Minutes*

Senate Research Committee
Monday, March 21, 2011
2:15 - 4:00
238A Morrill Hall

Present: Melissa Anderson (chair), Breanne Byiers, Arlene Carney, Margaret Catambay, Paul Cleary, Marc Dunham, Greg Haugstad, Seung-Ho Joo, Frances Lawrenz, Timothy Mulcahy, Kola Okuyemi, Federico Ponce de Leon, LaDora Thompson, Thomas Vaughan,

Absent: Mustafa al'Absi, Jerry Cohen, Robin Dittman, Tucker LeBien, Jennifer Linde, April Rose, Karen Williams, Lynn Zentner

Guests: Professors Jeff Kahn, Michael Oakes; Associate Vice President Pamela Webb (Sponsored Projects Administration)

Other: Peggy Sundermeyer (Office of the Vice President for Research)

[In these minutes: (1) clinical-care conflict-of-interest policy; (2) human-subjects research issues and questions; (3) grants job family; (4) procedures for establishing, operating, and evaluating University centers; (5) Minnesota Science Park and Minnesota Science and Technology Initiative]

1. Clinical Care Conflict of Interest Policy

Professor Anderson convened the meeting at 2:15 and thanked Committee members for voting on the clinical-care conflict-of-interest policy. The majority vote was to endorse the proposed policy without further discussion.

2. Human Subjects Research Issues and Questions

Professor Anderson next welcomed Professors Kahn and Oakes to the meeting. She noted that the Board of Regents had suggested that the University community take up issues that arose in connection with the Markingson case (the young man who committed suicide while a subject of a clinical trial of a pharmaceutical); the Board suggestion was made in a letter that Board of Regents' chair Allen sent to the faculty members in the Center for Bioethics responding to a letter they had sent to the Board. General Counsel Mark Rotenberg, in response to a request from the Faculty Consultative Committee (FCC), developed a set of questions he thought it might be useful for the community to address; Professor Anderson said that she and FCC agreed that three of them would be taken up by this Committee. The three questions are:

1. To what extent is U medical/health research dependent upon corporate funding? Is this typical of major research universities in the US/worldwide? How much of such research involves human subjects?

* These minutes reflect discussion and debate at a meeting of a committee of the University of Minnesota Senate; none of the comments, conclusions, or actions reported in these minutes represents the views of, nor are they binding on, the Senate, the Administration, or the Board of Regents.

2. What risks and challenges are posed by increasing reliance on corporate funding of this type of research?

3. What policies and procedures are in place at the U to address these risks and challenges? Are there policies and procedures at other major institutions, or under consideration elsewhere, that we should adopt here?

Professor Anderson emphasized that the Committee would discuss the issues related to the case, not the case itself; the Markingson case, she noted, has been well-aired in many venues and this Committee is not equipped nor charged to review it again.

Professor Anderson asked the two guests to introduce themselves and explain how their background is relevant to the issues posed in Mr. Rotenberg's questions. Professor Oakes, from the School of Public Health, explained that he is vice chair of the executive committee of the Institutional Review Board (IRB) and has been on the IRB for a number of years; he also serves as vice chair of the Academic Health Center Conflict Review Committee and serves as a member of FCC. He has been thinking about these issues for many years. Professor Kahn explained that he is Director of the Center for Bioethics and a faculty member in the Medical School; he is also an FCC member. His scholarly work focuses on the ethics of research, and the Center for Bioethics includes the faculty members who raised the questions with the Board of Regents.

Professor Kahn began the discussion by saying that an increasing amount of research is dependent on corporate funding, which brings challenges. The University of Minnesota is not in a position different from its peers, and some other institutions may be more dependent on corporate funding for research than it is. But the University is not alone in dealing with these problems and it can learn from other institutions what they are doing; faculty members here can also speak with colleagues elsewhere to learn what they are doing to address the issues that arise. Professor Kahn said the institution should talk about the principles apart from the Markingson case—and it has done so for a number of years. The University is not in better or worse shape than other institutions, nor is it alone in facing them.

Professor Oakes followed up by saying that if one looks at the evidence, the protection for human subjects at the University of Minnesota is stellar. The University has a nationally-recognized program in human-subjects protection that is a model. While it is not perfect, those who are responsible for it (Ms. Keane, Vice President Mulcahy, the IRB committees) look for mistakes so that the University does not repeat them. They are extremely self-critical, which serves the University well, and they promote a culture of research ethics based on the idea that there must be a partnership between the researcher and the compliance people. He said he believes that human-subjects protection is better here than at most places—and he has participated in audits of the programs at other institutions, so can make comparisons.

In terms of corporate funding, the University is dependent on it in many ways, ranging from a football stadium to pharmaceutical research, Professor Oakes observed. That is not the important question, because there is evidence that government funding, like corporate funding, can bias research. The question is who is doing the research. He said he was not sure that corporate versus government versus foundation funding streams systematically produced different results. He knew of a number of studies funded by the government or a foundation that were dismissed because findings were not what the researchers or sponsors hoped for.

There is also the question of consulting, Professor Oakes said. Even small sums can affect how one might approach research. The new clinical-care conflict-of-interest policy mitigates those problems, although it cannot eliminate them.

Professor Anderson asked Committee members for comments.

Professor Cleary said that it is his observation that when there are problems, they rise to the top and are forgotten, and the people who made the mistakes are still here receiving the same salary. What are the consequences for violating an IRB requirement, for example?

The consequences are profound for someone found in continual non-compliance, Professor Oakes said. The person can be prohibited from doing NIH-sponsored research. Letters go to the FDA and the Office of Human Research Protection (OHRP) at NIH. The person can be stripped of his or her ability to do research. That does not usually happen, however; they try to use carrots as well as sticks and behavior usually changes.

One problem is that IRBs give prospective approval, Professor Kahn said. Once it has approved a project, it is a huge challenge to do ongoing follow-up of individual research projects (this is true all across the country, not just here). That is a flaw in the protection regime created by federal regulations and implemented at research institutions around the country. There are issues related to human subjects who deserve protection (e.g., the mentally ill) but about whom the rules are silent. The University has the "gold standard" of human-subjects protection, but sometimes the rules and requirements are not sufficient. It would help if the University, and this Committee, would talk about what might be done to address these and other sorts of gaps in oversight.

Reporting is based on self-reports, Professor Anderson said; the investigators are to report if something bad happens. They are legally required to do so, Professor Kahn said. They do have post-approval monitoring, Vice President Mulcahy said, but with a limited staff, they cannot review every patient interaction in every clinical trial. They do intervene if they see something wrong.

Vice President Mulcahy responded to Professor Cleary's comment. That is not the first question, he said; the first question is whether someone receives a fair hearing when an allegation has been made against them. Anyone would want a review; if it is determined there has been a violation, the University deals with it directly and harshly. But one should not jump to conclusions. People's perspective changes when they've gone through the process; for anyone who has, and there has been a finding that there was nothing wrong, that should be the end of it—and the person should not have to continue to live with allegations for a long time after. One would expect institutional support if there has been a finding that there was no wrongdoing. It is easy to take a position if it is not me, Dr. Mulcahy said, and one needs to look at the issue both from the perspective of the one bringing the allegation as well as the one against whom the allegation is made. The allegations will be taken seriously and will be investigated—his office is committed to doing so, and to dealing with problems if they are discovered. If they look into the allegation and find no basis for it, they will say the matter is done.

Professor Oakes agreed with Professor Kahn that the IRB involvement is mostly prospective, but said there is also annual review. The investigator is legally obligated to the report to the IRB instances of serious adverse events and related unanticipated outcomes, and the IRB has the authority to halt a study

immediately. He said that Professor Kahn is also right about those with mental illness; the IRB thinks seriously about diminished capacity even though the regulations are not as clear as one might wish.

It is not permissible to recruit subjects for a study before the IRB approves it, Professor Kahn said. They cannot, however, monitor the process of recruitment and consent with each potential subject; there has to be trust in the investigator. There is also monitoring, self-reporting, and whistle-blowing. This is all a challenge with over 5000 studies at the University, he said, and the system relies on individuals behaving the way they are expected to. If they do not, there need to be repercussions.

Vice President Mulcahy said that it is not appropriate to use the institution's size as an excuse; they do not do so, and they do a good job in protecting subjects, but there are limits to the vigilance that can be maintained. Some people complain about the responsible-conduct-of-research training, but that is an opportunity to remind them of their responsibilities. He also noted that the University is fully accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP), a voluntary association to which the University voluntarily subjects its program for review. The University has a very good program and its director, Moira Keane, is a national figure who travels the world reviewing programs.

Professor Oakes speculated that even if the University increased the human-subjects-protection-program budget by fivefold, there would still have to be trust between the researchers, the institution, and the research subjects. This is not only about dollars, he said.

Ms. Catambay expressed interest in the problems associated with research using human subjects with diminished capacity. She said she sees a global trend in doing more research on such people because they have been under-researched in the past, but there is a problem because there should be more in the law protecting them. Professor Oakes responded that there has been more attention to diminished capacity (e.g., with children, those with Alzheimer's) because "we need to help them." People do research in order to improve their care and lives, and because they want to do innovative research—it is more difficult to that with "normal, happy people." The scientific mind is drawn to those who are ill, in need, or perhaps suffering from diminished capacity.

The ebb and flow of research oversight requirements bring to mind a pendulum, Professor Kahn said. Regulations were originally promulgated to protect "vulnerable" subjects from being taken advantage of, but at the same time those regulations had the effect of suppressing the amount of research performed on the very groups the regulations were intended to protect, which does not necessarily serve their collective interests. So rules were modified to encourage, and in some cases require, inclusion of historically-underrepresented groups. But if one is going to do the research, one must protect the rights and interests of individual subjects. The challenge is to strike the appropriate the balance, he said, and right now it feels as if society is moving back in the direction of providing more protection. IRBs probably try to balance between research to benefit those with diminished capacity and not taking advantage of them. Professor Oakes commented that these questions are always on the agenda at national meetings about human-subjects protection.

Professor Anderson turned to the first question that was posed.

Vice President Mulcahy said that total corporate sponsorship of research at the University amounted to perhaps 10-15% of research funding, a surprisingly small part of the portfolio. But there is a

growing trend in such support nationally. NIH created the Clinical and Translational Science Award (CTSA), the goal of which is to push research into practice. That introduces an important potential conflict about which the institutions must be vigilant, namely - the pressure to translate or commercialize research to practice and the growing regulatory pressures to restrict interactions with business and industry. The NIH director has announced a plan for a National Center for Advancing Translational Sciences to try to drive the process. Universities, whether in mechanical engineering or pharmacy, do not make products, but they have the responsibility to take research to the point where it can be developed to benefit people. Corporations are a part of the process that must be present; they carry the research into production. Dr. Mulcahy related that he "gets mugged" at the legislature because legislators do not believe the University is doing a good-enough job of translating research into products and treatment. Doing so is inherent in the land-grant mission, he said, and corporate funding of research will be a growing portion of the University's research budget, and there are increased expectations at both the state and federal level that institutions will do more to translate research into products and treatment. The University cannot shy away from the responsibility. The National Center for Advancing Translational Sciences is to coordinate the CTSA process because there is the view that there has not been enough conversion of research to treatment. It is most difficult to make the conversions in pharmaceuticals because of the regulatory gauntlet that must be run. Corporations do not usually run hospitals, so the University is a natural partner. He said he sees as symbiotic the university-corporate relationship (some oppose it), but the University must be aware of the risks inherent in the relationship.

Professor Anderson said she believed that the 10-15% is typical for the University's peer institutions, but some are on the edge of the spectrum. Dr. Mulcahy agreed; there are a few that receive 20% or more of their research funding from the corporate sector. The talk among his peers, however, is how to INCREASE the interactions.

Professor Oakes asked if there is any more harm to human subjects in corporately-funded research than in other kinds of research. He answered his own question: As far as he can tell, there is not. Dr. Mulcahy said he was not aware that there is nor is he aware of any institution that has a reputation for having problems with this kind of research. Problems pop up across the country, including at premier institutions; the point is, it is not a systemic problem. The more clinical trials that are conducted, the more likely there could be unfortunate incidents. At a place as large as the University, that does as much research as it does, things can happen, but the systems in place minimize the probabilities.

Corporate funding for human-subjects research creates different incentives, Professor Kahn said, for example the funds are not provided until after the research is completed and/or benchmarks have been met—so there is an incentive to keep subjects in a study. The IRB may not review projects differently based on the source of funds. Professor Oakes disagreed; he said the IRB does pay attention to the funding stream, the reputation of the investigator, and to conflict-of-interest issues; there is a system to navigate these issues. It does blunt the concerns, Professor Kahn agreed, but does not solve them.

Professor Cleary said that some of the most egregious situations have arisen from research funded by the U.S. Army and the federal government. Some companies do not want to spend $50 million to receive corrupt data; the companies can often be tough reviewers. There are different problems with government funding, Professor Kahn agreed; the investigator has an incentive for the research to be successful so that he or she can obtain another grant. Both sources of funding present problems.

Vice President Mulcahy said that "clinical research" is not a single entity. A company can be looking for other uses of an existing product, in which case the risks may be lower because the material is a known product. Research in places like the University is more risky because there is less known about the substance. He said he believes there is a robust system for review and to say that there is a problem with corporate research is too simple. Many times a corporate sponsor could be testing a product developed at the University.

Some would argue that a distinction is that some corporate-funded research is not investigator-driven, Professor Kahn said, but is more akin to contract research. Vice President Mulcahy said he did not have hard numbers. There are trials done at the University designed by the corporation and the University's IRB reviews and approves them if deemed appropriate. They could be corporate trials written by faculty members elsewhere; there are times when a University investigator works with the corporation to develop the trials. The University also does a lot of non-corporate work that does not include trials developed at the University, Dr. Mulcahy said, but the IRB still reviews them. The source of the funding does not matter when determining whether protocols require review or in determining whether safeguards for subjects are appropriate. All review and approvals focus on subject protections rather than funding source per se.

Professor Anderson concluded that answers to the first two questions had been provided and she turned to the third question. In particular, she asked, how has the policy environment changed since the Markingson case?

The University has a lot of policies, Dr. Mulcahy said, including training obligations, IRB reviews, audit trails, the conflict-of-interest policy, annual reporting on consulting, and FDA audits. The regulatory environment is quite robust. Are other institutions doing things the University does not know about? Dr. Mulcahy said he did not believe so; the University is on the leading edge, but all universities are dealing with the same issues.

Professor Cleary returned to the issue of the salary policy he raised at the last meeting. If a grant does not provide an augmentation to salary, but just pays a portion of the investigator's salary, there is less motivation to break the rules. The salary policy is a problem. For example, contrary to the expectations of professors in other colleges, clinical investigators pay a substantial portion of their salary from funded research projects and patient care. The base salary is considerably less than 50% of their actual or full salary. These salaries are not guaranteed by the institution and can be reduced if either source goes away. Whether income is based on the number of patients treated or participating in a study is a component of their full salary or extra income is inconsequential—the perceive conflict of interest is there. While this discussion is not about the Markingson case, Dr. Mulcahy said, in that case the investigators were not found to have benefited. It's not that case, Professor Cleary said; if dollars are important to someone, and he or she can increase the amount of money received from the research, that can be a problem.

The issue here is that faculty are expected to bring in funding for their salaries or augmentation of their salaries, Professor Anderson said. Is there is a distinction between Medical School faculty doing human-subjects research and a physics professor who writes a best-selling textbook, Professor Oakes asked? In the former case, human subjects are at risk; in the latter, the effect is on what students read. For the Medical School there are a lot more rules and the conflict-of-interest rules are tighter.

Is the clinical-care COI policy ahead of what other institutions are doing, Professor Anderson inquired? When it is implemented, it will be closer to state-of-the-art, Professor Kahn said. It has taken awhile to get there, and state-of-the-art continues to evolve. For example, the provision requiring that anyone who receives $100,000 or more from external consulting in a single year will be reviewed by both the COI committee and the conflict-of-commitment committee will put the University closer to the forefront of dealing with such issues, he said.

Professor Anderson thanked the guests for the discussion and concluded that the Committee had investigated the questions.

3. Grants Job Family

Professor Anderson turned next to Associate Vice President Webb to report on the grants job family.

Ms. Webb reported that this is a joint initiative between Human Resources and Sponsored Projects Administration (SPA) to create a career ladder and job descriptions for people involved in grants management. They believe that if they can do it right, the University can create a career ladder and enhance retention so that principal investigators can be optimally assisted by highly-qualified staff. They are working with a number of institutions on the project, including Duke, Johns Hopkins, Emory, and the University of Miami.

They are finding overlap with job families in accounting, administration, and research, and are sorting through those issues, Ms. Webb said. Eventually the job families can help guide the level of job and they may learn how best to deploy staff in appropriate clusters. In addition, the job levels and descriptions created through this project may be useful to faculty members who need to hire staff.

Ms. Webb said she will keep the Committee posted on developments and hopes to be able to share the job classifications that are developed within the next six months.

Is one possible unintended consequence that the job classifications will not allow people to do things they have done in the past, Professor Anderson asked? That is a possibility, Ms. Webb said. It may be that certain minimal-training certificates will be required for some positions, but there needs to be a way to meet that requirement if people have the knowledge that is needed. They hope to provide an incentive for relying on certified staff, such as expedited SPA proposal review. If classifications are established, current employees will have to be mapped to them, Ms. Webb added, and there could be a problem with certification and salaries. The changes may have to be rolled out over a period of time; this is something that Human Resources is examining.

Professor Okuyemi asked about the extent to which end users will be involved in the type of training required. Sometimes one hears from faculty members that the staff do not know as much as they should. They have not yet involved faculty members in defining the training, Ms. Webb said. They have eight classes so far, and have talked with the research associate deans about them. The Grants Management Advisory Committee is helping design them. They are open to working with faculty members but are not sure that faculty have an interest at the level of detail the courses are focused on. What they hope is that faculty will be beneficiaries of the curriculum.

Dean Ponce de Leon said that they have had some success with the training in his college. They find that most errors occur when PIs "do their own thing." Ms. Webb said they would welcome faculty members at any of the courses they offer, but wondered if that is the best way to deal with problems. If there is adequate administrative support that the faculty have confidence in, that would address the issues. Some faculty members will do their own work, however, and they are not proposing to force anyone to do anything; if faculty members want to write their own proposals, that will be fine, but SPA will strongly encourage the use of skilled professionals. There is unequal access to expertise, however, and they would like to enhance the quality of support across all colleges.

Professor Thompson said she could see the advantage of an expedited SPA review; that would instill confidence on both sides. They can also do post-approval monitoring, Ms. Webb said, to see if the quality is what is expected. But they are about a year away from fully implementing the certification program.

Professor Anderson thanked Ms. Webb for her report.

4. Procedure for Establishing, Operating, and Evaluating University-wide Centers

The Committee reviewed proposed changes in the procedure and had no objections to the changes.

5. Minnesota Science Park & Minnesota Science and Technology Initiative

Committee members next heard from Vice President Mulcahy about a proposed science park reported on in the news media.

Dr. Mulcahy said that a group envisions putting a science park next to the BioMedical Discovery District so that inventors and entrepreneurs could congregate next to the University. Across the country, some of the most successful science parks have developed near universities, and he said he believed this development would be good for the state and would also benefit faculty and students. But the University has no financial involvement in the proposal; it will be glad to participate in planning how it would work and it supports the idea, but cannot be looked on as a source of financial support. One idea behind the BioMedical Discovery district was that it would spawn private development.

Professor Anderson noted that Vice President Mulcahy was quoted in an article as saying that the University would put together a proposal to seek some of funding available through the "America Competes" act. If that act is funded, Dr. Mulcahy said, the University would participate in applications for federal funds. It would not play a solo role but would be part of a consortium if there is an appropriate role for the University.

Is there any state interest in the project, Professor Vaughan asked? Dr. Mulcahy said he hoped there would be. This is related to the next item on the Committee's agenda, the Minnesota Science and Technology Initiative. Many both inside and outside the University are concerned that the state is not well-positioned to compete in a science-and-technology economy. Over 30 states have approved funding to capture and retain part of the high-tech economy. Minnesota has been in a good position but there is an alarming complacency about its ability to stay there—other states are showing how to gain more of the benefits.

Vice President Mulcahy reviewed the development of the Initiative, which led to a report being prepared for the legislature last year. The legislature created the Minnesota Science and Technology Authority, which submitted a plan in January that fleshed out plans for what the state might do. The plan has been translated into legislation that says Minnesota must create and invest in a competitive scientific infrastructure and invest in a science park. The best programs elsewhere fund small business innovative research, internship programs, and support the development of entrepreneurial networks. The Initiative is not just for the University, it is to help connect people with good ideas to talent and support. For the long-term, the idea is to provide incentives to business and industry to sponsor research of interest in the public universities (the state would match company dollars to fund research at state universities). Minnesota needs to get in the game, Dr. Mulcahy said, and ultimately the Initiative could require hundreds of millions of dollars. It is a difficult time to think about that kind of effort, but at least the legislature is listening.

Professor Anderson thanked Dr. Mulcahy for his report and adjourned the meeting at 3:40.

-- Gary Engstrand

University of Minnesota