Minutes*

Senate Research Committee
Monday, November 3, 2003
1:15 - 3:00
238A Morrill Hall

Present: Gary Balas (chair), Dianne Bartels, Victor Bloomfield, James Cotter, Christopher Cramer, Dan Dahlberg, Sharon Danes, Kathy Ensrud, Steven Gantt, David Hamilton, Michael Hughey, Paul Johnson, Andrew Koch, James Luby, Mark Paller, Maria Sera, Virginia Seybold, George Trachte, Barbara VanDrasek, Jean Witson

Absent: Kathleen Conklin, Robin Dittman, Katherine Klink, Phillip Larsen, James Orf, Thomas Schumacher, Charles Spetland, Michael Volna

Guests: Associate Dean James Ysseldyke (Council of Research Associate Deans); Moira Keane (Institutional Review Board)

Other: none

[In these minutes: (1) issues from the college research associate deans; (2) policy on new drug applications; (3) results of the survey of Institutional Review Board users; (4) technology park]

Professor Balas convened the meeting at 1:20 and welcomed two new members of the Committee, Professor Dianne Bartels from the Center for Bioethics and Mr. Michael Hughey, a graduate student in Chemical Engineering and Materials Science.

1. Issues from the College Research Associate Deans

Professor Balas welcomed Associate Dean Ysseldyke to the meeting to discuss the issues of concern to the Council of Research Associate Deans (CRAD). He noted that he attends CRAD meetings and has learned that it deals with issues comparable to those taken up by this Committee, so he invited Dean Ysseldyke to join a meeting of the Committee.

Dean Ysseldyke outlined the categories of issues that CRAD deals with, and why.

-- Their charge is to serve in an advisory capacity to the Vice President for Research, and to provide suggestions and comments on policies and procedures governing the conduct and solicitation of research. This year they are reviewing major University policies affecting research; most are being revised so they are looking at and advising on them (e.g., academic misconduct, conflict of interest, external consulting, charging direct and indirect costs, and so on).

-- They have periodic sessions to educate the associate deans on such topics as cost transfers, reporting external professional activities (REPA), intellectual property issues, subcontracts, and so on.

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-- They felt it would be helpful to learn about what goes on in each other's colleges and the ways they are organized to provide infrastructure support for research, learn what does and does not work, accounting procedures, etc.

-- They hear from Mr. Schumacher in the compliance office about his first-year experiences.

-- CRAD revisits issues about the creation and dissolution of centers. There was a concern about the proliferation of centers that hang on for years even though no work is being done.

-- Other things crop up in addition to the agenda items.

There is overlap with the work of this Committee, Dean Ysseldyke said; he reads the Committee minutes and agreed that there is need for communication between the two groups.

Do all colleges have research associate deans, Professor Balas asked? Dean Ysseldyke said he believed they do, although the functions differ across colleges. Some individual have responsibility for both graduate education and research. CRAD has existed for about five years; it was established by then-Vice President Maziar when she came to the University, Vice President Hamilton said, although not all colleges have the specific position. If someone attends CRAD meetings, however, the person has been appointed to do so by the dean so does represent the college. How many different colleges are there? 26 on the Twin Cities campus (one of the highest in the nation, Professor Balas commented).

How do the research associate deans interact with faculty to let them know of new regulations, Professor Balas asked? That is why CRAD has sessions with each college and the issues confronting them, Dean Ysseldyke said. For example, his college (Education and Human Development) shares concerns with COAFES (Agriculture, Food, and Environmental Science): both do a lot of work for the state, which carries zero indirect cost funds, so their effective ICR rate is about 14%. The Institute of Technology, in contrast, gets a lot more funding from NSF so has higher ICR reimbursement.

What about research centers not linked to a specific college, Professor Gantt asked? They are not represented, Dean Ysseldyke said. Centers are hard to talk about. In some, people have tenure homes. In others, two people need to call themselves a center in order to bid for funding. The latter kinds of centers are all over the place and are indirectly represented by the research associate deans. It would, however, be worth thinking about representation for the larger centers. Especially when there are debates about funding across colleges, Professor Gantt commented. Those kinds of issues (funding, operations) are not what CRAD addresses, Dr. Hamilton said; those can be divisive and it is better for the deans to address them.

Committee members recently received an article describing how the federal government is not funding universities to support research as it used to, Professor Balas said, and he agreed with the analysis. There seem to be caps on what can be recovered. There is an uneven playing field, Dean Ysseldyke said. Only 2% of the total U.S. Department of Education budget is earmarked for research while 40% of the Health and Human Service budget is for research. There has, however, been a significant increase for education research funding, in interesting directions, and is worth talking about. The availability of those new funds makes his college wonder if it should do as much state work, with its zero overhead; should they turn down the state work? That leads to discussions about ICR distribution.

What is the history behind the state not paying overhead, Professor Balas asked? That decision was made before anyone in the room was born, Dr. Hamilton said. The state also does not like to pass through the overhead funds it receives for grants it gives to the University. The University, however, can trace those funds and does seek the overhead funds as well. What the state says is that it provides the overhead by funding buildings, Dean Bloomfield said.

One issue is that as costs increase, ICR funds are capped for administrative costs, Vice President Hamilton said. The University can document that there is an administrative cost of 32% for grants, but those costs are capped at 26%, so the University pays more and more. Agriculture grants are capped at 19%, so the University cannot collect the full negotiated rate for those grants. The result is that the University's total ICR recovery is about 25% rather than the 48% negotiated with the federal government, and it certainly does not recover the 53% costs that it can document. He said he would like to have a discussion with the Committee about the negotiation process after the current negotiations are completed. Moreover, Dean Bloomfield added, federal agencies are increasingly asking for matching funds. NSF requires them, Dr. Hamilton said, as well as a match of 30% for equipment (and for a $1.6 million electron microscope, that is a lot of money).

Is there any policy to discourage faculty from seeking certain grants, Professor Balas asked? Absolutely not, Dr. Hamilton said; if they can get the grant, the University will find the money to support it. They have a matching pool--that is always in debt.

One issue that CRAD has addressed in the past, but that this Committee may not have, is the practice of many agencies of adding the ICR funds on top of the grant while others award a grant and require that the ICR funds be taken out of the grant. Given graduate student fringe benefit costs, some units are hiring fewer graduate students and more research associates. This has implications for the University in training researchers. A related issue is the disparity in graduate student salaries across colleges, which leads to problems in how to pay the students. Are these concerns for this committee, he asked?

Professor Balas said the Committee has talked about these issues with Dean Bloomfield in the past. There is a growing concern also about the increasing number of research contracts and fewer grants, which makes it more difficult to staff research with graduate students to provide them an education. There appear to be more business-oriented funds and less money for long-term research.

Dr. Bloomfield said that the statistics show that enrollment in Ph.D. programs is fairly constant or increasing slightly. There does not seem to be any dramatic change in the hiring of postdocs or others, but he agreed that the stresses are there. Health care costs keep going up, and tuition keeps increasing, but the University must be competitive in the national market for students. There is no easy answer on how to cut costs. In his college, Dean Ysseldyke said, the number of graduate students has not declined but the number who are funded to work on research projects is, which affects the kind of research experience they are receiving.

Is there a mechanism to keep track of postdocs, Professor Balas asked? There are a variety of positions that are used and the total number could be rising while the number of graduate students is flat. They are working with Human Resources to regularize appointments, Dean Bloomfield said. To make

them properly, college human resource staff must know the proper categories. The number of postdocs, however, appears to be relatively unchanged for the last couple of years, at about 900.

Professor Balas thanked Dean Ysseldyke for joining the meeting and said the Committee would stay in touch with CRAD. Perhaps a joint meeting would be useful at some point, he said.

2. Policy on New Drug Applications

Professor Balas now turned to Assistant Vice President Paller to lead a discussion of a new policy on "Submitting Documents relating to Sponsor-Investigator Investigational New Drug Application (IND) or Investigational Device Exemption (IDE)."

This policy, Dr. Paller explained, relates to an FDA regulation about research that uses human subjects in the investigation of new drugs and medical devices. Investigators who do such research must follow both FDA and Health and Human Services regulations; this policy has to do with the FDA regulations. If one wants to test a new drug on human subjects, the investigator must obtain approval both from the Institutional Review Board (IRB) and the FDA. The regulations concerning INDs apply even if there is no commercial application in mind, and is different from the subsequent step, the New Drug Application or NDA, which is the request for approval to market a new drug.

The sponsor of an IND or IDE must file with the FDA and must follow certain protocols. The details required vary with the drug and purpose but the basic requirements are essentially the same. In testing new drugs, a pharmaceutical company may be the sponsor, but it will go to clinical sites for testing; each site would have a principal investigator. Normally faculty serve as investigators but are not sponsors. Even if a drug is developed by a faculty member, it is typically licensed to an existing or start-up company, which is the sponsor. More and more, however, in developing new drugs, the PI serves as the sponsor, so there is a category of sponsor/investigator, and anyone in that position must follow two sets of regulations. Faculty are generally familiar with the regulations that cover investigators but not with those that cover sponsors.

Dr. Paller said that they have set up an IND/IDE Assistance Program to help faculty submit INDs to the FDA in order to test products in clinical trials. That office has been very well received. The FDA is interpreting its own regulations more stringently now. In the past, the IRB could decide if it was safe to test something, even though the ultimate responsibility rests with the FDA; increasingly, however, the FDA wants to make the decision, in addition to the IRB. The IRB has helped advise faculty whether they need an IND. A brand new agent requires an IND; using an approved drug in a different way may or may not require an IND. The IND/IDE Assistance Program helps faculty get an answer to that question.

What is not addressed in all this is the institutional responsibility to be sure that people are doing things correctly. The FDA will not communicate with the institution, only with the investigators who hold the IND. Dr. Paller said he even ASKED the FDA about this and that is what he was told. That leaves the University in the position that its faculty are communicating with the FDA about the research they are doing and the University is not part of the process. All INDs require an annual report and other periodic reports; how is the University to know about them? The FDA will send the PI a letter if the report is delinquent, and eventually will threaten to pull the authorization to do human subjects research if the report is not filed. The University only learns about this after the fact or from the FDA website.

This policy seemed to be the best way to deal with the problem, Dr. Paller said. Any faculty member who holds a sponsor/investigator IND must provide copies of the FDA filings to the IND assistance office so the University can help in the process. If he or she does not do so, they will be referred to the Office of Regulatory Affairs. They are proposing this policy to help faculty and also to provide assurance to the University that its faculty are complying with the regulations.

How have the faculty reacted? In the Academic Health Center, they have a translational research advisory group with a large number of faculty with INDs; that group is very positive about this because it is linked to the IND assistance office, which helps them with the technical work. They find this an acceptable mechanism. The office, for example, will send a reminder when the annual report is due; the office will provide assistance in preparing the report. If the faculty member does not want help, he or she must still send a copy of the report to the office so the University is sure that the regulatory obligations have been met.

This policy is not a reaction to specific incidents here or elsewhere, Dr. Paller said, and is more a response to the faculty saying they have difficult regulations to comply with and need help. He said he believed this policy and the assistance office are unique to the University of Minnesota.

What about adverse event reports, Ms. Witson asked? It already has to be filed with the IRB and the FDA; now another copy has to go to this office? Dr. Paller said that a copy of the report to the IRB must go to this office (and faculty may not even be aware that a copy has to go to the FDA; the assistance office works with the IRB to be sure the report is sent to the FDA). It is up to faculty to decide how to do the report--they can do it themselves or the office can help.

Does the office deal with scientific issues or clerical/government issues, Professor Johnson asked? With regulatory issues, Dr. Paller said; the policy requires faculty to do something not previously required by the University. The scientific issues are dealt with by the FDA and IRB.

Professor Balas asked about the sponsor/investigator category. He said he thought the University discouraged people from developing and testing the same drug. That is handled by the conflict of interest policy, Dr. Hamilton commented.

Sponsor does not necessarily imply a financial gain to the project; it merely identifies the individual or organization that has the obligation to talk to the FDA. (For example, a drug for something that a faculty member wants to pursue even where there is no personal financial consideration. After the study, the beneficiary could be the company that makes the drug. The company may say it is not interested in performing the research project, perhaps because of liability concerns, so the faculty member needs to be the sponsor/investigator).

In terms of submitting copies, Professor Balas confessed that he was not great at doing so--he could be in compliance but not send the copies until a year later. Dr. Paller said he would not be in compliance if he communicated with the FDA and did not send a copy to the IND assistance office. They will try to make the process as easy as possible. They will pick up the copy of the report if need be.

How many faculty-sponsored INDs are there at the University, Dean Bloomfield inquired? Perhaps two or three dozen, Dr. Paller said, and the number is increasing.

The federal government deals only with investigators, Dr. Hamilton said again, but if it turns out that someone at the University is not complying with regulations, even if the University knew nothing about the problem, the federal agencies can wreak havoc on the institution. This is a good policy to get on the books in order to be able to deal with something that could be very damaging to the University and to human subjects in research.

Dean Bloomfield observed that doctors in practice can use drugs for uses for which they have not been approved.. Are the University of Minnesota Physicians able to do so? New uses of drugs are allowed in clinical practice (off-label usage), Dr. Paller said, but if the physician is recording the results, it is research. There is a standing joke that doctors can do anything they wish to ALL of their patients, but if they only do it to HALF the patients, they have to have the permission of the FDA and IRB.

Are the consequences specified if a matter is referred to the Office of Regulatory Affairs? Normally the director of ORA (or other regulatory units in the Office of the Vice President for Research) would send a letter and a second letter. If there is no response, the sponsor/investigator will receive a letter from the Vice President, who has various options, including stopping the research, Dr. Hamilton said.

At present the University is out of the loop; it is in the loop enough to be able to remind an investigator that documents are due, Professor Luby asked? As long as the individual starts the process and lets the University know when he or she has contacted the FDA, the University will be in the loop. This is still up to the investigators; if there are adverse events and the investigator tells no one, there will be unknown non-compliance, Dr. Paller said. If the investigator tells the IRB, the University will be informed. And the University can help; it cannot do everything, but if it knows about things it will be in a better position to help solve problems. There are tricky parts to this, he observed. If someone files for an IND and it is approved, an annual report must be filed. But the investigator may not obtain the money or may drop the project--but there still has to be a final report to the FDA. An error with the FDA is an error; the assistance office tries to get problems cleared up.

Initially, policing will be in Dr. Paller's office, Vice President Hamilton said; he is the overlord. They have in process a project on compliance that integrate the IRB, clinical research, the Cancer Research Center, and various units--a project stimulated by a plea from Professor Balas to have the REPA and other forms put all in one place so they can be completed on line. The system will include automatic notification of when a report is due or if there is a paper to sign.

Professor Sera said that one concern she has is that she has been on the Committee for three months and has been asked to endorse three policies that increase the work for investigators--at the same time there are more students and more work in general. She said she believed this is a good policy that the faculty wanted, but faculty are concerned about paperwork, which is what the faculty here hate the most. The University must not keep piling on the paperwork. Dr. Hamilton said he was sympathetic to Professor Sera's point--he is still a faculty member who teaches and maintains a lab--but these are regulations the University must comply with. It has no control over them but is trying to make compliance as easy as possible. The investigator must file with the FDA anyway, Dr. Paller said; this policy does not require any additional forms, only that the University receive a copy. He said he could sleep at night because this policy will also end up helping faculty.

Have there been abuses in the past that led to this policy, Professor Dahlberg inquired? Perhaps ALG, Dr. Paller said. The policy was not designed to have prevented the ALG problems per se, but the University would have been helped in knowing what was going on. The policy deals with people who are not in compliance because they do not send the forms to the FDA, which the University can help with. A lot of people in the trenches say that the people who do wrong get off and the rest get punished, Professor Dahlberg said. That happened with ALG--the University was put on exceptional status, had to have extra lawyers and paperwork, but Dr. Najarian came out fine. "If I do wrong, I expect the system to punish me, not my colleagues in the department," he said. Dr. Hamilton said that while Dr. Najarian was not convicted in court, he lost his endowed chair, his faculty appointment, his Regents' Professorship, and cannot function as a faculty member. He can only do surgery as an adjunct surgeon. And he was not the only one who was punished as a result of ALG.

This is work that she does, Ms. Witson said. If there is any way to simplify the process, or the forms for the IRB and the assistance office, that would help. Some documents, she noted, are 50 pages long. Dr. Hamilton said he would talk about this problem when he brings the integrated compliance plan to the Committee in January. Dr. Paller noted that the FDA only accepts paper forms; Dr. Hamilton said that the University can nonetheless do them electronically; Dr. Paller added that the University would make all the needed copies for the investigator.

Professor Balas asked for a motion to endorse the policy. The Committee voted 14 in favor, none opposed, with one abstention. Professor Dahlberg, who abstained, said he was not against the policy but that it would be better for the Committee to hear about a policy, have a discussion, and then have time to think about it--and have the item brought back for action at the next meeting. He said he was hesitant to vote for something he has not had time to think about. Dr. Hamilton said he agreed entirely. He noted Professor Sera's point that the Committee has seen three policies so far this year; there will be many more coming, he said; part of the process needs to be that he gets draft policies to the Committee early. He said he believed firmly in consultation with the governance system and that Committee members cannot know the pros and cons of a policy without discussion.

Is Minnesota still in front in terms of making things easier, Dr. VanDrasek asked? It is and it is not, Vice President Hamilton said. It is ahead of the other Big Ten schools, but some institutions have begun using an outside company to assist with compliance and regulatory issues. The University cannot afford to do so.

Professor Balas thanked Dr. Paller for his presentation.

3. Survey of Institutional Review Board Users

Professor Balas now turned to Vice President Hamilton to discuss the results of the survey of IRB users.

The survey was developed and conducted because of a concern initially expressed by the Faculty Consultative Committee that there were substantial problems with the IRB in practice at the University, Dr. Hamilton reported. Professor Dan Feeney proposed a survey of faculty and developed a proposal. He (Dr. Hamilton) brought in professional survey people to rework and refine the survey; he and Professor Feeney agreed it would go out over both of their signatures and would be sent to 3022 faculty who have

IRB protocols. They received 864 returns. The results were assembled in Epidemiology by Professor Michael Oakes, who is an expert on IRBs.

Ms. Keane said that what sparked the effort originally was the problem that customer service surveys typically do not reach the threshold of coming to this Committee or the Vice President for Research. The issues involved in the survey arose from both national and local concerns. The University had a brush with federal agencies about 10 years ago and since has gotten ahead of the curve on regulatory compliance issues. Other institutions have had more recent entanglements with the agencies, which have gotten tougher, so there is angst about whether institutions are doing things right. In addition, social science researchers were concerned that they were being held to standards for the clinical sciences, not the behavioral, and the IRB was applying rules it should not. Coupled with the notion that a campus should be more service-friendly, the question was whether the University was getting the best it could from the IRB. The survey tried to get at the issues: Were people getting reliable information from the committees? Were they getting what they needed from the educational program?

Ms. Keane said she was pleased with the results. For the most part, investigators believe the review they receive is appropriate, they have seen a significant increase in customer service, and they are receiving the education they need. The survey dovetailed with the application for accreditation of the IRB, she said, and helped push improvement of information on the web site and the educational efforts.

There were also open-ended results which are currently being analyzed. Ms. Keane said she would bring them to the Committee when they were completed.

Some concerns were from the social/behavioral sciences but the report provided to the Committee lumps the responses together so there is no way to tell how that group of researchers felt about the issues, Dean Bloomfield said. Ms. Keane noted one of the graphs in the report does get at the issue. Professor Dane said she had the same question; the social/behavioral scientists might have very different answers.

Professor Balas noted, in another graph, that 46% of the respondents said they disagreed or were uncertain whether the IRB added value. That seems to be high, he said. The "uncertain" category needs to be broken down, Ms. Keane said; it may include people who do not know. Professor Seybold said she had received the survey, but since she does not do human subjects research, she would have marked the "uncertain" choice.

Professor Luby said he was concerned about the responses that may have come from faculty with different levels of involvement. He said he always applies to the IRB for the "exempt" category so for him the process is relatively easy. He said he put down "agree" on the survey but he also barely gets into what touches many faculty. Professor Johnson said the results needed to be broken out by individual scientific experiences. Of the nearly 900 responses, 800 could be clinical and the remainder social and behavioral scientists. If there is a problem on the social/behavioral side, one does not know what to conclude from these data; they need to be broken up.

It also appeared to be the case that the more often one applies to the IRB, the less satisfied one is with the process, Professor Balas noted. For a lot of the categories, the number who answer negatively is 10-20%, which is a lot of people who do not the think the forms communicate appropriately and so on, Professor Sera said. If one is making a customer service argument, Professor Johnson agreed, one wants that number to be zero.

Ms. Witson said that it was her understanding that social/behavioral scientists believe the model for oversight of medical research is sometimes inappropriate for social science research and that that belief was one of the motivations for developing the survey. She asked Ms. Keane how the survey questions get at that issue. Ms. Keane said the IRB tries to tailor information to the faculty so that they can sure faculty are receiving what is relevant to what the faculty member is doing. Ms. Witson said she interpreted that to mean that the problem lies with the social science faculty--they do not always understand how human subjects protection applies to their research--rather than with over-exuberance on the part of IRBs. Perhaps it is not just the faculty who need education but also the IRBs. That is true at many institutions, Ms. Keane said, but Minnesota has two panels for the social and behavioral sciences and those projects are not mixed up with those of the doctors.

A lot in the social and behavioral sciences are unhappy, Dean Bloomfield said, not how this IRB does its work but that the federal IRB rules apply at all to their research or they apply in a way that is not sensitive to their disciplinary needs. There are a lot of complaints but it could be a case of shooting the messenger, he said.

Ms. Keane said she would not maintain that the survey answered all the concerns; there are still gaps. They do have initiatives underway to address the reasonableness of application of the rules, but everyone must recognize that their customer is the research subject. The best way to protect research subjects is to help the researcher do things right.

One question he gets from colleagues, Professor Johnson said, is about students doing something in a class, or quasi-research. There could be more communication about what it is necessary to do in those instances. He said he has gone through the website materials and the answer is not clear. Dr. Hamilton said he was not sure anyone knows the answers; the social/behavioral scientists and the federal government are debating the matter. What about a small classroom setting, Professor Dahlberg asked? If the students are asked to react to a question, Professor Sera added? Professor Johnson responded, a la Dr. Paller, if the instructor asks a single student, there is no problem; if the instructor collects data and analyzes it, then it is research.

They do not just tell people to look at the website, Ms. Keane said. They have people to answer the telephone and help troubleshoot projects. One of their favorite things to do is tell a researcher they do not have to the paperwork.

Professor Dahlberg asked if there was concern about the large percentages of answers that were "uncertain." That raises a flag with him, he said. Dr. Hamilton said that Committee members were raising valid questions and they would have to see if the data could be examined to address them.

Professor Balas thanked Ms. Keane for joining the Committee and said it would await the results of the open-ended questions with interest.

4. Technology Park

The Committee concluded it had insufficient time remaining to deal with the issues of the technology park and the relationships with Minneapolis and St. Paul that were raised in documents distributed by Vice President Hamilton. It agreed that individual Committee members would use the

committee listserv to make comments and ask questions because the process could not wait until the next meeting.

What will happen if the University does not act in a timely way, Professor Johnson asked? The two cities will go their own way and not listen to the University, Dr. Hamilton said. He said if there were no agreement it would be difficult for him to work with the two cities.

Professor Dahlberg recalled that there was a technology corridor that disappeared; will this effort fail for the same reasons? Dr. Hamilton said this would not fail. It is along the transit corridor and both cities are interested in developing the technology park. He said he was troubled by other aspects of the development. He has put into the agreement various things he believes the University must control and believes that there must be a benefit to students at the University. There is also the issue of faculty retention: Some faculty are very entrepreneurial and want an opportunity to do a start-up company; they will leave if they do not have that chance. By the same token, prospective faculty will not come to the University because the opportunity is missing.

Dr. Hamilton said he wanted ideas about the documents more than he wanted endorsement, because he would like to make them better. The documents have already been approved by the academic vice presidents and the President.

Professor Balas adjourned the meeting at 3:00.

-- Gary Engstrand

University of Minnesota