/Provost's Office, i.e., Vice Provost for Research for review, and consideration for approval.

3.2.12 Feasibility Review

The PI and Research Support Service Manager will determine what resources are needed to conduct the trial or study, whether the PI has access to these resources, and if not, if is there a plan to obtain resources not currently available in the AHC. The areas of review will include among other things:

3.2.13 Patient Population

The PI and Research Support Service Manager will review the subject population. The PI will be responsible for assuring that an adequate number of potential subjects exists from which to recruit for the study. The PI and Research Support Service Manager will discuss the recruitment strategy for reaching the potential subjects. Human subjects rules for recruitment will be addressed with the PI during this discussion. The Research Support Service Manager will use this information to complete the human subjects application as the study passes the protocol review stage.

3.2.14 Core Facilities and Resources

The PI and Research Support Service Manager will discuss the need for core facilities: inpatient and outpatient services, laboratory services, other clinic and hospital services, and research nurses. The availability of these services will be determined. The Research Support Service Office will negotiate with existing internal service providers, on behalf of the PI, in an attempt to obtain the optimal prices or service. The Research Support Service Manager will also try to obtain facilities or resources that are needed but not available internally. In addition, to optimize efficiency of relative costs and services, outsourcing will be considered to fulfill any of the needs generated by a project.

3.2.15 PI Commitment - Time and Other

The Research Support Service Manager and PI will discuss the PI's commitment to following the protocol. Any potential risks for non-compliance will

be identified, i.e. does the PI have time to complete the assessments they are agreeing to make.

The Research Support Service Manager will document concerns regarding PI commitment, if any, and review the responsibilities the PI agrees to accept by signing the FDA 1572 form.

3.2.16 Naming the Research Team

The Research Support Service Manager and PI will review the protocol and sponsor requirements to determine the need for other professionals to assist with performing and managing the trial. The Research Support Service Manager will facilitate finding any needed sub-investigators for the study. However, the PI will have the ultimate authority for determining the addition of any co-investigators or sub-investigators. The PI must assume authority and be responsible for the conduct of all other members of the research team involved with the clinical trial.

3.2.17 Sponsor Regulatory Documents

The Research Support Service Manager will be responsible for completing all the required regulatory documents and assisting the PI in organizing and executing the long term document retention requirements. The Research Support Service Manager, in consultation with the PI, will complete the FDA form 1572; collect the C.V.s or biosketches of all staff members listed on the form, provide the IRB committee the staff member list, and collect laboratory certification documents, normal ranges, and lab directors' C.V.s.

3.2.2 Conflict of Interest Review and Management

The Research Support Service Manager will assist the PI in complying with the University of Minnesota conflict of interest policy. The Research Support Service Manager, the Research Support Service Office, and the Vice Provost or dean for research will share the ultimate responsibility for identifying and managing potential conflicts of interest with the PIs.

The PI is responsible for providing complete and accurate information in disclosing external relationships and commitments. The Research Support Service Manager is responsible for assuring the information provided is properly defined, and for identifying a plan to manage any potential for a conflict of interest that could be perceived to bias the research outcome. The Conflict Review and Management Committee will review cases where there is a potential for conflict of interest or commitment, making recommendations to the Research Support Service Office Director, or AHC Vice Provost or dean for Research, as to whether the management plan should be approved. The senior AHC person overseeing research is responsible for final approval of the plan. The University has an institution-wide conflict resolution group - the Public Private Partnership Committee. Recommendations of the Public Private Partnerships Committee may be solicited to assist the AHC in making the final determination.

The Research Support Service Manager will also assure that research investigators are familiar with their rights and responsibilities with respect to the Regents' Policy on Academic Misconduct.

Regents' Policy on Conflict of Interest will guide the conduct of research in the AHC when a research investigator's external financial relationships may be perceived to potentially compromise the integrity of data produced by a study. The Research Support Service Manager will guide research investigators through the policy and the procedures in cases where there is a potential for conflict of interest.

3.2.21 Review of Faculty Members and Research Investigator's External Relationships

The Research Support Service Manager will check the PI database for the completed Report of External Relationships for the PI, and for any co-PI/sub-investigator serving in a capacity which could be perceived to allow any potential bias in the outcome of the study. The report will be reviewed by the Research Support Service Manager, and the PI(s) will be contacted (via e-mail) to ask if there have been any changes since the report/data base was last updated (if more than 30 days have passed since the report was last updated). If there have been changes, the PI will be asked to make the changes and the report will be printed for the Research Support Service Office file. If there have been no changes, the e-mail response to that effect will be printed and placed in the Research Support Service Office file. The Research Support Service Manager will review funding sources for the PI's entire research program.

3.2.22 Review of the Study Research Design

More rigorous management of potential for conflict of interest is required for studies in which the evaluation of bias resulting from conflict of interest is difficult to assess by other means.[1] Studies falling into this category include: open label, unblinded studies of a non-pharmacokinetic nature, study designs with subjective endpoints, single investigator studies, or multicenter studies in which the University of Minnesota is expected to provide a disproportionate number of subjects. In these situations, a review to assure appropriate experimental design and documentation, coupled with the review of data generated and performed with industry is required to comply with federal regulations. This will objectively address circumstances surrounding a research study where concern about bias might exist in a more meaningful way, perhaps, than through inferences drawn from financial disclosure statements.[1]

If it is determined that no significant potential for conflict of interest. exists, the Research Support Service Manager will note this in the Research Support Service Office file and the review of external financial relationships for the project will end. A copy of the report of external relationships will be sent to the Department head and to the Dean and, as appropriate, to any relevant center or institute director.

When it is determined that a potential for conflict of interest exists, the Research Support Service Manager will inform the PI of the potential conflict and a management plan will be developed. If the PI opts to end the relationship with the sponsoring corporation, written documentation of the end to the relationship must be provided. If the financial relationship is terminated, the application will be noted as acceptable by the Research Support Service Manager on the BA 23 and the application will be forwarded to the AHC SPA representative for review.

Only in cases in which a potential conflict of interest is determined to exist will applications be reviewed by the Conflict Review and Management Committee (CRMC). The Committee will meet as often as necessary (no less often than bi-weekly) to review applications. The Conflict Review and Management Committee review process will be limited to addressing the issue of investigators' external financial relationships, and review and approval of the proposed plan to manage the conflict. The Committee will review applications in less than 10 working days, and may recommend approving or denying the plan for managing the potential conflict. The final decision authority rests with the AHC, e.g., Vice Provost or dean for Research who may seek the advice and recommendation of the Public Private Partnerships Committee.

3.2.23 Responsibility Indicated by Conflict Review Document Signatures

PI: Signature by the PI, co-investigator, or sub-investigators means that he/she has complied with all the disclosure requirements of the Regents' Policy on Conflict of Interest, and that the management plan for any potential conflict of interest will be followed.

Research Support Service Manager: Signature by the Research Support Service Manager means that the proposed activities have been administratively reviewed, a conflict of interest management plan has been developed and that the affected academic employees have received information about the action plan, the disclosure requirements, other University policies, and any pertinent federal or local regulations.

Conflict Review and Management Committee: This Committee will have authority to approve cases in which a potential for conflict of interest exists, to approve a proposed management plan, or to recommend management plans which mitigate this situation and make a potential conflict acceptable. It is expected that the norm will be to approve corporate sponsored research where a management plan has been developed to deal with a potential conflict of interest. Thereafter University administration at all levels will vigorously defend the employee and the activity so long as the academic employee complies with the plan of action, the disclosure requirements, other University policies, and any pertinent regulations.

Provost's Office: Depending on the ultimate organization of the Provost's Offices, the Research Support Service Office director, Vice Provost or Dean for Research signature on the BA 23 indicates final approval of the research project with respect to conflict of interest.

[1]Testimony of the American Association of Pharmaceutical Scientists on the FDA's Proposed Rule on Financial Disclosure by Clinical Investigators [Docket No. 93N-0445].

3.2.3 Budget Preparation and Negotiation

The Research Support Service Office responsibility for working with the PI in the preparation of the budget is to assure that the funds budgeted will cover all the anticipated research costs - including the PI/co-investigator/sub-investigator efforts. The Research Support Service Manager, working with the PI, will determine the costs of the study and prepare the proposed budget for review by the PI. The PI and Research Support Service Manager will negotiate the budget with the sponsor. The PI may elect to give the major share of the responsibility for budget negotiation to the Research Support Service Manager but the PI would have final review authority.

The Research Support Service Manager will have the authority to complete all approvals in the Research Support Service Office protocol review process. The project will be forwarded beyond the Research Support Service Manager only in the event there is a question/concern about performing the study at a financial loss that cannot be resolved by the Research Support Service Manager and the PI. In a case where the PI, Research Support Service Manager and sponsor can't come to agreement on a fiscally sound budget the senior authority, Vice Provost for Research and unit head of the PI would make a determination on whether or how to go forward and who would assume financial risk.

3.2.31 Determination of Actual Costs

During the early stages the Research Support Service Manager will work with the PI and his or her colleagues to develop a list of all procedures and services required to perform the study. Given this, all personnel required to perform the study and fulfill its requirements will be determined.

- Negotiation with Internal Service Organizations (ISOs)/Other Internal Service Providers

The Research Support Service Manager, working on behalf of the faculty member will negotiate with and/or arrange the purchase of service from ISOs and other internal service providers. This will include all Fairview University Medical Center services such as laboratory, radiology studies, inpatient and outpatient charges for facilities, etc.

- Separation of Standard Care from Research Procedures for Clinical Trials

The Research Support Service Manager will determine, in consultation with the PI, which (if any) procedures, diagnostic tests, clinic and hospital charges, etc., are related to standard care. Charges that are explicitly part of standard care will be billed to the patient/subject and/or his third party payer. All charges not explicitly part of the patient/subject's standard care will be built into the study budget.

- Personnel

Over time experience will allow the Research Support Service Office to determine the Research Support Service Manager time necessary to develop the proposal through the point of submission to the sponsor This cost will be borne by the Research Support Service Office. The Research Support Service Manager and the PI will discuss the extent to which other Research Support Service Office support during the project management phase will be required, e.g., biostatistics, etc. The ongoing Research Support Service Office effort during the project management phase will be projected and determined with the PI based on the PI's need. A schedule of tasks, projected time required to perform them, and the hourly rate of staff (including fringe benefits) will be prepared for the PI's approval. With the PI's approval, these personnel costs will become part of the study budget.

The costs of PI/co-investigator/sub-investigator effort will be reflected in the budget, as will the costs associated with research nurses required to oversee and perform clinical assessments.

3.2.32 Preparation of the Draft Budget

The Research Support Service Manager will prepare the draft budget and attach worksheets for calculating Research Support Service Office charges and all personnel charges. (Worksheets will be for internal distribution only.)

- Process of Review, Change, Approval

In the interest of expediency, no one other than the PI and the Research Support Service Manager will be required to review the budget. However, departments or other units that wish to review proposed budgets prior to budget negotiations with the sponsor will have 8 hours in which to respond to the Research Support Service Manager with requested changes. Again, in the interest of minimizing unnecessary steps, avoiding duplication, and expediting proposals, communication between Research Support Service Managers and department staff will be solely electronic at the stage of draft budget preparation.

Research Support Service Managers and PIs will have the authority to approve the budget and proceed to negotiation with the sponsor.

- Indirect Costs and "Margin"

The current indirect cost recovery rate for industry-sponsored research at the University of Minnesota is 20% of the direct costs. Arrangements with the PI and unit heads will be made about the use of any funds remaining after expenses.

3.2.33 Negotiation with the Sponsor

The Research Support Service Manager will fax the proposed budget and the standard U of M contract to the sponsor. The Research Support Service Manager (or the PI if he/she prefers) will negotiate the budget with the sponsor. Agreement will be reached between the PI and the Research Support Service Manager, prior to negotiation, to assure clarity in the areas in which there may be room for negotiation. In no case will the PI or the Research Support Service Manager negotiate downward without the express knowledge and agreement of the other. The PI and/or Research Support Service Manager will continue the process of negotiation until the budget is negotiated to their satisfaction.

3.2.4. Contract Review and Negotiation

It is a desirable and laudable goal to create mutually beneficial, highly effective and respectful relationships between the University (in accordance with its mission and rights) and a sponsor (with its mission, rights and market demands) that does not compromise either party's position. Understanding this operating principle is the basis on which these contracts need to be written, negotiated, executed, and monitored. Without this foundation for the relationship, a contract has yet to be written that will be sufficiently detailed or litigation-proof to assure absolute respect for each party's rights. Absent this understanding neither party should enter into an agreement.

The Research Support Service Office will work on behalf of the PI and institution and will be responsible for reviewing the contract or grant to assure that the:

- intellectual property rights of the faculty member and University are protected,
- projected income schedule is structured to be compatible with the expense schedule,
- academic freedom of the faculty member and research is maintained, and
- confidentiality of the sponsor's assets is protected.

3.2.41 Initial Contract Review

Preliminary contract review will be performed by the Research Support Service Manager. To the degree possible, the standard University contract will be used.

- Standard University and AHC Contract

Terms will be developed by the PI, any collaborating investigators, and the Research Support Service Manager. General concurrence on the terms of agreement will be reached prior to submitting it to the sponsoring organization for their review. Any review by legal counsel will also be performed at this time. Changes that the sponsor requests will be negotiated by the Research Support Service Manager, in conjunction with the PI, the Research Support Service Office director, and Research Support Service Office legal counsel, the Research Support Service Office financial leader, as needed.

- Sponsor's Contract

The Research Support Service Manager will review the sponsor's proposed contract in all aspects. The Research Support Service Manager, functioning with or on behalf of the PI and in conjunction with Research Support Service Office finance and legal counsel as needed, will negotiate any changes that are desired. These will be agreed upon and signed for by the PI. The financial terms will also be reviewed by a financial officer in the Research Support Service Office/Provost's Office.

3.2.42 Negotiation and Approval of Contracts

- Proposed Long-Term Plan

In order to save faculty time (with the concurrence of the faculty member) the Research Support Service Manager will lead the negotiation process with Research Support Service Office financial and legal assistance, as needed. The Research Support Service Manager will sign off on all contracts where intellectual property is not involved. If intellectual property is or may be involved, the Research Support Service Office staff member designated to review intellectual property, will guide the review and negotiation process. In the interest of efficiency, delegation of responsibility and accountability to the Research Support Service Office would be such that they should have the authority to sign contracts for the Board of Regents. In any of the dealings with corporate sponsors there may be faculty who wish to lead these negotiations, and if so, the Research Support Service Manager will work with them to facilitate and expedite this process.

- Proposed Short-Term Plan

The Research Support Service Manager, functioning on behalf of the PI and with the Research Support Service Office legal and financial assistance as needed, will lead the negotiations and keep the site-based ORTTA representative apprised of these. Upon reaching closure, the site-based ORTTA representative will review (with <4 hr turnaround) the contract. If acceptable, the ORTTA representative will sign the proposal, indicating the University's acceptance of the agreement and that the interests of the University and the faculty member will be protected.

Experience suggests that there may be a variety of questions that arise when a contract is reviewed by ORTTA. Ideally, associated with the new process envisioned, most of the kinds of issues that ORTTA has been concerned with in the past would already have been resolved. Notwithstanding these good intentions however, there may be issues that need to be resolved with the sponsoring organization. Over time, continual fine tuning should reduce this time to a minimum.

In the current system, the Conflict Review Committee reviews "batches" of contracts and grants, and then sends these same "batches" on to Sponsored Projects Administration for approval. Given the nature of this work flow, it has added to the backlog at Sponsored Projects Administration. Some contracts are managed in a more expeditious manner than others. In the new system, as a general operating principal, we recommend that verbal or electronic contact with sponsors occur within 24 hours of receipt of the contract. For any changes that must occur we recommend that a university official must contact a sponsor within 24 hours of a need to execute some modification or negotiation, and to do so in an iterative fashion if needed.

In all cases, the PI's signature on a contract indicates the faculty member's awareness and acceptance of the terms of the agreement and a willingness to abide by the same.

3.2.5 Protection of Human Subjects

The Research Support Service Office will be responsible for assisting and supporting faculty members so that they can, as best as possible, follow regulations which govern research involving human subjects. The support and assistance provided by the Research Support Service Manager will allow the PI to develop the best planned and developed materials for the IRB; the better the preparation the greater the likelihood that investigators will get IRB approval for their protocols as expeditiously as possible. The Research Support Service Manager will review and develop human subject research plans with PIs and their associates, provide information, and support faculty and their associate investigators as they prepare applications and consent forms.

Research Support Service Managers will be responsible for knowing human subjects research regulations, and for assuring, to the greatest degree possible, principal investigator compliance with regulations through all the steps of the project approval phase.

3.2.51 Protocol Review

The PI and Research Support Service Manager will review the protocol to discuss the overall management of the study and to determine whether or not the study would qualify for an expedited review (almost none will). Through this discussion, the Research Support Service Manager can assist the PI in identifying issues critical to managing the project with the highest regard for each subject's safety, confidentiality, and right to be completely informed before deciding whether or not to participate in the research study. This process will provide answers to questions the Research Support Service Manager will answer as he/she completes, or assists the faculty member in completing, the human subjects application form. Among other things, the Research Support Service Manager will address these types of issues:

- Roles and Responsibilities of Principal and Associate Investigators

The roles and responsibilities of the study team will be identified. The role of each study team member will be defined explicitly, especially with respect to their role in the process of obtaining informed consent.

- Identification and Recruitment of Subjects

The Research Support Service Manager and PI will discuss the method by which potential subjects will be identified. The Research Support Service Manager will be responsible for developing an alternative method that will be acceptable to the IRB if, in the judgment of the Research Support Service Manager, the PI's approach appears one that might prove unacceptable to the IRB.

- Vulnerable Populations

As the protocol is reviewed, the Research Support Service Manager will identify any vulnerable populations that the study may involve. The Research Support Service Manager and PI will discuss the regulations that apply to studies involving a vulnerable population(s). Together, the PI and the Research Support Service Manager will apply the tests IRBs must use to approve research in a vulnerable population. This process will improve the faculty/research investigator's understanding of the IRB guidelines and processes, improve the quality of the application, and assure the IRB that the PI has made the necessary special considerations required. Documentation that a clinical investigator has considered, answered, and justified (where necessary), the questions IRBs must ask regarding the recruitment of vulnerable subjects will raise the level of awareness, knowledge and compliance with these requirements throughout the entire research process.

- Financial Considerations

The Research Support Service Manager and PI will discuss plans for paying incentives to research participants. Together, decisions can be made about the appropriateness of payment, the "approvability" of the amount, the plan for payment, and how a subject who is terminated from the study before completion will be compensated.

- Assessment of Risks and Benefits from Participating in a Study

The PI and Research Support Service Manager will assess the potential benefits and risks to subjects participating in the trial. Proposing research in vulnerable populations requires particular attention to this issue. Determination and an accurate description of the alternative treatment the subject could receive (if any) will be made at this step. Assessing the benefits and risks for subjects participating in the study must be reviewed in the context of the subject's general condition. Principal investigators will be encouraged to objectively consider the patient's assessment or recognition of risks.

- Plan for Managing Emergencies

After considering the potential risks to study subjects, the PI and Research Support Service Manager will develop a plan for dealing with emergencies that may occur. This will include describing the roles of the members of study team in an emergency, and what other treatments will be available in the case of emergency.

- Confidentiality and Records Retention

The Research Support Service Manager will be responsible for determining the most appropriate plan for maintaining confidentiality of study records. The Research Support Service Manager will be responsible for consulting the PI and informing him/her about the importance of adhering to the

plan for maintaining confidentiality. The Research Support Service Manager will be responsible for informing the PI about federal records retention requirements for IRB documents and communications. In order to facilitate this, the Research Support Service Manager will assist the PI and/or his/her staff in developing a master plan for records retention.

- Consent Process

The PI and Research Support Service Manager will determine the process by which informed consent will be obtained. The Research Support Service Manager will assume responsibility for developing a consent process that will assure that no subject is enrolled without an approved member of the study team participating in the process of obtaining informed consent with the potential subject. During this process, the research protocol will be explained to the subject, the subject will be allowed to ask questions and receive answers, the study team member will ask questions of the subject to assess his/her understanding of this, and given full understanding on the part of the patient the consent form will be signed if the potential subject agrees to participate. The PI will be informed and educated about the importance of obtaining consent before any study related procedures are performed, allowing the potential subject time to consider what is being asked of him/her, using language the potential subject can understand, and taking time to consider each individual in precisely the manner in which he/she would hope a parent, spouse, or child of his/her own might be regarded.

- Consent Form

The PI and Research Support Service Manager will discuss the sections of the consent form not previously addressed. The PI will be informed of the importance of assuring none other than the most currently approved version of the consent form is used when recruiting subjects. A consent form log will be given to each PI for the purpose of recording each subject, the version of the consent form signed and the date consent was (or was not) obtained. Research regulated by the FDA must have complete and accurate records about consent forms for subjects who agree to sign, and also for potential subjects who decline the invitation to participate.

3.2.52 Preparation of Human Subjects Application and the Consent Form

The Research Support Service Manager will prepare the application and draft the consent form. The PI/co-investigator/sub-investigator will review and approve the application and the consent form before it is submitted to the IRB. The Research Support Service Manager and the PI will have thoroughly discussed the research and will have addressed the questions that it is well known the IRB must ask. The Research Support Service Manager will complete these tasks, but will do so only after thorough consultation with the PI. Throughout this process, the Research Support Service Manager is working on behalf, not in lieu, of the PI. It is common for the sponsors of industry supported

research to request their own review of the proposed consent form prior to submitting the application and consent form to the IRB.

- Review and Approval Prior to Submission to the IRB

The PI/co-investigator/sub-investigator must all sign the human subjects application form before it is submitted to the IRB. Their signatures indicate agreement with the information in the application, a pledge to make no changes without first informing the IRB (except in life-threatening circumstances), and a promise to follow the plan for the research outlined in the application form. This means, for instance, enrolling no more subjects than the application indicates will be enrolled, drawing no extra blood or other fluid samples than those indicated in the application, and assuring the consent process outlined in the application is followed. The Research Support Service Manager will certify that no other application for the project has been submitted to the IRB, and that all items the IRB will check during its "triage" process are addressed and included in the application.

3.2.53 Protection of Human Subjects Application Review Process

Human subjects applications and consent forms prepared by the Research Support Service Office will be approved by the IRB within 10 working days of receiving the completed application. The Research Support Service Manager will be informed of the IRB committee meeting date and whether the faculty member/research investigator might be needed to answer questions via some telecommunications method such as video conferencing. The Research Support Service Manager will assist the faculty member in preparing his/her response.

3.2.54 Management of Protocol Changes

Changes to industry-sponsored protocols must be approved by the FDA prior to being distributed to the clinical sites involved in the trial. These changes come in the form of what is termed "protocol amendments" from industry sponsors. These protocol amendments cannot be implemented prior to review and approval by the IRB. When the PI receives a protocol amendment, it will be given to the Research Support Service Manager as quickly as possible. (Ideally, they would be notified contemporaneously.) The Research Support Service Manager will review the amendment in the same manner in which the original protocol was reviewed. In conjunction with the PI, the Research Support Service Manager will determine whether or not the protocol amendment involves any change in the risk to study subjects. The changes will be listed and addressed in a letter to the IRB. If the consent form requires changes as a result of the amendment, these will be made by the Research Support Service Manager and a proposed new version of the consent form will be sent to the IRB Committee for review and approval. Any protocol amendments, changes, or corrections will also be reviewed and approved within 10 working days following the IRB Committee's receipt of the information.

3.2.55 Reporting Serious Adverse Events (SAEs)

- Local Site

The Research Support Service Manager will discuss with each PI the protocol specific requirements for reporting serious adverse events to the sponsor of the study and to the IRB. The FDA has defined a list of events as "serious", however, due to the nature of some protocols and subject populations, the definitions listed in each protocol should always be reviewed for what represents a serious adverse event in the given study. Prior to beginning the clinical trial, the Research Support Service Manager and PI will discuss assessing the causality of any adverse events, and how to assess the relationship of the test article to the event. If a serious adverse event occurs, the PI will report the event to the Research Support Service Manager as quickly as possible after learning of the event. A report (usually a sponsor form) will be completed by the PI and/or a study nurse and faxed to the sponsor within 24 hours of learning of the event. This report will then be given to the Research Support Service Manager so that the essential facts known at that time can be included in a notification letter to the IRB. The Research Support Service Manager will prepare this notification letter within 24 hours of receiving the information from the PI or members of their team. If more information becomes available regarding resolution of the event, the PI will provide this information to the Research Support Service Manager for notification of the IRB. There will be instances in which the IRB will ask for more information. There will also be instances in which a change to the consent form may be required resulting from the occurrence of an adverse event for which a specific risk is not already listed. The Research Support Service Manager will discuss this possibility with the PI. If a change is required, the Research Support Service Manager will modify the consent form and send the proposed revised version to the IRB with the serious adverse event notification letter.

- Other Sites

Industry sponsors of multicenter clinical trials are required to report serious adverse events (SAEs) experienced in a clinical trial at one center to all participating centers. (Many sponsors refer to the notification letters as "IND letters".) Investigators at each center are required to consider each event that may occur at any participating center and to report it to the IRB at their own institution. The IRB will consider whether or not the local consent form must be changed based on the SAEs reported at other centers. The Research Support Service Manager will review the IND letters, organize the information for the PI, and prepare an IRB notification letter (and revised consent form, if necessary). These sponsor IND letters will be batched and submitted to the IRB no less often than quarterly. The sponsor may require a more frequent than quarterly submission of the information to the IRB.

3.2.56 Retention of Records

The Research Support Service Manager and PI will discuss the requirements for records retention related to IRB documents and correspondence. The FDA requires that all correspondence between the IRB and the PI be retained in chronological order. In addition, the complete original application, protocol, Investigational Drug Brochure (IDB), and all approved consent form versions must be retained. Each subject's consent form bearing the original signature must be retained by the PI. All of these documents are subject to review by the sponsor and by the FDA.

3.2.6 Protection of Animal Subjects

The Research Support Service Office will be responsible for supporting research investigators so that they are guided in how to effectively follow regulations that govern research involving animal subjects. The Research Support Service Manager will review and develop animal subject research plans with PIs, provide information, and support PIs and their staff as they prepare the University of Minnesota Animal Usage Form .

Research Support Service Managers will be responsible for knowing animal care and use regulations, and to the degree possible, for assuring PI compliance with various regulations in the project approval phase.

The Institutional Animal Care and Use Committee (IACUC) is guided by the following principles in making determinations about the acceptability of animal use applications:

U.S. Government Principles

- The transportation, care, and use of animals should be in accordance with the Animal Welfare Act (7 U.S.C. 2131 et seq.) and other applicable federal laws, guidelines and policies.
- Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.
- The animals selected for procedures should be of an appropriate species and quality, and the minimum number required to obtain valid results. Alternatives such as mathematical models, computer simulation, and in vitro biological systems should be considered.
- Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain is imperative when consistent with sound scientific practices. Unless the contrary is necessitated, research investigators should consider that procedures causing pain or distress in human beings may cause pain or distress in other animals.
- Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgery, or other painful procedures, should not be performed on unanesthetized animals paralyzed by chemical agents.

- Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved, should be painlessly euthanized at the end of the procedure or, if appropriate, during the procedure.
- The living conditions of animal should be appropriate for their species and contribute to their health and comfort. Normally, the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of that species. In any case, veterinary care must be provided as indicated.
- PIs and other personnel shall be appropriately qualified and experienced in the proper care, handling, and use of the species being maintained or studied. In any case, veterinary care must be provided as indicated.
- Where exceptions are required in relation to the provisions of these principles, the decision should not rest with the research investigator directly concerned but should be made, with due regard to Principle 2, by an appropriate review group such as an institutional animal research committee. Such exception should not be made solely for the purposes of teaching or demonstration.

Research Support Service Managers will be responsible for knowing animal subjects research regulations, and for assuring to the greatest degree possible investigator compliance with regulations through all the steps of the project approval phase.

3.2.61 Protocol Review

The PI and Research Support Service Manager will review the protocol to discuss the overall management of the study. Through this discussion, the Research Support Service Manager can assist the PI in identifying issues critical to managing the project with the highest regard for compliance with regulations governing the care and use of animals in research. This process will provide answers to questions the Research Support Service Manager will ask as he/she completes, or assists the researcher in completing, the University of Minnesota Animal Usage form. The Research Support Service Manager will address these issues:

- Experiments Which May Produce Pain or Distress

Pain is defined as the sensation resulting from a stimulus which (1) would be perceived as painful by people, (2) produces escape behavior in animals, or (3) approaches or exceeds tissue damaging proportions.[1] Distress is defined as any disruption of physiologic equilibrium manifested by abnormal or maladaptive behavior.[2] The Research Support Service Manager will assist the PI in identifying procedures which may produce significant pain or distress, including but not limited to: survival surgery, experimental induction of disease, testing procedures, sampling procedures, use of adjuvants, dietary or environmental manipulation, physical trauma, or restraint. If any of these procedures are to be used in the proposed research project, the Research Support Service Manager will assist the PI in writing a justification to indicate the alternative approaches that were considered, and how pain and distress will be alleviated.

- Euthanasia

The Research Support Service Manager will assist the PI in identifying the/an acceptable method for euthanizing laboratory animals. The University of Minnesota has adopted a chart of acceptable methods.

- Experiments Involving Nonsurvival Surgery

The Research Support Service Manager will assist the PI and their staff in completing the required documentation for these experiments. This documentation includes: a description of the surgical procedure, the location of surgery, the personnel responsible, anesthetic and other drugs that would be used, and the method of euthanasia.

- Experiments Involving Survival Surgery

The Research Support Service Manager will assist the PI and their staff in completing the required documentation for these experiments. This documentation includes: a description of the surgical procedure, the surgeon's name and qualifications, the building and room number where the surgery will be performed, provisions for post-surgical care, generic names of all anesthetics, analgesics, tranquilizers or other drugs used during surgery or post-operatively, including dosage, route of administration and persons responsible for their administration. The Research Support Service Manager will assure that the PI provides justification for any distress or functional deficit that may result in animals from the surgery and that he/she will describe how the distress will be alleviated.

- Dietary Manipulation

Nutritional distress is defined as a level of malnutrition that significantly interferes with the normal physiology and behavior of the animal. Nutritional distress may occur as a result of feeding nutritionally unbalanced, physically unfamiliar, inappropriate or unpalatable food. If significant nutritional distress may be induced by the proposed research, the Research Support Service Manager will assure that the PI provides a description of the methods, a justification of the rationale and a description of the way in which each animal will be monitored and evaluated.

- Environmental Stress

If the study requires that environmental conditions vary from those proscribed by the NIH Guide, the Research Support Service Manager will assist the PI in providing a description of the conditions, the rationale for this, the proposed duration of treatment and the methods of monitoring animals.

- Studies Involving Physical Restraint

The Research Support Service Manager will assist the PI in assuring that any research involving animal restraint is adequately justified. A course of action will be developed for any instance in which the restrained animal shows signs of distress (inappetence, abnormal behavior) or clinical abnormalities (e.g., decubitus ulcers, etc.).

- University Animal Usage Form Signature

The form must be signed by a member of the faculty and the Research Support Service Manager assisting with the application. The PI signing the form takes responsibility for all work done on the research protocol, and agrees to execute the work as described. The signature indicates that the PI agrees to execute the work as described; will request approval from the IACUC for any changes; will comply with the guidelines in the University Animal Care and Use Manual; will follow Environmental Health and Safety guidelines, and will be responsible for the work and supervision of staff. The signature of the PI further indicates that the proposed research activities described in the study do not unnecessarily duplicate previous experiments or the general working knowledge in the field, and that the use of animals described in the protocol matches the use of animals described in all grant applications covered by the protocol.

- Animal Certification Statement

The Research Support Service Manager will assure that the principal and associate investigators, as well as all personnel who will have animal contact, have completed an animal certification statement and filed it with the IACUC.

3.2.62 Protection of Animal Subjects Application Review Process

It is recommended that animal usage applications prepared by the PI working with the Research Support Service Office be approved by the IACUC within 10 working days of receiving the completed application.

3.2.63 Management of Research Protocol Changes Using Animals

Changes to protocols cannot be implemented prior to review and approval by the IACUC. When the PI decides to amend a protocol, the Research Support Service Manager will be notified. The Research Support Service Manager will review the proposed amendment in the same manner the original protocol was reviewed. In association with the PI, the Research Support Service Manager will determine whether or not the protocol amendment involves any change to the risks of pain, distress, etc. for animal subjects. The changes will be listed and addressed in a letter to the IACUC. It is recommended that protocol amendments/changes/corrections will also be reviewed and approved within 10 working days following the Committee's receipt of the information.

[1]Kitchell RL, Erickson H, Carstens E, and Davis LE, editors, Animal Pain: Perception and Alleviation, Am. Physiol. Soc., 1983, Williams and Wilkins, Baltimore.

[2]ILAR News, Fall 1991; Committee on Pain and Distress in Laboratory Animals, Institute of Laboratory Animal Resources, National Research Council, National Academy of Sciences.

3.2.7 Biohazards and Other Health and Safety Compliance

The Research Support Service Office will be responsible for assuring, to the greatest degree possible, research investigator compliance with any biohazard and/or other environmental health and safety compliance regulations the proposed research may be required to follow. The Research Support Service Manager will assist the investigator in obtaining any approvals required and for documenting the approvals by other internal committees and/or departments.

3.2.71 Review of Potential Hazards

The Research Support Service Manager and research investigator will review the proposed research plan to identify the following hazards:

- Recombinant DNA, Biological Toxins, or Infectious Agents

If the proposed research involves any biological hazards, the Research Support Service Manager will provide the PI with the appropriate application forms, assist in completing the forms, and consult as necessary with the Biosafety Officer to develop an appropriate plan to procure, store, handle, administer, and dispose of the agent.

- Radiation

If the proposed research involves radiation, the Research Support Service Manager will provide the research investigator with the appropriate application form, assist in completing the form, and consult as necessary with the University's Radiation Officer.

If the proposed research is a clinical trial involving radiation exposure, the Research Support Service Manager will assist the research investigator in applying to the Health Sciences Radiation Committee.

- Highly Toxic, Flammable, or Reactive Chemicals

To our knowledge, there is currently no institutional committee in place to review the use of hazardous chemicals in research.

- Known or Suspected Carcinogens

To our knowledge, there is currently no institutional committee charged to review the use of known or suspected carcinogens in research.

3.2.8 BA 23 and Account Assignment

The Research Support Service Office will be responsible for reviewing the research proposal and completing the BA 23 on behalf of the PI. Information needed to complete the form (including required approvals) will be obtained by the Research Support Service Manager. Issues for review will be identified, and supporting documentation will be provided to departments/units/centers as required to attempt to iron out any problems. The Research Support Service Manager will be available to attempt to resolve any questions raised prior to sending the proposal forward for any approvals.

3.2.81 Completing the BA 23

In working with and on behalf of the PI, the Research Support Service Manager will complete the BA 23. The Research Support Service Manager will determine, where appropriate, PI eligibility, the potential for DEHS hazardous materials issues that may need to be resolved, and the potential for conflict of interest. Issues of the space to perform the studies, credit to what department, equipment, and cost-sharing will all be identified by the Research Support Service Manager prior to routing the BA 23 for signature (if it continues as it currently has). This will be discussed with the PI so that they are cognizant of these issues. The budget and contract will have been approved by the PI and in the Research Support Service Office prior to routing the BA 23 for signature.

3.2.82 BA 23 Review and Approval

The BA 23 will be signed by the Research Support Service Manager and the PI. The BA 23 will then be routed for review and signature as required by each department/unit/center, if necessary. The PI will be responsible for informing the Research Support Service Manager of the review and approval signatures required by his or her department/unit/center. Alternatively, a data base will be established that provides this. This will be integrated with recommendations forthcoming from the Interdisciplinary Taskforce which is developing a model for assigning advisory and accountability functions between departments, programs, centers and institutes.

3.2.83 Responsibility Indicated by Approval Signatures

Research Support Service Manager: The Research Support Service Manager's signature on the BA 23 will indicate that all information on the form is true, complete, and accurate to the best of his/her knowledge.

Principle Investigator: The PI's signature on the BA 23 indicates that the information provided is correct and that equipment budgeted in the application is not otherwise available for use on the project from existing departmental or collegiate inventories. The PI indicates his/her agreement to abide by all applicable institutional and sponsoring agency policies and procedures (including the Patent and Technology transfer Policy of the University of Minnesota) and to

follow commonly accepted scientific practices in recording and maintaining records of research.

Department head or other similarly designated head of a "unit": They will assume approval authority for on and off campus space, prorating department/institute/center credit, equipment requests, and cost sharing arrangements.

Dean: The dean will share approval authority for on and off campus space, and approval of requests for indirect cost waivers. Local oversight authority for prorating department credit, equipment requests, and cost sharing arrangements is indicated by the dean's signature.

Provost's Office: For certain grants and activities of interdisciplinary programs, centers and institutes the provost's office or a vice provost would take the place of a dean's signing. Also, a director of one of these centers, programs, or institutes might take the place of a department head.

3.2.84 Reporting the Project to Departments/Institutes/Centers

The PI will be responsible for informing the Research Support Service Manager of the project reporting requirements of his/her department. The Research Support Service Manager will send the department a copy of all study documents upon request.

3.2.85 CUFS Account Number Assignment

A CUFS number will be assigned to the account within 24 hours after the contract or research agreement is signed. The site-based ORTTA representative will assure the account number is provided to the PI, the department administrator, and the Research Support Service Manager within 24 hours.

3.2.9 Managing and Reporting Investigator and/or Protocol Changes

The Research Support Service Office will provide project management service to PIs. The Research Support Service Manager will manage changes with the local oversight committees or offices that require notification, review, or approval of changes to the research plan. The Research Support Service Manager will manage changes in the following areas:

3.2.91 Conflict of Interest

All investigators associated with a study will be reminded to report any changes within 30 days of the change in external financial relationships and/or time commitments. The Research Support Service Manager, in conjunction with the Research Support Service Office director and senior academic official in the Provost's Office, e.g., Dean or Vice Provost for Research, will assume responsibility for identifying changes that may require review of a current potential conflict of interest management plan. Changes that may require a potential conflict of interest management plan will also be identified and developed by the Research Support Service Manager.

3.2.92 Budget

Budgets may need to be reviewed and amended during the course of conducting sponsored research. Industry sponsors will often amend a protocol to add a test, or an overnight stay, or a study visit, without suggesting the budget be amended. The Research Support Service Manager will review all proposed amendments or changes that may or should affect the budget. The Research Support Service Manager will be responsible for re-writing the budget and obtaining approvals much as in the protocol approval phase.

3.2.93 Contract

A contract may need to be amended during the course of conducting sponsored research study. Some examples of these changes occur when the sponsor amends the protocol to extend the length of the study or increases the number of patients to be enrolled at a center. The Research Support Service Manager will assist the PI in proposing, reviewing and seeking approval of contract changes. The site-based ORTTA staff will also review any proposed changes to the contract to assure protection of the interests of the University and the investigator.

3.2.94 Biohazards

The Research Support Service Manager will assist PIs in identifying the proper course of action to take when a change is made in the use or management of a biohazard.

3.2.95 Human Subjects

The Research Support Service Manager and the PI will be responsible for assuring that the protocol is executed in exactly the manner reflected in the application and consent form. Whenever any change to the most currently approved version is proposed, it must be reported to the IRB. IRB approval is required prior to instituting the change (except in cases of responding to life-threatening circumstances - these can be reported after the fact).

- Changes in Protocol or Staff

Any time there is a change in the manner in which the protocol is executed, the IRB must be informed. Essentially any change made to the plan outlined in the original application to the IRB, and any subsequently approved change, must be reviewed and approved prior to implementation. The PI will be responsible for informing the Research Support Service Manager of any such changes proposed to be made. All changes in staff, particularly those responsible for making any study related assessments and/or individuals authorized to participate in the consent process, must be reported to the IRB.

- Serious Adverse Events (SAEs)

If a serious adverse event occurs, the PI will report the event to the Research Support Service Manager as quickly as possible after learning of the event but within no more than 24 hours. A report (usually a sponsor form) will be completed by the PI and/or a study nurse and faxed to the sponsor within 24 hours of learning of the event. This report will then be given to the Research Support Service Manager so that the essential facts known at that time can be included in a notification letter to the IRB. The Research Support Service Manager will prepare a notification letter within 24 hours of receiving the information from the research investigator. If more information becomes available regarding the resolution of the event, the PI will provide this information to the Research Support Service Manager, and the Research Support Service Manager will notify the IRB. There will be instances in which the IRB will ask for more information. There will also be instances in which a change to the consent form may be required by the occurrence of an adverse event for which a specific risk is not already listed. The Research Support Service Manager will discuss this possibility with the PI. If a change is required, the Research Support Service Manager will modify the consent form and send the proposed revised version to the IRB with the serious adverse event notification letter.

- Protocol Deviations

While every effort will be made to avoid these situations, there will be instances in which the protocol is not followed. There are some cases, however, in which the PI may receive approval from the sponsor to make an exception to the protocol. These instances must be fully documented. Should such a circumstance occur, the PI will inform the Research Support Service Manager as quickly as possible after it occurs. The Research Support Service Manager will

collect information and then document the protocol exception/deviation in a letter to the sponsor (copied to the IRB). In this way, the PI and the University will have documentation of the circumstance and report in the event the study is selected for a quality assurance review by the sponsor or FDA review. Every effort will be made to keep protocol deviations and exceptions to a minimum. Although a research sponsor may approve a protocol deviation, the FDA will document all protocol deviations as deviations without regard to the fact that the sponsor may have granted approval for them.

- Consent Form and Consent Process Changes

As is the case with any changes to the IRB approved plan for implementing the protocol, changes to the consent process or the consent form must be reviewed and approved by the IRB prior to their implementation. The Research Support Service Manager will make any changes the PI proposes to make to the consent form and guide him/her in making the changes so that they are as "likely as possible to be approved" by the IRB. Changes to the process will be discussed with the PI and the IRB will be informed by way of a letter.

- Continuing Review of Approved Research

Once each year the IRB will request the PI to complete a form called *Continuing Review of Approved Research*. The Research Support Service Manager will complete this form for the PI's review and signature. If the PI has worked closely with the Research Support Service Office from the beginning of the project, the Research Support Service Manager will have most of the information required to complete the form. If the PI has not, this will be more problematic.

3.2.96 Animal Subjects

- Changes in Protocol

Any time there is a change in the manner in which the protocol is executed, the IACUC must be informed. Essentially any change made to the plan outlined in the original application to the IACUC, and any subsequently approved change, must be reviewed and approved prior to implementation. The PI will be responsible for informing the Research Support Service Manager of any such changes proposed to be made.

3.2.97 FDA 1572

Any changes made to staff listed on the FDA Form 1572 must be reported to the FDA on a new 1572 FDA form The Research Support Service Manager will be responsible for completing the new form, obtaining the relevant faculty member or research investigator's signatures, and sending it to the sponsor (with a copy to the IRB.)

3.2.98 Data Monitoring and Audits by Sponsor/CRO/FDA

A copy of the site visit reports filed by the sponsor/Contract Research Organization after each monitoring visit will be sent to the Research Support Service Manager. If there are problem areas indicated in which the PI or staff need more information in order to improve data collection or retention, the Research Support Service Manager will be responsible for providing such information and suggestions for improving their processes. If the study is chosen at any time for a sponsor quality assurance audit or an FDA audit, the Research Support Service Manager will be responsible for managing the audit with the PI and his/her staff.

3.2.10 Managing Research Funds

In conjunction with the PI and their staff, the Research Support Service Office will be responsible for oversight and managing project funds. The Research Support Service Manager will have assured, to the greatest degree possible, proper budget writing, contract negotiation and will also assume responsibility for the proper administration of the funds.

This will be completed in cooperation with the PI and the PI's department administrator where the grant is administered. It is expected that the Research Support Service Manager's involvement will vary slightly in working with departments across the AHC. The Research Support Service Manager will fulfill a role in administering the funds that may range from minimal review to extensive responsibility for the account in conjunction with the PI and their staff.

The critical review of financial information for industry-sponsored research is important for providing assurance that no fixed price contract is performed at an unexpected loss to the AHC. This review can be very difficult for staff to perform if they are unfamiliar with the project. The Research Support Service Office and Research Support Service Manager will be aware of the budget, the protocol requirements, the agreements/arrangements for internal services, and the payment schedule in the contract.

3.2.101 Approving Purchases

The Research Support Service Manager will review and provide approval recommendation of charges currently reviewed only by ORTTA (>$500). In the interim, the Research Support Service Manager will be responsible for getting or expediting approval of the expenditure from the site-based ORTTA person.

3.2.102 Monitor Contract Benchmarks and Payment Schedules

The Research Support Service Manager will monitor the progress of the study and assure that payments are being received in a timely manner for the sponsor according to the agreement with the sponsor. The Research Support Service Manager will negotiate with sponsors for any late payments.

3.2.103 Monitor Charges by ISO's and Other Internal Services

The Research Support Service Manager will review the charges assessed against the study account for any internal services. Experience suggests that it is easy to make errors - particularly when a study subject is admitted as a patient to the hospital. The Research Support Service Manager will likely be unable to review every charge - but will review at least some charges for all studies against which internal services may bill.

3.2.104 Report to Investigators and Departments

The Research Support Service Manager will provide a "usable" report of the financial status of the account once each month to the PI and their department or unit administrator.

3.2.105 Monitor Effort Certification for the Project

The Research Support Service Manager will work with the PI and the PI's department to assure the proper assignment of and billing of effort for the project. While the PI will retain approval authority on the project, the Research Support Service Manager will provide corrected information to the PI to assure that effort drives salary and that funds are available to pay for personnel.

3.2.11 Study Close Out

The Research Support Service Office will be responsible for reviewing regulatory documents for the final study record. The Research Support Service Manager will write the final report to the IRB for the faculty/research investigator's review and signature.

The Research Support Service Office will be responsible for final financial review of the research study account. This final review will include: review of the contract terms, the performance, and the payments received, total expenses, shortfalls or funds left above expenses. The Research Support Service Office will provide a final financial report to the faculty researcher and to the PI's department or other appropriate administrative unit. After the report is accepted by the PI and his/her department, the account will be closed by the site-based ORTTA representative.

3.2.111 Regulatory Documents Review

The Research Support Service Manager will provide the PI with a checklist of all the regulatory documents which must be retained at the end of the study. A final review by the sponsor/CRO will be reviewed by the Research Support Service Manager and s/he will provide any assistance which may be required to obtain/provide any outstanding documents that the PI, their staff or others within the institution may have.

3.2.112 Final Report to the IRB

Study sponsors require a final report be filed with the clinical site's IRB. The essential elements of the report vary from sponsor to sponsor. The Research Support Service Manager will be responsible for writing the final report for the PI's review and approval. The original report is sent to the IRB and a copy is sent to the sponsor/Contract Research Organization.

3.2.113 Final Report to the Sponsor

The Research Support Service Office will provide assistance to PIs in writing the final research reports for the sponsors.

3.2.114 Review of Final Account Status and Contract Terms

The Research Support Service Manager will review the final account status. Payment terms will be reviewed and any deviations noted. Any expenses not covered by the contract will be documented and sent to the sponsor for collection (i.e. subjects screened but not enrolled). The Research Support Service Office will assure that all funds due the University are collected or take steps to accomplish this.

3.2.115 Closing the Account

After it is certain that all funds have been collected and all bills paid, the Research Support Service Manager, in cooperation with the PI, the investigator's department or unit, and the site-based ORTTA representative, will close the study account. There are a variety of things that might be done with any balance of funds remaining after the completion of a study. These could be, for example, deposited in the faculty members discretionary fund or as determined by prior arrangement with their department or unit or distributed as indicated in the initial agreement with the Research Support Service Office.

3.2.116 Final Report to the Department

A final financial report will be provided to the research investigator and if applicable, to the department, center, or institute. This same report will be used to document the fund close-out request made to the site-based ORTTA representative.

3.3 Business Development Office

3.3.1 Introduction

Corporate sponsorship is one of many funding sources that faculty may use to support their research. In contrast to applications for competitive funds, pursuit of corporate support is somewhat more complex, inefficient and in the opinion of many, is in need of optimization within the AHC. That is, generally, individual faculty take it upon themselves to seek out corporate partners and the AHC corporate research program is what these faculty make of it. It appears that insufficient resources have been allocated to develop this very important area.

The result of this situation is that:

- some faculty are extremely accomplished at attracting corporate support, while most are not.
- there is no strategic plan with specific goals for corporate sponsored research within the AHC, i.e., what are the different goals, objectives and metrics used to see how good a job we are doing: are we moving ahead, staying the same or falling behind?
- there is no strategic investment plan to enhance the faculty's technology or services to make them more attractive to corporate sponsors within the AHC.
- there is, to the degree we can ascertain, no department or office specifically responsible for promoting or marketing faculty services.
- often interaction between ORTTA's Patents & Technology Marketing personnel, faculty and corporate partners is reactive. Additional ways to make this more proactive need to be developed.
- there is probably a need for more aggressive broad based marketing of University of Minnesota/AHC faculty's technology and services.
- there is an unfavorable environment for faculty entrepreneurship.

The AHC has a given base of corporate sponsored research, theoretically it has a certain defined capacity for the amount of corporate-sponsored research that can take place. Although this capacity is difficult to estimate, we believe that the AHC has substantial room for growth in corporate sponsored research. What is a level of enhanced corporate sponsored research one might seek? This might be akin to the enhanced revenues of >15% a high technology company like Medtronic might attempt to achieve in a year. Our goal for growth of corporate sponsored research in the AHC is 15% per year. However, we believe that there are constraints to our growth, due to bureaucratic and administrative bottlenecks. In order to achieve this growth we will have to examine our processes to approve and submit contracts and grants, and reduce the time required to approve project proposals. The fact that many of the processes aren't linked contributes to our poor user friendliness. This gauntlet manages to turn off many but the most resilient corporate sponsors.

As discussed elsewhere in this document, one of the goals of the Research Support Service Office is to improve the quality of submissions and expedite the approval process such that at least 75% of proposals get all the internal approvals and signatures within 10 working days. As approval time decreases and we become more able to help and support faculty and service

corporate sponsors better, we anticipate that the volume of corporate-sponsored research will increase. In order to do this there needs to be greater focus on promoting and marketing AHC faculty technology and services. How do we accomplish this? Greater institutional resources must be allocated to do this at a much higher level. We must develop a system for the provision of "seed" funds. Also, we must work on development of an environment that fosters and does not hinder faculty entrepreneurship.

The AHC is uniquely positioned to dramatically alter the current paradigm for corporate sponsored research. For many reasons, the University is searching for innovative ways to serve its constituents and at the same time enhance its ability to perform our missions of education, research and clinical service. Also, untapped synergies exist within the University that could stimulate innovative approaches to developing and marketing new technologies, services and products. Most importantly, industry is looking for innovative partners who are willing to share their vision, risks and goals and work with them in a timely, seamless and non-bureaucratic manner - partners who understand that from a company point of view - time is money.

3.3.2 Recommendations

To accomplish this new way of doing business, we recommend the following:

- Form a Business Development Office be formed that would be an identified, accountable function within the AHC - Research Support Service Office.
- Move the responsibility, identification or disclosure, protection and marketing of technology and services generated within the AHC to individuals who provide these services out of the Business Development Office of the AHC.
- Help faculty define the technology or services they might have that could be of value to external constituents. This office would then coordinate an intellectual property strategy and aggressively promote and market faculty technology and services to various corporate sponsors, locally, nationally and internationally.
- Set a goal to enhance the faculty's ability to compete for corporate sponsored research and increase the overall rate of corporate sponsored research by 15% a year.
- Increase patent filings from the AHC by 25% per year.
- Enhance the ease for faculty to submit corporate sponsored research.
- Develop a process to provide "seed" funds to enhance the value of AHC faculty technology or services that might enhance the value or likelihood of out licensing a technology to a corporate sponsor.
- Determine via periodic surveys of faculty that there is >95% satisfaction with the Business Development Office/Research Support Service Office.
- Determine via periodic surveys of corporate sponsors that there is >95% satisfaction with the Business Development Office/Research Support Service Office.
- Promote, monitor and show evidence of stimulating faculty entrepreneurship and creation of jobs in the private sector. An article from the

San Francisco newspaper shows that the Midwest is a "wasteland" for biotechnology; it is not even listed. This needs to change.

- Employ Service and Technology Managers who will build relationships and work with AHC faculty to identify, reveal and disclose new technologies. These individuals are "miners", prospectors or scouts for technology and services that may have value to a corporate sponsor. In addition to this there will be Technology & Service Marketing specialists who will market AHC services and technologies to potential partners locally, nationally and internationally.
- Establish a Technology Investment Pool (see following discussion.)

The Taskforce recommends that the AHC establish a technology investment pool to enhance the marketability of AHC faculty, technology and services. There are many sources this might come from, one obvious source might be from the 33% of net income royalty that is generated from AHC technologies. This could be supplemented by other funds from the faculty member's school or even investors who may wish to invest in faculty research.

This pool will be used to:

- invest in promising AHC technologies and discovery research that could have high commercial interest or value,
- match investment funds on some ratio basis of industry funded Research & Development within AHC,
- provide incentives to faculty research investigators for filing disclosures that lead to licensing deals with the AHC
- enhance an entrepreneurial research environment for faculty
- make investments in companies starting up with AHC technologies that may or may not have faculty as entrepreneurs.

The overall goal of this investment effort will be to assure that the AHC receives a reasonable return for its investment in corporate-sponsored research. For the AHC what are some of the "upsides" that makes up a return and what are the components of the investment?

Return	**Investment**
• royalties	• space
• other investments of development: agreements bringing money into the U to assist faculty research	• faculty time
• new business venture based on faculty technology	• support staff and other personnel
• enhance scholarship of faculty - new refereed articles	• University or AHC competitive funds
• scientific presentations surrounding work	• Technology Investment Pool funds
• AHC/University recognition locally, internationally, globally	
• quality teaching	
• patents	

To optimize the return on these funds, the Taskforce envisions a portfolio of investments based primarily on each project's scientific feasibility and its potential attractiveness to the "marketplace", i.e., the likelihood of investment by corporate sponsors or investors (Figure X).

- Feasibility

This will be a measure of the likelihood of achieving the necessary technical progress in the study in a cost-effective manner. It is a function of two factors. First, the scientific potential of the project refers to the extent to which the research being proposed is specific, realistic and worth achieving in a "business sense". The second factor is the likelihood or probability of the proposed research team to carry out the project but also in a given time frame based on the resources available. This will depend upon their track record, their skills, facilities, and the proposed time frame.

- Relative Attractiveness

The relative attractiveness of a project is a measure of the likely benefit of successful research. It is a function of two factors. The first is the potential benefit of the project. The potential benefits are rather variable and include the economic, environmental, and social returns possible from the technological improvement as a result of this research. Some key factors implicit in the assessment of potential benefits are:

- attributes of the technology,
- size of the market,
- contribution of the research to increased productivity (especially in agriculture),
- projected market growth,
- exports / imports replacement,
- neutral or positive environmental impact, and
- enhanced social amenity.

The second factor is our ability within the AHC to capture these benefits. The ability of the AHC to capture the benefits from the technology will depend upon, among other things, our ability to identify and negotiate with appropriate corporate partners, and the ability of the partner to exploit the full potential of the product in a timely fashion.

Having assessed every project's feasibility and attractiveness, we then propose the Research Support Service Business Development effort have a process in place for investing and allocating funds with a strategy that maximizes return. Each proposed study will be compared on its relative merit to those projects already in the portfolio or "on the table for consideration". In the matrix below (see figure x), the anticipated returns from studies 1 and 6 are most and least attractive. Studies 2-5 are intermediate.

Return on AHC investment can come in many ways. A series of papers (some in abridged version) in the appendix and others from the AUTM

(Association of University Technology Managers) speak well to the various value matrices that could be used.

In the most basic sense, this can be measured by a financial equation such as internal rate of return. The graph below shows a hypothetical investment, where research investments totaling $500,000 were made in a particular project for 5 years. A licensing agreement was successfully negotiated and revenues to AHC were initiated in year 6 and ended in year 15. The internal rate of return on the investment of $500,000 was 11.7%. By forecasting the investment needed to bring each project to fruition and the anticipated stream of licensing revenues or other "consideration" the AHC might receive, we can estimate each project's rate of return (see comparison of projects 1-6 as measured by net present value (NPV), in figure below).

The strength of this evaluation process is in the process itself, not in the numbers. This process assures that scientists and marketing managers become equally familiar with each project's riskiness as well as its potential market impact. In so doing, the process of identifying potential corporate partners will occur coincident with the research and development effort. If someone makes a discovery that might be patentable they have to initiate an action to attempt to protect this.

Contrast this proposed approach with the current practice. As funds come in to support research they are approved through ORTTA. Basically, ORTTA may not hear much from the faculty researcher until an invention may be in hand. At this point, the researcher may contact personnel from Patents and Technology Management (PTM). If they do, a report of the disclosure is initiated by PTM staff when such a report to the research sponsor is required. PTM staff will work with faculty members to initiate the preparation of patent applications which are uniformly outsourced. Experience suggests that PTM works very well with faculty and outside counsel during this process. Thereafter, PTM staff conduct the negotiation and processing of licensing agreements which may result from the invention.

As is discussed elsewhere in this document, Patents and Technology Marketing is one of the two divisions of ORTTA. PTM is controlled centrally within the University (see figure X for current reporting structure and see appendix for detailed reporting structure). PTM goals are as follows:

- make a decision on >75% of disclosures within 4 weeks
- spend approximately 30% time on marketing efforts
- increase licenses from 15/yr at present to 20/yr

From 1992- 1996, the AHC averaged 79 disclosures / year which represented 48% of the UMN total (see appendix). AHC disclosures have a disproportionate effect on royalty income to the University. In FY 1996, AHC generated $5,879,626 in royalty income which represented 92.8% of total UMN royalty income (appendix). It is our understanding that PTM is funded through royalty and license income and other funds from the University. Of the royalty flowing into the University, 1/3 is distributed to ORTTA. PTM Health Technology's budget is substantially less than this. In the past, it appears that royalty income to ORTTA beyond expenses has been diverted to other University functions. It is the Taskforce's view that PTM, especially relative to the AHC, is

under-resourced and that more professionals, an increased rate of filing patents, and establishing a seed fund needs to occur.

3.3.3 Financial Administration

One of the goals of the Research Support Service Office is to be fiscally responsible and financially self-sufficient. The research support service and business development functions will have separate revenue sources, budgets and cash flows.

Research Support Services Office Has Two Functions

Research Project Support Services	Business Development Service

3.3.31 Revenues

- Research Project Service Function

At the outset, the object of this effort is to facilitate developing all the accompanying information for a grant or contract, to shorten the time necessary to seek internal approvals, and to make faculty and the University of Minnesota more competitive at securing corporate sponsored research.

Since this service will be voluntary, it is likely that some faculty may wish to use it while many others will not. Because of the need to assist faculty as much as possible, the recommendation of the Research Support Service Taskforce is to make it as convenient as possible to use the Research Support Service Office. That being the case, the AHC would offer these services gratis to "jump start" the process. Subsequently, if there were to be significant interest on the part of faculty to utilize this service, a number of scenarios are laid out, costs of providing various levels of service would then be developed.

- **Service Level 1**
  - general overall project or protocol review
  - assistance in developing and filling out IRB forms
  - assistance in developing and filing animal care forms
  - assistance in developing and reviewing budgets
- **Service Level 2**
  - all basic services provided in Level 1
  - up to XYZ number of hours consultation with a biostatistician for assistance in developing the research plan and experimental design and statistical analysis
  - to work in consultation with faculty member in the development of conflict of interest management plan
- **Service Level 3**

- all of the services provided in Levels 1 and 2 (e.g., biostatistical support, etc.) plus
- development of project management or GANNT charts to assist faculty and staff in understanding how the project is laid out and how over time it should evolve
- ongoing monitoring of the project by the Research Support Services Manager; determination of project roll out relative to GANNT chart

- **Service Level 4**

  - all services from all preceding service levels
  - ongoing support from the Research Support Service Manager to handle any project changes, IRB resubmissions
  - assist in developing project close out report to the sponsor and/or Food andDrug Administration
  - assistance prided by a technical writer to assist in developing the original project request or any subsequent reports during or associated with the completion of the project

We would charge established rates for each level of service. It is anticipated that we may need to put "caps" on the given amount of time that a Research Support Manager or biostatistician might work on a given project for a flat fee. This would avoid any one or a few faculty monopolizing personnel. However, additional time would be available like other internal service organizations on a fee for service basis. It is believed that this would be self correcting since faculty would determine if they were getting their fair value relative to the services provided. Since it would be paid for, only that service needed beyond base level would be used because it would cost something.

We envision that the Research Support Service Office will have a positive cash flow within 24 months. Once positive cash flow develops, one thought is that perhaps 25% of this balance be distributed back to PIs as a dividend, sort of a "frequent buyers program", proportionate to their financial expenditure with the office for that year. The remaining 25-75% funds plus (depending on the amount) will be used as a bonus pool for the staff of the Research Support Service Office. This bonus could be based not only on each individual's productivity, but also will be distributed to all staff based on the overall achievement of the Research Support Service Office.

- Business Development Office

We propose that 33.3% of all royalty revenues generated from AHC technologies be used to fund the AHC Business Development Office and support investments in faculty who may have commercially attractive technologies. In time, projects which have had Research Support Service Office investment will start to generate royalty income.

It is recognized that for human products it might take as long as 10 years to realize any royalties, therefore, we need to be realistic. If an investment pool or bank is established, the AHC should consider the "payback" or replenishment

if you will of this prior to distributing royalties. Subsequent to the investment pool being paid back, royalty payments would be paid 33.3% to the PI, 25.3% to the PI's lab, 8.67% to the dean (as is currently done) and 33.3% to AHC.

Currently, AHC royalties are approximately $6.0 million/year (33.3% or $2.0 million). Current PTM annual expenditures for the AHC are substantially less, and estimated to be about $1 million. Given the above considerations, there should be considerable finances available to file more patents, hire more professionals, and set up a seed fund.

The task force believes that PTM is currently under-resourced and that additional investment in staff is needed to optimally market AHC faculty expertise so expenses might be higher. Income beyond expenses will go towards and be one means for funding the technology investment pool.

3.3.32 Budget & Cash flow

The Research Support Service Office will employ Research Support Service Managers and Clinical Trial Coordinators. In addition, over time and given a need, access to one or more biostatisticians, technical writers and accounting personnel will be provided. We propose that hiring of staff will reflect demand for services.

The Business Development Office will employ Technology Managers and Service & Technology Marketing Specialists. Again, the technology managers will work with faculty to help them define the technology or services the faculty that could have commercial value and may need protection of this intellectual property. The technology managers would process and develop relationships with faculty and faculty leadership to "mine" and "prospect" for faculty technology and services.

The technology marketing specialists' job would be to focus externally. They would direct all of their time and energy towards the marketing of faculty technology and services. Because of this focus it should be relatively easy to measure accomplishments.

The Research Support Service Office director, working with the technology marketing director, would also look at how they can encourage and foster entrepreneurial activities of faculty. Over time, a series of metrics could be developed that would allow us to determine how well we were making progress in this area.