Karen Muskavitch's Commentary on "Pregnancy Results?"

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Pregnancy Results?

[Experimental Design of the Study]

[The Informed Consent Process]

[The Dissertation Committee]

The primary questions in this case cluster around beneficence, the ethical principle that one should avoid doing harm and seek to do good. How one answers these questions will then affect how one designs the informed consent process for this study. A secondary set of questions concerns the dynamics between a graduate student and the faculty on her dissertation committee.

Experimental Design of the Study

Conducting a risk/benefit analysis is more than just a required task that a researcher must perform in filling out an application for IRB approval. Coming from the ethical principle of beneficence in the Belmont Report,The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 1979. http://ohrp.osophs.dhhs.gov/humansubjects/guidance/belmont.htm. it is the obligation of researchers to scrutinize the experimental design of their proposed studies, and to put themselves in the proposed subjects' shoes to consider what potential harms and benefits may result from their work. If one looks at the mandated criteria for IRB approval of research,45 CFR 46, http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm. one notes an emphasis on evaluating potential risks and benefits of a proposed study in the context of its research design. While the federal regulations do not clearly require

IRBs to review a proposed study's experimental design,Office for Human Research Protections, The Institutional Review Board Guidebook. http://ohrp.osopht.dhhs.gov/irb/irb_guidebook.htm, Chap. IV. some institutions do ask this review of their IRBs (see, for example,Office of Human Subjects Research, National Institutes of Health, IRB Protocol Review Standards. http://ohsr.od.nih.gov/info/checklist_IRB_protocol.html.) and, as in this case, it frequently becomes important in the consideration of potential risks and benefits.

A number of questions need to be answered before a decision can be made about making the results of the hCG analyses available to the subjects. First, what is the goal of this study? What is the hypothesis being tested? What does Wilma hope to learn from this study and then contribute to the scientific literature? The case as written offers no clear answers to these questions, and so these points may need to be addressed in the case discussion.

Then, knowing the study's goal(s), one can begin considering possible alternatives and refinements to the experimental design. Who are the subjects of this study? What, if anything, will be presented to them as the potential benefits of participation in this study? How will potential subjects be recruited or excluded? Will the men in each couple answer the questionnaire and consequently be subjects, or will only the women fill out the questionnaire as well as providing urine samples? Will the nurses gather any additional information when they collect the month's samples? Will Wilma contact the subjects for any follow-up data, such as reports of pregnancies clinically confirmed within three months of the completion of the study? All of these aspects of the experimental design affect the potential risks and benefits to the subjects and thus affect how Wilma will design the informed consent process and form. Let me give a couple of examples.

If only women are recruited, complete the questionnaire and provide samples, then only they are subjects of the research, and their male partners have no claim upon data generated by the study. However, possible harms and benefits to the male partners who are not subjects should also be considered in the research design. Stakeholders beyond the immediate subjects of the research, such as the subjects' families and communities, should also have their interests considered and protected.

If Wilma recruits from among patients of clinics specializing in the treatment of infertility, then her subjects, and possibly their doctors as well, will be very interested in obtaining their hCG data even six to twelve months later. However, if

she recruits from among the general population and restricts her study to women who have been trying to conceive for less than three months, she is better able to argue that there is very little benefit in making the data available. Nevertheless, one must wonder what benefits or inducements Wilma can offer her subjects to make them willing to collect approximately 90 daily urine samples. Women who have been unsuccessfully trying to conceive for more than more than a year may be more willing to collaborate if there were the promise of data that might help them and their doctors determine the source of the problem. How (pure numbers or with interpretation) and to whom (the woman or her physician) the data are given could be important in minimizing possible distress if an otherwise unrecognized pregnancy is indicated.

Throughout the process of reviewing and fine-tuning the experimental design, Wilma, like all researchers, must take care to evaluate the potential harms and benefits of the research and work to minimize possible risks in a manner that is consistent with good science, even if the risks appear minimal.

The Informed Consent Process

The design of the informed consent process and form for this study will depend on how Wilma answers the questions posed in the previous section concerning the identity of her potential subjects. Both Ready and Supply are overstating their positions, but there is some truth in each of their statements, as well as quite a bit of room for a creative middle ground. While the regulations do not require that the researcher provide test results to research subjects,45 CFR 46, http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm. one can argue that there is little other benefit that Wilma can offer her subjects for all their inconvenience. Unlike Supply's assertion, daily hCG levels could be useful to women having difficulty conceiving even if the data are received six to twelve months after the samples are collected, but these data could also cause distress to the woman if they reveal an early spontaneous abortion. Determining the study's potential harms and benefits and the steps that should be taken to minimize the potential harms will depend upon the details of the experimental design and the pool of potential subjects. Once these are determined, however, the informed consent process and form must be designed to clearly inform the potential subjects of "any reasonably foreseeable risks or discomforts . . . any benefits to the subject or to others which

may reasonably be expected from the research," as well as stating who will have access to confidential data generated by the study and in what circumstances.45 CFR 46, http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm. The consent process should also be consistent with the ethical principle of respect for persons.The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 1979. http://ohrp.osophs.dhhs.gov/humansubjects/guidance/belmont.htm. Perhaps the best option for Wilma is to give her potential subjects a choice about whether they want to receive their hCG data.

The Dissertation Committee

The interactions of Wilma with Knowledge, her adviser, and Ready and Supply, members of her dissertation committee, are typical and can be used to initiate discussion of several aspects of graduate students' relationships with faculty members.

First, we see Wilma consulting with her adviser on the proposal that will be submitted to the IRB. Knowledge carefully reviews the proposal and recommends some additions and modifications based on his more complete knowledge of the ethical and regulatory concerns associated with research involving human subjects. That is as it should be. It is Knowledge's responsibility as Wilma's research adviser to help her learn how to design an experiment and acquaint her with the norms of the profession.Committee on Science, Engineering and Public Policy of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. Adviser, Teacher, Role Model, Friend: On Being a Mentor to Students in Science and Engineering. Washington, D. C.: National Academy Press, 1997, p. 7 and Chapter 2. http://www.nap.edu/readingroom/books/mentor. In addition, at many universities faculty advisers must cosign IRB applications, indicating that they will supervise the research and are aware that they are responsible for seeing that it conforms to ethical and regulatory standards (see, for example,Office for Research and the University Graduate School, Indiana University, Researcher Responsibility. http://www.indiana.edu/~resrisk/resresp.html, and IRB Application Packet Forms http://www.indiana.edu/~resrisk/forms.pdf.).

Second is the committee meeting where Ready and Supply provide Wilma with very different advice. That is not necessarily a bad thing. One usually tries to get faculty with varied expertise and a variety of perspectives on a dissertation committee Committee on Science, Engineering and Public Policy of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. Adviser, Teacher, Role Model, Friend: On Being a Mentor to Students in Science and Engineering. Washington, D. C.: National Academy Press, 1997, p. 7 and Chapter 2. http://www.nap.edu/readingroom/books/mentor.. However, if the conversation does not continue toward a compromise, it could be a problem. First Wilma should present her reasoning and offer some other possible courses of action. Then Knowledge should speak up. As Wilma's research adviser, he needs to help Wilma work with her committee to devise an ethically acceptable course of action upon which all can agree. If that is not possible, it may be time to rethink the project or change the committee membership.