Karen Muskavitch's Commentary on "Informed Consent for Use of Stored Specimens"

Commentary On
Informed Consent for Use of Stored Specimens

Overview

This case challenges us to consider one of the fundamental questions in ethics: How ought people to treat each other? Yes, it's a human subjects case that emphasizes the issue of informed consent. However, if we only talk about "human subjects," we can too easily forget what this term really means, and that is people, like ourselves. Here, the subjects are 10,000 women who were initially recruited for the study when they were pregnant five to ten years ago. Those considering the ethical issues in the case are two senior researchers who have collaborated on the study since its beginning. In their discussions in this case, Smith seems to concentrate on the research subject aspect of those who participated in the study while Jones tends to view them more as individual people.

At one level, this case can be discussed as a means to clarify what the regulations are and how one goes about fulfilling them. That is a necessary part of educating researchers in the proper procedures to follow in human subject research, and should not be overlooked. However, this approach leads one to discuss rules and legalities more than ethics and can result in protocols that, while technically correct, do not truly treat the subjects respectfully and/or fail to consider all the possible consequences of the study. To get at the ethical issues, one must move from just considering the letter of the regulations to their spirit; to exploring the ethical principles that underlie all those rules. For research involving human subjects, these are the three principles delineated in the Belmont Report:

1. Respect for persons involves a recognition of the personal dignity and autonomy of individuals. . .
2. Beneficence entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm.
3. Justice requires that the benefits and burdens of research be distributed fairly. (National Commission, 1979)

If researchers got into the habit of looking beyond the rule itself to consider the reason for the rule, and then asked whether their protocols and procedures were consistent with the underlying principles, a lot of the difficulties that have come up in human subjects research could be avoided.

Discussion Questions

Part 1

The question asks whether the researchers are obligated to recontact the participants for their consent before doing a genetic analysis on the specimens donated by the participants for the previous study. The short answer is "yes," both for legal and ethical reasons.

I use the term "previous" study because it has "been five years since the end of data collection," and I assume that the analysis of these data and presentation of the researchers' interpretations at meetings and in journals would have already occurred. Thus, the primary work on the study is probably completed, but the samples are still in the freezer. I make this point because, acting on a point made by Wallace (1982) and noted in the IRB Guidebook (NIH 1993), most current IRBs would require that the experimental protocol specify what would happen to the data and specimens at the conclusion of the study. That does not seem to have been the case here, and probably was not required for most older studies. The fate of the data and specimens should be a concern of all researchers carrying out research using human subjects.

Why all this concern about a few blood samples and a few proposed "look-see" preliminary tests? After all, scientists are trained to keep samples just in case

something comes up in the future such as a question about the previous work, or an opportunity to extend the investigation previously conducted. Most scientists have freezers and storage cabinets bulging with materials from earlier research. In this case, it is important to note that those 10,000 blood samples that Smith has in her freezer are not the same as the thousands of slices from a sediment core drilled out of a lake bed that a geologist across campus may have carefully stored in her cabinet. Smith's samples come from human beings, and therefore the issues of respect for persons and confidentiality need to be considered as well as scientific merit when new analyses are contemplated.

The women who participated in the study have a right to have a say in what is done with these specimens taken from their bodies. It is interesting to note that some universities have gone so far as to broaden the official, federal definition of human subjects to include living individuals "as well as human embryos, fetuses, cadavers, and any human tissue or fluids." (Indiana University, 1997) This definition emphasizes that these research materials are different from others scientists may use in their work, like the sediment core noted above, and that these samples must be treated with respect. The concept of respect for persons comes largely out of the writings of Immanuel Kant who asserted that one should:

> Act so that you treat humanity, whether in your own person or in that of another, always as an end and never as a means only. (Kant, 1785)

In this case, Smith is in danger of forgetting that the participants in the study are people, not just a means to advance her research. I'm sure that she has good intentions, but she can't skip asking permission of the study participants just because she believes the end will be beneficial for science and society.

Genetic analyses were not listed in the original consent form, and they yield information that is fundamentally different from that yielded by the analyses listed. The original analyses looked at characteristics that were environmental in nature; things that could be changed by treatment or modification of the women's behavior. The genetic analyses could yield information about characteristics of the women over which they have no control, and that could be passed on to their children. This information could cause harm if it became known to either the women themselves, or to others with whom they interact such as employers or insurance companies. Even for oneself, genetic self-knowledge is not always a benefit. It can be a burden if

no available corrective treatment is available, and particularly if the knowledge is unwanted and is forced upon a person. What Smith proposes is not just an extension of the previous analyses. The women have a right to decide whether the genetic analyses are to be done on their samples, particularly in light of possible consequences.

The issue of confidentiality will be discussed further in the commentary on later questions in this case.

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Part 2

Question 1. In response to Jones' objections, Smith suggests that they just destroy the list that links the study participants' names with the other data collected in the study. That would seem to solve the problem of confidentiality since no one could find out the participants' names after the list was destroyed. In addition, it would seem to qualify their work for an exemption from the need for informed consent based on the federal regulations. This suggestion raises several issues.

First, the proposed course of action is disingenuous. It's not the case that the researchers never had the participants' names. They have simply destroyed them because it seemed the easiest short-term solution. This approach is not the best way to enhance the public's trust of scientists. Also, as Jones points out, those names might be needed later if they decide to pursue a follow-up study.

Second, destroying the names does not really eliminate the linkage between those samples in the freezer and the women who donated them. The relevant regulations state that an exemption from the requirement for informed consent may be granted

> . . . if the information is recorded by the investigator in such a manner that subjects can not be identified, directly or through identifiers linked to the subjects. (45 CFR 46.101(b)(4)).

However, that is not the situation here because of the other data collected by these researchers. What the regulations refer to as "other identifiers" could still be used to link the genetic results to the women. Information that might facilitate the linkage are such items as maternal age, date of delivery, days preterm, baby's weight,

location of interview and delivery hospital. It would not take too much work by a private investigator to identify the women to whom these data referred. Thus, confidentiality must still be a concern of the researchers, and they do not qualify for an exemption from the requirement for informed consent.

Question 2. This question is largely addressed in the commentary for Question 1 above, but there is an additional reason why the researchers should contact the participants for their consent before doing the genetic analysis: The genetic analysis poses potential risks that differ from those presented by the earlier analyses. If confidentiality is broken somehow, the women could be burdened with self-knowledge that they did not want; they may lack support in dealing with this information; and their new knowledge could have a negative impact on them and their children. Depending on the genetic markers that Smith selects for her work, the information derived may simply enable molecular geneticists to estimate the risk of premature delivery for the participants and their daughters.

However, if genetic markers with known associations with other diseases or conditions were used, the information could be even more damaging. For instance, if Smith checks for the alleles at the BRCA1 locus, one of the so-called breast cancer genes, she may or may not gather data that will help predict if a woman is in danger of giving preterm birth, but she will have information that bears on the current health of these women and their blood relatives. This information could be devastating to a woman, especially if she did not expect to receive it, and could be detrimental to her future employment and insurability if it became known to others. Because of these considerations, the new informed consent form would need to be different from the original one in order to address the potential risks associated with genetic analyses. The women should also be asked to indicate if they want to be informed of any information the researchers may gather that could have an impact on the participants' health. They have a right to determine what information will be gathered about them, and to control who will have access to the information, including themselves.

Question 3. Asking whether the researchers have an obligation to inform the women of the results of the genetic analysis assumes that the researchers went ahead with the analyses without obtaining additional consent from the study participants. Of course, it would be best to avoid the dilemma posed by discovering that Mary Brown, for instance, has an 80 percent chance of breast and/or ovarian cancer, but not knowing how she will react if you send her a letter containing this information.

This scenario could be avoided by getting additional consent, before doing the analyses, in which one also asks the women if they want to be informed of the results of the genetic tests.

Assuming that they didn't ask, Smith and Jones must now consider the possible consequences of their decision to contact Mary Brown with the bad news. Here it is valuable to take a closer look at the principle of beneficence.

In the Belmont Report, the committee discussed what they meant by the principle of beneficence as it applies to research involving human subjects.

> In this document, beneficence is understood . . . as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not do harm and (2) maximize possible benefits and minimize possible harms. (NIH, 1993)

Note that the first rule listed is "Do not do harm." Many philosophers assert that one has a greater obligation to avoid doing harm than to attempt to do good (Frankena, 1973), and that is an important consideration in this case. What "goods" might the researchers do by carrying out the analyses and then contacting a participant if they discovered something they felt she should know? What "harms" might occur as a result of this course of action? In the "goods" column, a list might include advancing scientific knowledge for the benefit of society, and aiding in the health care of study participants. In the "harms" column would go such things as psychological harm to the participants who are told bad news, and risk to future employment and insurability if confidentiality is broken. Many of the potential benefits are to science, society and the researchers, while almost all of the potential harms are to the study participants themselves. Thus, one must consider both the principle of beneficence and the principle of justice in answering this question. In my analysis, the potentials for harm and injustice were so much greater than the potential benefits that I would argue that the woman should not be informed of the results of the genetic analysis unless they have said they wanted to know.

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Part 3

In a situation like this, a vague statement on a consent form is of benefits to no one, although it might be technically in compliance with the regulations. One must question whether the researchers are really demonstrating a respect for the participants when the consent process is so vague. In addition, the vague wording, while sanctioning the genetic analyses Smith wants to do, does nothing to help her resolve the dilemma of how to respond if data are found that could have an impact on the participants' health. For the benefit of the participants, the researchers and the enterprise of science, it is best to be as through and forthright as possible in the consent form and in the recruiting interviews with the potential subjects.

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