Informed Consent for Biorepositories: Assessing Prospective Participants' Understanding and Opinions

Laura M. Beskow[1] and Elizabeth Dean[2]

[1]Duke Translational Medicine Institute and the Duke Institute for Genome Sciences and Policy, Duke University, Durham, North Carolina and [2]RTI International, Research Triangle Park, North Carolina

Abstract

Purpose: **Obtaining informed consent for the collection, storage, and future research use of biospecimens is challenging, as potentially complex and controversial information must be communicated clearly. We gathered input on a consent template developed for the Duke Biorepository from individuals representative of those who might one day consider contributing specimens.**

Methods: **Forty subjects were recruited from the Durham, NC area and screened to achieve diversity by race/ethnicity, education, age, and sex. Cognitive interviews assessed participants' (*a*) understanding of information in the template, and (*b*) opinions about that information. Participants also completed a survey assessing trust in medical researchers.**

Results: **Interviewees seemed to understand the template. Although responses were diverse, majority views emerged: more than half were comfortable with indefinite biospecimen storage, periodic contact to update information and to inform participants of additional research opportunities, the prospect that commercial products could be developed, and the fact that profits would not be shared. More than half were willing to provide medical record access, although this was a primary concern for others. More than two thirds were comfortable with not receiving individual research results as a matter of routine, but many thought they should be informed of findings with serious health implications. Lack of trust in researchers was associated with declining certain consent options.**

Conclusions: **Protecting and promoting trust in research is essential to fostering widespread participation in biorepositories. Biorepositories should also devise ways to communicate clearly about the research being conducted and what is being learned.** (Cancer Epidemiol Biomarkers Prev 2008;17(6):1440–51)

Introduction

Biorepositories are an invaluable resource for basic, epidemiologic, and translational research. The application of molecular technologies to collections of human biological specimens represents an unparalleled opportunity to discover new ways to prevent, diagnose, and treat cancer and other diseases (1). Efforts to compile health information and collect biological specimens from large populations are already under way in the United States and around the world (2), with the ultimate goal of unlocking the genomic basis of disease and ushering in an era of personalized medicine (3). Such achievements, however, depend on the ready availability of high-quality specimens, annotated with relevant clinical data and collected with scrupulous attention to ethical, legal, and social concerns. In particular, issues related to informed consent are among the most pressing in human biospecimens research (4, 5). In addition to questions about when informed consent must be obtained, there is considerable debate about what information and options should be incorporated into the consent process (6-10).

Several previous studies from the United States have focused on attitudes among persons who had already contributed tissue for research (11-15); others involved population-based surveys of specific groups regarding use of stored tissue for research and the need for consent (16-20). Still, questions remain: how can the collection, storage, and future research use of specimens and data be described so that prospective participants can make informed decisions? What do prospective participants think about controversial aspects of biorepositories, such as indefinite storage, links to medical records, future contact, development of commercial products, access to research results, and the ability to withdraw? What effect do these issues have on the willingness of potential subjects to participate?

We sought to gather input on a consent template developed for the Duke Biorepository from individuals generally representative of those who might one day consider contributing specimens. Specifically, we conducted cognitive interviews to explore the following questions: (*a*) how do prospective participants understand or interpret the information conveyed in the consent template, and (*b*) what are their opinions about the information conveyed?

Materials and Methods

The Duke Biorepository consent template was developed based on federal regulations (21, 22) and best practice guidelines (4, 23-26), as well as guidance from the Duke University Health System Institutional Review Board (27)

Received 1/28/08; revised 3/7/08; accepted 3/17/08.

Grant support: NIH Clinical and Translational Science Award 1UL1RR024128-01 (Duke University).

Requests for reprints: Laura M. Beskow, Duke Institute for Genome Sciences and Policy, 240 North Building, Box 90141, Durham, NC 27708. Phone: 919-668-2293; Fax: 919-668-0799. E-mail: laura.beskow@duke.edu

doi:10.1158/1055-9965.EPI-08-0086

Table 1. Interviewee characteristics (*N* = 40)

	n (%)
Age group (y)	
18-24	1 (2.5)
25-34	6 (15.0)
35-44	8 (20.0)
45-54	16 (40.0)
55+	9 (22.5)
Sex	
Female	24 (60.0)
Male	16 (40.0)
Race	
American Indian/Alaska Native	2 (5.0)
Asian	6 (15.0)
Black/African American	20 (50.0)
White	9 (22.5)
Other	2 (5.0)
Hispanic	
Yes	5 (12.5)
No	35 (87.5)
Education	
High school diploma/GED	10 (25.0)
Some college, no degree	12 (30.0)
Associate's or other 2-year degree	1 (2.5)
Bachelor's degree	8 (20.0)
Master's degree	8 (20.0)
Doctorate or professional degree	1 (2.5)
Research participant in past year	
Yes	6 (15.0)
No	34 (85.0)
Duke Health patient in past year	
Yes	14 (35.0)
No	25 (62.5)

and publicly available sample forms from other institutions. It was further revised following input from senior Duke investigators. For the purposes of our study, we developed a cognitive interview (28) protocol about the template, based on a review of literature regarding informed consent and attitudes toward biobanking and research using stored tissue. The interview focused on participants' comprehension and opinions, and the decisions they would make if asked to participate in the Biorepository. The research was determined by the Duke and RTI Institutional Review Boards to be exempt from review (45CFR46.101[b][2]).

Subject Recruitment. We recruited interview participants from the Durham, NC area, using newspaper advertisements, Internet postings, and flyers placed in Duke clinics and in several community locations. Respondents were screened by telephone and selected to oversample minorities and people with lower educational attainment, to achieve diversity by age and sex, and to avoid habitual research participants. A sample of 40 participants was expected to achieve saturation (i.e., no additional insights gained from further interviews). The purpose of cognitive interviewing is not statistical estimation; thus, sample sizes are not selected to supply statistical power for hypothesis testing. The goal is to maximize the diversity of the sample and to attain insights by interviewing a variety of individuals who will be useful in informing the issue (28, 29).

Subject Interviews. Interviews took place from May to October 2007. We used an iterative approach, revising the template and the interview questions based on feedback gathered in each of four rounds of interviews. Participants were interviewed in person by one of two professional interviewers at RTI's Laboratory for Survey Methods and Measurement. Participants first completed a brief written survey that collected basic demographic information, as well as answers to four validated questions intended to assess trust in medical researchers (30). Interviews were conducted by non–Duke personnel in a nonclinical setting in part to avoid biasing the response to these questions. After reading the entire consent template (Appendix A), participants were interviewed (script available upon request). All interviews were digitally recorded and lasted an average of 30 min. Participants gave oral consent and received $40 for participating.

Interviews were analyzed using standard inductive qualitative methods (31, 32). One author (E. Dean), who conducted most of the interviews, compiled a detailed

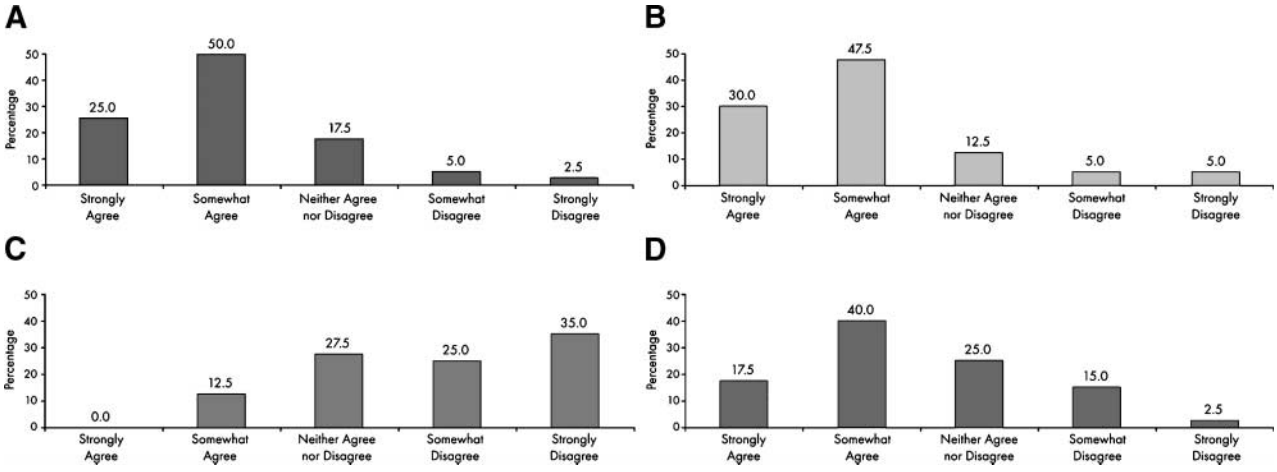

Figure 1. Participant responses to validated survey questions designed to assess levels of trust in medical researchers. (**A**) Doctors who do medical research care only about what is best for each patient; (**B**) Doctors tell patients everything they need to know about being in a reserch study; (**C**) Medical researchers treat people like "guinea pigs", (**D**) I completely trust doctors who do medical research.

report based on interview notes and recordings. She characterized the nature of interviewee responses to questions, wherever applicable, as positive/comfortable, mixed/neutral, or negative, and also itemized reasons interviewees gave for their responses. The other author (L.M. Beskow) listened to all recordings and independently characterized the nature of interviewee responses. She also categorized interviewees' reasoning using content codes initially developed based on expert knowledge of the field, and refined over the course of listening to the interviews to ensure the integrity of the categories identified and to ascertain that no new categories were emerging during the interview process. Findings were then reconciled by both authors. Fisher's exact test, a test specifically intended for small sample sizes, was used to make preliminary quantitative comparisons of responses to the brief written survey using STATA version 8.0 (StataCorp LP).

Results

Interviewee Characteristics. The study sample was demographically diverse (Table 1). Responses to the four survey questions assessing trust in medical researchers revealed varying degrees of trust (Fig. 1), although overall, responses tended to indicate neutral feelings or some level of trust, rather than distrust. In this sample, trust did not differ by age, sex, race, education, research experience, or status as a Duke patient, with one exception. Most (75%) interviewees either strongly or somewhat agreed with the statement, ''Doctors who do medical research care only about what is best for each patient.'' There were, however, differences by research experience: 33% of those who had participated in research in the past year disagreed with this statement, compared with only 3% of those who had not ($P = 0.05$).

Purpose of the Biorepository. When asked to describe what the consent form was asking them to do, all but two interviewees mentioned ''research,'' and nearly three quarters correctly mentioned the concept of ''leftover blood.'' Interviewees typically described a biorepository as a place where blood is stored and studied. As one stated: ''It's kind of like a blood bank except that it's not for people who need blood to live, it's for people who need blood to study'' (ID 22).

When asked what kinds of research they thought would be conducted, more than half of the interviewees mentioned research on specific conditions. Cancer, diabetes, heart disease, Alzheimer disease, and hypertension were most frequently cited; other examples included asthma, bird flu, HIV-AIDS, and obesity. Half described research involving DNA or genes. Some mentioned general concepts, such as ''developing new drugs'' and ''things you could find out by testing blood.''

Later rounds of interviews included the question, ''How would you feel if this consent form were asking you to have your blood drawn just to give to the Biorepository?'' Among 22 interviewees asked this question, half said it would pose no problem. Others expressed concerns that included dislike of needles, lack of personal benefit, lack of association with their personal physician, lack of association with a specific study, and inconvenience (Table 2).

Duration of Storage. Almost three quarters of interviewees thought their blood would be kept as long as it was needed, or forever. The remainder generally knew that the consent form made reference to indefinite storage, but had doubts about how long their blood would actually last. About half of these were unsure how long it would last; the other half gave estimates ranging from 3 months to ''25 to 100 years.''

When interviewees were asked how they felt about indefinite storage, more than two thirds reported feeling either positive or comfortable (Table 2). Some cited the option to withdraw or to not participate as the reason they were comfortable. Reservations expressed by those less comfortable included concern for their descendents and unforeseen events at the Biorepository.

Update Contact. Nearly three quarters of interviewees correctly thought they would be contacted once per year to update basic information. When asked what frequency would be reasonable, over half said once per year and about a third said more than once per year, with answers ranging from two to six times per year. Other answers included ''one time only,'' ''never,'' and ''it depends on the length of the interview.''

Medical Record Access. Almost all interviewees thought that personal medical information (e.g., test results, diagnoses, medications, procedures, and biometric data) would be collected from their medical record. Approximately one third mentioned family history information, and several mentioned other kinds of information, such as race, lifestyle information, and health insurance status. A few were unsure what kinds of information would be collected.

More than half of interviewees said that providing access to their medical record would not affect their decision about participating, citing reasons such as altruism and lack of concern about risks (Table 2). Others, however, expressed concerns about confidentiality, changes in health status, and uncertainties about what information would be collected and how it would be used.

In later interviews, those who expressed discomfort about medical record access were asked, ''Are there any ways the Biorepository's procedures could be revised to make you more comfortable?'' Among 10 interviewees asked this question, 6 said they wanted to be asked permission each time. One wanted an ''iron-clad guarantee'' of confidentiality, one wanted to know exactly what was being studied, one wanted to designate certain parts of her medical record ''off limits,'' and one said there were no circumstances under which she would agree to ongoing access.

Withdrawal. When interviewees were asked what kinds of things would cause them to change their minds about participating, a breach of security or a scandal were the most frequently cited reasons: ''If you heard on the news that it got broken into or the samples were stolen. That would probably do it for me... or if I heard on the news that a worker from the place was caught doing something with the samples, nonethical stuff'' (ID 2).

Other common reasons included negative news stories about research in general, changes in health status, excessive or burdensome contact from researchers, and negative responses from peers (Table 2).

Types of Researchers. We asked interviewees about the statement that ''researchers from other universities (other than Duke), the government, and drug or health-related companies'' could apply to study materials stored in the Biorepository. Nearly three fourths were comfortable with the idea of other academic researchers having access to the Biorepository. Frequent themes included ''strength in numbers'' (i.e., allowing other academic researchers access could amplify research benefits), shared goals among researchers, and putting materials to ''good use'' (Table 3). Interviewees who expressed concerns mentioned issues such as the prestige of the university, whether universities outside the United States would have access, and lack of control over research use.

More than half of the interviewees were concerned about government researchers having access to the Biorepository. Several made reference to ''Big Brother.'' Other common themes included misuse of information and government intrusion into private areas (Table 3). Among those comfortable with government researchers, a common refrain was ''research is research,'' no matter who is doing it.

More than half of the interviewees were either positive or comfortable regarding health care industry access to the Biorepository (Table 3). Profit motive was mentioned both favorably and unfavorably; for example, one person seemed more comfortable with the idea of profit-driven research than with research purely for the sake of inquiry, whereas others expressed reservations about the motivations of for-profit researchers.

Contact about Additional Research. Almost three fourths of interviewees were comfortable with being contacted about additional research. Most correctly

Table 2. Representative responses to selected interview questions: collection and storage of specimens/data

How would you feel if this consent form were asking you to have your blood drawn just to give to the Biorepository?
Concerns
Dislike of needles: ''I don't like needles; I'd have to get past that.'' (ID 34)
Lack of benefit: ''At least for blood being drawn for my physician, I know it's going to give me some idea about my health, a condition, that sort of thing.'' (ID 27)
Lack of association with personal physician: ''I don't mind answering questions, but when it comes to giving blood, taking medication, unless my doctor prescribes it, I wouldn't do it.'' (ID 30)
Lack of association with specific study: ''I would want to know more information... Narrow it down so that I know my blood goes to cancer (research).'' (ID 28)
Inconvenience: ''I wouldn't go out of my way to do it. If I'm already at the hospital and I'm sitting there anyways... But not if I was just in and out—I wouldn't even read this (form).'' (ID 33)
How do you feel about the idea that your blood will be kept indefinitely?
Positive or comfortable
''I actually think that's pretty cool keeping your blood forever.'' (ID 1)
''It takes years to get an outcome, so you can't assume you're going to give blood and then within 90 days destroy it if you guys don't have an answer.'' (ID 4)
''I don't think it matters...It said you can always say you don't want them to use it anymore.'' (ID 9)
''I think (indefinite storage) is not a bad idea, because they ask your consent...You can always say no if you don't want to.'' (ID 3)
Uncomfortable
''I would not want it kept after I passed away because then I wouldn't have the option to opt out. It could affect your offspring.'' (ID 33)
''I guess I'm bothered by the 'forever.' If their funding runs out, does that mean that at that point, would everything be destroyed? If all the researchers associated with this decided to leave, my sample is still just sort of sitting there?'' (ID 27)
How does collection of information from your medical record affect your opinion about participating in the Biorepository?
Comfortable
Altruistic motivations: ''It doesn't hurt me, cost me a thing to participate. I want to help.'' (ID 13)
Lack of concern about risks: ''There's nothing there that's harmful, that would be shameful to me.'' (ID 37)
Uncomfortable
Confidentiality: ''It makes me a little bit worried. Once you start letting more and more people get access to your private information it sort of opens up a whole can of worms.'' (ID 5)
Changes in health status: ''There might be something that changes in my medical history that I don't want people to know.'' (ID 16)
Uncertainties about information collected: ''It talks about things like medical diagnoses, but there are a whole lot of things that could be considered a diagnosis that don't necessarily have anything to do with medical research.'' (ID 27)
Uncertainties about research use: ''Sometimes they tell you one purpose but it is really used for something else.'' (ID 31)
What kinds of things would make you change your mind about participating in the Biorepository?
Negative news about research: ''You read some creepy thing that happened in research, not even at Duke, but it would make you think about what if that happened to you.'' (ID 40)
Changes in health status: ''If something happens in their life that they want to seal their medical history, they no longer wanted their medical history to be open.'' (ID 16)
Excessive contact: ''Beginning to feel like it's harassing.'' (ID 13)
Peer opinion: ''Any type of negative fears, like if you told someone you signed up for the Biorepository and they responded negatively.'' (ID 25)

Table 3. Representative responses to selected interview questions: research use of specimens/data

How do you feel about the statement that ''researchers from other universities, the government, and drug or health-related companies'' may apply to study Biorepository materials?
Other universities
Strength in numbers: ''You would think the more research being done would increase the chances of medical breakthroughs.'' (ID 23)
Common goals: ''One facility might have certain researchers in one area, another might have some in another area, or they may have facilities that are somewhat different. But they can all come together as a team, with a common goal.'' (ID 8)
Putting materials to good use: ''I don't care who uses it, as long as they put it to good use.'' (ID 32)
Lack of control over research use: ''I don't like it. There are so many researchers and you don't know what they have in their mind. You don't know what they're doing it for. Some people could be a great scientist, but be doing it for the wrong reasons—who's going to figure that out?'' (ID 31)
The government
Misuse of information: ''Historically, there's always issues of the purpose of the research, how that information may be used, the intentions of the researchers.'' (ID 19)
Government intrusion: ''The government gets into this stuff having to do with terrorism and that gives me the creeps. I don't want the government creeping around in my medical record.'' (ID 40)
Drug or health-related companies
Positive: ''I think drug companies are the ones that should do the research. They're making the drugs.'' (ID 26)
Comfortable: ''I wouldn't have a problem because it might help me out or somebody I know.'' (ID 2)
Profit motive—favorable: ''I'm a little more comfortable with private sector because they're trying to make something to make money, not just experiment for the sake of experiment.'' (ID 5)
Profit motive—unfavorable: ''Maybe I'm jaded, but money has a tendency to drive people to do things they might not ordinarily do when the bottom dollar becomes the bottom dollar.'' (ID 27)
How would you feel about being contacted at a later time to participate in additional research?
Comfortable: ''I have a choice of saying no if it's not something I thought I could do.'' (ID 37)
Uncomfortable due to too much contact: ''I would look at being contacted as an inconvenience. I don't like getting calls during dinner—I would kind of put it in that same category.'' (ID 10)
Uncomfortable due to lack of benefit: ''I wouldn't want to do it for free.'' (ID 8)
In your own opinion, what do you think are the risks involved in taking part in the Biorepository?
Loss of privacy/confidentiality: ''If this information is not protected, it could really cause some serious damage. I would compare it to your social security number.'' (ID 8)
Technological advances: ''If medical science changed, what limits could you have on what type of research could be done?'' (ID 5)
Loss of control: ''It will be there for decades, even after you're dead. It may even affect your descendants or something. Basically, you are losing control over a tiny portion of yourself.'' (ID 40)
Uncertainties about research use: ''Give me a heads up, tell me the progress you are making, what exactly you're doing with the blood. Don't just come and take my blood and that's it, I never hear from you again. That would make me feel even more like a laboratory rat.'' (ID 17)
How important or how much of a concern are these risks to you?
Very important
Legal/financial consequences: ''It would give me more confidence to know that it is just not their word, that there may be criminal penalties or possibly even financial penalties where, if they misuse my information, that I could sue for compensation.'' (ID 10)
Not important
Researcher self-interest: ''I don't think anyone would just purposely put themselves out there to mess up. . .their reputation, when research is their career and that's what they do.'' (ID 4)
Age: ''For me personally, it is not important right now because I am already retired. But for younger person. . .this might be very critical and very limiting.'' (ID 14)
Trust in the research enterprise: ''I don't think a place that's doing research could very well be slack in keeping things confidential. I would trust them.'' (ID 26)
Do you perceive any benefits to participating in the Biorepository?
Long-term personal benefit: ''No direct benefit, but hopefully in the future they can find some sort of solution to a particular disease or condition that I have.'' (ID 14)
Altruism: ''You're aiding research, and for society there's the benefit. But to (me), no benefit whatsoever, other than maybe that would be another thing, when I get up to the Big Gate. It's something good that I did.'' (ID 10)

believed they might be contacted once or twice a year; most also considered this a reasonable frequency. One cited the possibility of opting out of any proposed research as a reason for feeling comfortable about such contact. Concerns included excessive contact and lack of personal benefit (Table 3).

When interviewees were asked what they thought additional research would involve, common responses included giving more blood, participating in a survey or interview, and participating in a clinical trial. However, the most frequent answer was related to selection criteria: more than one fourth of interviewees thought

they would be contacted because of something that had been found in their blood. One person, for instance, said, ''I can't imagine they would contact me unless they saw something in my blood that interested them and they needed more, needed to know more'' (ID 13). Some who expressed this belief felt positively about the prospect of research contact, although others felt negatively: ''I don't think I would like that too much, additional research based on what they found in the samples. Me personally, I'd rather volunteer for studies. I don't want anyone calling me out of the blue because that would make me feel like 'what did you find that makes you want to do the study so much?'' (ID 5).

Table 4. Representative responses to selected interview questions: commercialization and access to research results

What do you think about the prospect that commercial products could be developed?
Positive: ''I think that's excellent. That's a good reason for doing it.'' (ID 20)
Comfortable: ''Well, it's the American way. That's what they would do, with the economic system that we have, that's the way things are distributed.'' (ID 22)
Negative: ''I don't think that's right. I think some of the drug companies could keep the drugs less expensive. If people are willing to participate in studies like that, then they should help the public as much as the people help them.'' (ID 26)
What do you think about the statement, ''You should not expect to share in any of the profits''?
Comfortable
Large number of subjects: ''I'm sure they'll collect a lot of blood samples. They can't give money to everybody.'' (ID 1)
Lack of prior expectation: ''I'm doing this on a voluntary basis. It's understood I'm not going to receive any compensation.'' (ID 23)
Researchers do the work: ''Just because I helped within the study, it's not like I worked in the lab and helped develop the drug.'' (ID 20)
Confidentiality concerns: ''If I'm one of 100,000 people, the check would be for $2. So in order to send me a check for 2$, they would have to access my name, my address, and the more times they access it, the more chances there are for the data to get out.'' (ID 33)
Uncomfortable
Profit should be shared: ''If it's going to help them make a lot of money and with my help they're going to make the money, I feel like I should share in that benefit from it.'' (ID 30)
Uncomfortable, but profit share not expected: ''It's sad but you don't expect it. If my drop of blood helped produce a million dollar drug, it'd be nice to get a percentage, but of course you don't expect it.'' (ID 31)
Benefit sharing at a societal level: ''If it was used for developing any kind of drug, I'd hope the drug would be affordable'' (ID 16).
What do you think about the statement, ''You should not expect to get individual results from research done with your blood''?
Comfortable
Limited research resources: ''I can only imagine if they had to give information to everybody who participated, that'd be a lot of money and a lot of time.'' (ID 1)
Research versus medical care: ''I'm sure they're going to have millions of samples, so they're not going to individually contact each person. It really is not that type of testing anyway. . .it's not like a regular doctor visit.'' (ID 35)
Lack of prior expectation: ''Once I give it, it's theirs, it doesn't bother me.'' (ID 37)
Personal physician would be aware of health problems: ''Prior to (researchers) getting that, I would hope that my doctor would have figured all of that out.'' (ID 25).
Ambiguity of research results: ''Because if they're not absolute, they'll cause another problem.'' (ID 34)
Uncomfortable
Reciprocity: ''If I'm helping you out doing this big study, the least you could do is make one phone call. . .that wouldn't be too much to ask for.'' (ID 17)
Clinical utility: ''I think (the statement) is practical, that I shouldn't expect it. However, I would hope that if there were something wrong with me and . . . there was as easy fix, that somehow there should be a way for that information to get back to my doctors.'' (ID 10)
If researchers discovered something serious about your health, do you think they should let you know?
Reciprocity: ''I would hope so. . . Not only would I be helping by giving them the blood, if they found something I would hope they would help me.'' (ID 39)
Common courtesy: ''Forget the research part of it, it would just be human decency. Even if you're maybe not supposed to, it's just the right thing to do.'' (ID 29)
Clinical utility: ''If it's serious, and it's something that wouldn't ordinarily be detected by symptoms or a physical or a regular check up, then yes, they should.'' (ID 33)
New knowledge: ''Maybe they have newer tests, different tests the average doctor wouldn't have.'' (ID 17)
How important would it be to you to be able to get general news about studies being done through the Biorepository?
Benefit: ''For me that would be like compensation. Not payment, but a compensation—you've helped people, so you get that information back.'' (ID 36)
Fair exchange: ''It would be real important. If I'm going to provide my time, my blood, why not?'' (ID 8)

Risks and Benefits. When asked about risks involved in participating in the Biorepository, most interviewees mentioned loss of privacy or confidentiality. Other concerns included technological advances that might expand the scope of research, loss of control (potentially affecting family members), and lack of knowledge about what uses were being made of specimens (Table 3).

Approximately one fourth of interviewees thought there were no risks involved. Interviewees who mentioned at least one risk were asked, ''How important or how much of a concern are these risks to you?'' About one third considered the risks to be very important (Table 3). One asked whether there were legal penalties or financial recourse for breaches of confidentiality; another felt that no matter how many precautions were taken, ''The bottom line is the trust you put in people to keep their mouths closed and do the right thing. That's all you can do'' (ID 11).

About one third of interviewees believed the risks were not important, citing reasons such as researcher self-interest, age, and trust in the research enterprise (Table 3). One person said she was not concerned because ''Who would really want to know that stuff? Even if they saw it, unless they're a doctor or a researcher, they wouldn't even know what it was'' (ID 13).

No interviewees expected direct benefit, although a few mentioned the possibility of long-term benefit resulting from research done on their biospecimens, and more than three fourths mentioned altruism and/or social benefit (Table 3).

Commercialization. About a third of interviewees felt positively about the prospect that commercial products could be developed through biorepository research; another third were comfortable with the idea (Table 4). About one fifth, however, responded negatively to the idea of others profiting from their specimens or data.

When asked about the statement ''You should not expect to share in any of the profits,'' comments from about two thirds of interviewees suggested they were comfortable. Common themes were the large number of subjects participating, lack of prior expectations, and the fact that the actual work would be done by researchers (Table 4). One interviewee was specifically positive about not receiving a profit share because of confidentiality concerns.

Among those uncomfortable with the statement, a few thought participants should share in profits (Table 4). Most, however, still said a profit share was not expected, and others expressed a desire for more benefit sharing at a societal level. Some interviewees expressed dislike for the presence of the statement itself in the consent form. One thought it ''sounds selfish'' (ID 17); another, who did not expect a profit share, stated: ''That was kind of offensive, given the fact that medications, medical bills are sky high and climbing. I think that was one of the statements that shouldn't be there'' (ID 34).

Access to Research Results. Nearly two thirds of interviewees were comfortable with the statement, ''You should not expect to get individual results from research done with your blood.'' Common themes were acknowledgment of limited research resources, differences in research versus medical care, and lack of prior expectations for receiving individual results (Table 4). Some interviewees thought their physician would already know about any problems with their health, and one expressed concern that disclosing ambiguous research findings might create additional problems.

The remaining third of interviewees expressed concerns about not getting individual results, citing a desire for reciprocity for having rendered assistance, and a desire to be contacted if the findings had clinical relevance (Table 4). One person disliked the tone of the statement itself: ''I would still participate, but I think they could have made that statement sound a little nicer'' (ID 32).

After the first round of interviews, we added the question, ''If researchers discovered something serious about your health, do you think they *should* let you know about it?'' Among 30 interviewees asked this question, over three fourths said ''yes.'' Reasons for doing so included reciprocity, ''common courtesy,'' clinical utility, and the possibility of access to potentially beneficial new medical knowledge (Table 4).

Nearly half of the interviewees thought it would be very important to receive general news about studies being done through the Biorepository. Several thought it would be beneficial or would constitute a fair exchange for having volunteered for a study (Table 4). Many thought it important to determine whether their samples were being put to good use; for example: ''I would like to know what happened. I mean, did it help? I would like to know what they're focusing on, what they're finding out. Just to see the result, to know that this research is contributing to something or someone, helping somebody or society'' (ID 31).

Of the remaining interviewees, about half said access to general news was somewhat important; half said it was not important.

Consent Statements. Most (85%) interviewees said that, if asked, they would allow their blood and information to be stored indefinitely at the Biorepository for use in future research (Table 5). Among the six interviewees who declined or were unsure, privacy concerns were a major factor; five of the six had characterized the risks involved as ''very important.''

Table 5. Consent statements (*N* = 40)

	Yes, *n* (%)	No, *n* (%)	Unsure, *n* (%)
I voluntarily agree that my blood and information can be stored indefinitely at the Biorepository for use in future research to learn about, prevent, or treat health problems	34 (85.0)	4 (10.0)	2 (5.0)
Someone from the Biorepository can contact me once a year to update my personal information	31 (77.5)	6 (15.0)	3 (7.5)
My medical record can be used from time to time to get updated information about my health	24 (60.0)	14 (35.0)	2 (5.0)
Someone from the Biorepository can contact me to tell me about up to two studies each year that involve contact with a researcher	34 (85.0)	5 (12.5)	1 (2.5)

In this sample, there were no differences in responses to the consent statements based on demographic characteristics or on answers to the survey questions about trust in medical researchers, except for the following.

Someone from the Biorepository can contact me once a year to update my information. Most (78%) interviewees indicated that they would say ''yes'' to this statement. There were, however, differences by trust in medical researchers: 100% of those who disagreed with the statement ''Doctors who do medical research care only about what is best for each patient'' said ''no'' or were unsure about update contact, compared with only 16% of those who had agreed or were neutral ($P = 0.01$).

My medical record can be used to get updated information about my health. Most (60%) interviewees said they would agree to this statement, but differences by education emerged: 59% of those with a bachelor's degree or higher said ''no'' or were unsure, compared with 26% of those with less education ($P = 0.05$).

Someone from the Biorepository can contact me to tell me about studies that involve contact with a researcher. Most (85%) interviewees said they would say ''yes'' to this statement. However, 67% of those who disagreed with the statement ''Doctors who do medical research care only about what is best for each patient'' said ''no'' or were unsure about medical record access, compared with 11% of those who agreed or were neutral ($P = 0.05$).

Discussion

Unprecedented advances in biomolecular and informatics technologies are providing new ways to derive more valuable data from human biological specimens (26). Biorepositories are therefore a key resource for accelerating discovery and development of new cancer diagnostic, therapeutic, and preventive agents (1). Realizing the promise of such research, however, depends on maintaining the trust and goodwill of potential participants; thus, participants' understanding of, and reaction to, information conveyed in the informed consent process will be pivotal to the success of the research enterprise.

In this study, we obtained prospective research subjects' perspectives on an array of issues affecting participation in biorepositories within the context of detailed information provided in a consent document. Interviewees seemed to understand the information and voiced a wide range of opinions about it. Even so, majority views emerged on many issues. Considerably more than half of the interviewees were comfortable with unlimited duration of biospecimen storage; periodic contact to update their personal information and to inform them of additional research opportunities; the prospect that commercial products could be developed from the research; and that profits, if any, would not be shared among participants. More than half of the interviewees were willing to provide continuous access to their medical records, although this aspect was a primary concern for others. Interviewees generally accepted the concept of a variety of researchers having access to the Biorepository, as long as their samples and information were being put to ''good use'' and their confidentiality was protected. More than two thirds of participants were comfortable not receiving individual research results as a matter of routine, but many thought they should be informed of findings with serious implications for their health.

At least two overarching lessons can be drawn from these findings. First, the importance of protecting privacy and confidentiality cannot be overstated. Our survey questions intended to assess participants' level of trust in medical research seemed to indicate that the majority of this sample were either neutral or well disposed regarding the trustworthiness of medical researchers. In addition, many interviewees expressed trust in protections described in the consent form and referred to them directly in the context of other questions (generically, ''it's okay as long as they don't get my name''). However, concerns about privacy were nonetheless prominent among reasons given for not participating. Furthermore, the possibility of a breach in confidentiality was foremost among likely motivations for withdrawal. Lack of trust in medical researchers also seemed to play a significant role regarding whether participants said they would refuse additional contact and continued medical record access. Protecting and promoting trust in the research enterprise is therefore essential to fostering widespread participation in biorepositories and to realizing the ultimate goals of biorepository research.

Second, biorepositories must operate in a framework of transparency and accountability. Participants are typically asked to allow their specimens and data to be used for an unlimited time and for unspecified research. Such an arrangement clearly enhances the scientific usefulness of the Biorepository, but entails risks for the participant without any countervailing direct benefits. Our findings suggest that many people are nevertheless willing to take part, and biorepositories' operating procedures should honor this altruism. Rigorous processes must be in place to ensure that samples and data are put to ''good use.'' Biorepositories should devise ways to communicate clearly about the research being conducted and what is being learned.

A significant strength of our study was the diversity of the study sample. Samples for previous studies have tended to be relatively homogeneous, e.g., predominantly white (11-14), predominantly or all female (12, 16), or all older adults (14).

Our study design, which constituted an in-depth ''pre-test'' of the consent form using surrogate subjects, was also novel. Because subjects were asked only hypothetically whether they would take part in the Biorepository, further study of actual participation rates will be needed when the consent form is put into practice. It is reasonable to expect that such rates will be lower. Pentz and colleagues (33) reported that at two health care facilities in Atlanta where cancer patients are routinely asked whether leftover tissue can be stored for research purposes, 73% of patients consented, 9% refused, and 17% took the consent form but did not return it. The opinions collected by our study, however, are useful for informing the development of biorepository policies as well as consent documents and processes.

Although our study sample was diverse, it was geographically limited, with participants drawn from

the Durham, NC area only. Thus, socioeconomic and cultural factors particular to this region might have affected the nature of responses to our questions, and our findings may not be generalizable to all geographic regions.

In addition, our sample size was selected based on our primarily qualitative study design. Thus, we had limited statistical power to detect differences in the relationships among demographic characteristics, trust in medical researchers, and responses to consent statements. Future research could reveal such differences, which may prove useful for refining approaches to informed consent.

Future improvements to the consent template should focus on developing language and consent options regarding new federal policies for widespread data sharing (34) and further clarification of issues surrounding ownership of specimens and data (35, 36). In addition, research is needed on ways to enhance and simplify consent processes to maximize prospective subjects' opportunities to make an informed decision about participating in a biorepository.

Appendix A. Duke Biorepository Consent Template

Researchers are trying to learn more about cancer, heart disease, diabetes, and other health problems. Much of this research is done using human tissue or blood. Researchers often study tissue or blood from people who have health problems and from people who do not.

You are being asked to let some of your blood be stored for possible use in this kind of research. This is because you had blood drawn for medical tests ordered by your doctor. After all these tests are finished, there may be some blood left over. This leftover blood would usually be discarded because it is not needed for your care. If you agree, we would like to keep any leftover blood and some information about your health so it will be available for future research.

Your blood and information will be kept at a central place called the Duke Biorepository (just called the ''Biorepository'' in the rest of this consent form). Important details about the Biorepository are given below. Please read this information carefully and take your time making your decision. Be sure to ask us about anything that does not seem clear.

Some general things you should know about taking part in research are:

- Research is meant to gain knowledge that may help people in the future. You may or may not get any direct benefit from taking part. Taking part may also involve some risks.
- Research includes only those people who choose to take part. You should feel free to talk over your decision with your family, friends, doctor, and health care team.

What is the purpose of the Biorepository?

The purpose of the Biorepository is to collect and store tissue samples (such as blood) and health information for use in medical research. Researchers can do many kinds of studies using these materials. Some may use the samples and information to look for new ways to diagnose, treat, and maybe even prevent or cure health problems. Others may use them to study how genes affect health and disease, or how genes affect response to treatment (genes, which are made of DNA, give the instructions for building all the proteins that make our bodies work). Some of these studies may lead to new products, such as drugs or tests for diseases. (Insert name) is the director of the Biorepository.

What is involved if I decide to take part?

Here is what will happen:

1. We will obtain a leftover sample of your blood.

Your doctor plans to draw some of your blood for medical tests. He or she will give you the results of these tests, which will be used to plan your medical care. Even though your doctor will only take the amount of blood needed for your care, there may still be some left over after all the tests are done. This leftover blood is what we will keep.

2. We will collect some information about you and your health.

First, we will ask you for some basic information. This will include things like your name, age, and racial or ethnic group. We will also ask about your family's health history. If you agree, someone from the Biorepository will contact you no more than once a year to update this information. This will happen for as long as your sample is stored in the Biorepository.

Second, we will collect some information from your medical record. Examples include information about your diagnoses, lab results, medical procedures, and medications. This is because future researchers will need to know if you have any problems with your health. They may also need to know about any treatments you have had and how well the treatment worked. If you agree, this information will be updated from your medical record from time to time. This will also happen for as long as your sample is stored in the Biorepository.

3. We will store your blood and information.

Your blood and information will be kept at the Biorepository along with those from all the other people who decide to take part. There is no limit on the length of time we will keep your blood and information. We will keep them as long as they are useful, unless you decide you no longer want to take part or we close the Biorepository.

4. Researchers may use your blood and information in future research studies.

Researchers can apply to study the materials stored in the Biorepository. A part of your blood and some information about your health might be given to some of the researchers, along with those from many other people. However, we will not give researchers your name or any other information that could identify you without your permission. There are more details about this in the part below called ''How will information about me be kept private?''

Materials stored in the Biorepository will be used mainly by Duke researchers. Researchers from other universities, the government, and drug or health-related companies can also apply to use them. Only skilled

researchers will be allowed to use the samples and information. A research committee at the Biorepository must approve each study. An ethics review will also be done. This kind of review is to make sure that people who take part in research are protected.

5. Researchers may ask to do studies that involve contact with you.

You will not be notified every time your blood and information are used in a study. However, some researchers might apply to do a study for which they would need to contact you. For example, a researcher might want to do a telephone interview with people who gave their blood. If a study like this is approved, someone from the Biorepository will contact you first. We will tell you about the study so you can decide if it is okay to give the researcher your name. If you agree, the researcher will then contact you to tell you more about the study. There will be a new consent process just for that study so you can make your final decision about taking part.

We will make sure not to contact you about more than two studies like these each year. You can also decide, now or later, that you never want to be contacted about studies like these.

What are the possible risks or discomforts?

There are no physical risks to you. The main risk is that someone could get access to the data we have stored about you. If that data suggested something serious about your health, it could be misused. For example, it could be used to make it harder for you to get or keep a job or insurance. There are laws against this kind of misuse, but they may not give full protection.

We believe the chance of these things ever happening is extremely small. However, we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us and we will make every effort to protect them. These efforts are described in the next section.

How will information about me be kept private? Blood samples will be stored in locked freezers in locked buildings. Health information and research data will be stored on secure computers that have many levels of password protection.

Your blood and health information will be labeled with a code number. Your name and anything else that could identify you will be removed and kept in a separate file. There will be a master list that links the code number to your name. This list will be stored on a secure computer with many levels of password protection. Only a few of the Biorepository staff will have access to the list and they have signed a pledge to keep your identity a secret.

Researchers who study your blood and information will not know who you are. We will only give them the code number and not any information that identifies you. The researchers must promise that they will not try to identify you. They must also promise that they will keep the coded materials secure and will not give them to anyone else.

To further protect you, we obtained a Certificate of Confidentiality from the NIH. With this Certificate, the Biorepository cannot be forced to disclose information that could identify you, even under court order, except as explained below.

The Certificate may not be used to keep information from the government that it needs to evaluate federally funded projects or information that is needed by the U.S. Food and Drug Administration. If information is disclosed to such an agency, it is no longer protected by patient privacy regulations (called 'HIPAA'), but it will be protected by other federal privacy regulations. The Certificate does not stop you from giving information about yourself or your involvement in this project.

What are the possible benefits? You will most likely not benefit directly from giving your blood for future research. The main reason you may want to take part is to help researchers make discoveries that will benefit people in the future.

Are there any costs or payments? There are no costs to you or your insurance. You will not be paid for taking part in the Biorepository. Your blood will be used only for research and will not be sold. You should know that research sometimes results in discoveries that may one day have commercial value. For example, discoveries could eventually lead to new tests, drugs, or other products. If this happened, you should not expect to share in any of the profits. Development of new products relies on the study of samples from hundreds or thousands of people, not on any one person.

Will I find out the results of the research? You should not expect to get individual results from research done with your blood. Researchers must study samples from many people over many years before they can know if the results have meaning. The results will not affect your care right now. They will not be given to your doctor and will not be put in your medical record. You can get general news about studies being done through the Biorepository at (insert URL).

What if I change my mind? You can change your mind at any time about taking part in the Biorepository. Just call us at (insert phone number) and let us know. If some of your blood has already been given out for study, it cannot be taken back. Also, knowledge already gained from research using your blood cannot be destroyed. However, we will send you a form so that you can tell us in writing what you would like us to do with any of your blood that remains.

What are my options? Taking part in the Biorepository is completely voluntary. If you choose to take part, you can change your mind at any time. No matter what you decide, now or in the future, it will not affect your medical care. There will not be any penalty and you will not lose any benefits you would otherwise be able to get.

What if I have questions? You should feel free to ask any questions. Your questions should be answered clearly and to your satisfaction. For questions about the Biorepository, contact (insert name, phone number). For questions about your rights as a research volunteer, contact the Duke University Health System Institutional Review Board at (insert phone number). We will give you a signed copy of this consent form to keep.

Statement of consent. The purpose of the Duke Biorepository, the procedures involved, and the risks and benefits have been explained to me. I have asked all the questions I have at this time and I have been told whom to contact if I have more questions. I have been told that I will be given a signed copy of this consent form to keep.

I voluntarily agree that my blood and information can be stored indefinitely at the Biorepository for use in future research to learn about, prevent, or treat health problems.

In addition, I have made the following optional choices.

1. Someone from the Biorepository can contact me once a year to update my personal information.

YES _____ (initials) NO _____ (initials)

2. My medical record can be used from time to time to get updated information about my health.

YES _____ (initials) NO _____ (initials)

3. Someone from the Biorepository can contact me to tell me about up to two studies each year that involve contact with a researcher.

YES _____ (initials) NO _____ (initials)

_____ _____

Signature of Research Subject Date

_____ _____

Signature of the Person Obtaining Consent Date

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

The authors thank Jonathan McCall for editorial assistance and manuscript preparation. We also gratefully acknowledge Drs. John M. Falletta, Geoffrey Ginsburg, Amy L. McGuire, Ross McKinney, and Debra Skinner for their input on earlier drafts of this manuscript. Timothy Flanigan, MA of RTI International, assisted in conducting the cognitive interviews.

References

1. National Cancer Institute. National Biospecimen Network Blueprint. http://biospecimens.cancer.gov/global/pdfs/FINAL_NBN_Blueprint.pdf. Accessed January 20, 2008.
2. Kaiser J. Biobanks. Population databases boom, from Iceland to the U.S. Science 2002;298:1158–61.
3. Collins FS, Green ED, Guttmacher AE, Guyer MS. A vision for the future of genomics research. Nature 2003;422:835–47.
4. Dressler LG. Human specimens, cancer research and drug development. Washington (DC): Institute of Medicine and National Research Council; 2005.
5. Vaught JB, Lockhart N, Thiel KS, Schneider JA. Ethical, legal, and policy issues: dominating the biospecimen discussion. Cancer Epidemiol Biomarkers Prev 2007;16:2521–3.
6. Greely HT. The uneasy ethical and legal underpinnings of large-scale genomic biobanks. Annu Rev Genomics Hum Genet 2007;8:343–64.
7. Roche PA, Annas GJ. DNA testing, banking, and genetic privacy. N Engl J Med 2006;355:545–6.
8. Rothstein MA. Expanding the ethical analysis of biobanks. J Law Med Ethics 2005;33:89–101.
9. Maschke KJ. Navigating an ethical patchwork—human gene banks. Nat Biotechnol 2005;23:539–45.
10. Cambon-Thomsen A. The social and ethical issues of post-genomic human biobanks. Nat Rev Genet 2004;5:866–73.
11. Helft PR, Champion VL, Eckles R, Johnson CS, Meslin EM. Cancer patients' attitudes toward future research uses of stored human biological materials. J Empir Res Hum Res Ethics 2007;2:15–22.
12. Kaphingst KA, Janoff JM, Harris LN, Emmons KM. Views of female breast cancer patients who donated biologic samples regarding storage and use of samples for genetic research. Clin Genet 2006;69:393–8.
13. Chen DT, Rosenstein DL, Muthappan P, et al. Research with stored biological samples: what do research participants want? Arch Intern Med 2005;165:652–5.
14. Wendler D, Emanuel E. The debate over research on stored biological samples: what do sources think? Arch Intern Med 2002; 162:1457–62.
15. McCarty CA, Nair A, Austin DM, Giampietro PF. Informed consent and subject motivation to participate in a large, population-based genomics study: the Marshfield Clinic Personalized Medicine Research Project. Community Genet 2007;10:2–9.
16. Fong M, Braun KL, Chang RM. Native Hawaiian preferences for informed consent and disclosure of results from genetic research. J Cancer Educ 2006;21:S47–52.
17. Schwartz MD, Rothenberg K, Joseph L, Benkendorf J, Lerman C. Consent to the use of stored DNA for genetics research: a survey of attitudes in the Jewish population. Am J Med Genet 2001;98: 336–42.
18. Pulley JM, Brace MM, Bernard GR, Masys DR. Attitudes and perceptions of patients towards methods of establishing a DNA biobank. Cell Tissue Bank 2008;9:55–65.
19. Kettis-Lindblad A, Ring L, Viberth E, Hansson MG. Genetic research and donation of tissue samples to biobanks. What do potential sample donors in the Swedish general public think? Eur J Public Health 2006;16:433–40.
20. Wong ML, Chia KS, Yam WM, Teodoro GR, Lau KW. Willingness to donate blood samples for genetic research: a survey from a community in Singapore. Clin Genet 2004;65:45–51.
21. Code of Federal Regulations. Title 45, part 46, Protection of human subjects. http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm. Accessed January 20, 2008.
22. Code of Federal Regulations. Title 45, parts 160 and 164, HIPAA administrative simplification: enforcement, final rule. http://privacyruleandresearch.nih.gov/pdf/FinalEnforcementRule06.pdf. Accessed January 20, 2008.
23. National Bioethics Advisory Commission. Research involving human biological materials: ethical issues and policy guidance, volume 1. Rockville (MD): National Bioethics Advisory Commission; 1999.
24. Eiseman E, Bloom G, Brower J, Clancy N, Olmsted SS. Case studies of existing human tissue repositories. ''Best practices'' for a biospecimen resource for the genomic and proteomic era. Santa Monica (CA): RAND Corporation; 2003.
25. International Society for Biological and Environmental Repositories (ISBER). Best practices for repositories I: collection, storage, and retrieval of human biological materials for research. Cell Preserv Technol 2005;3:5–48.
26. National Cancer Institute. Best practices for biospecimen resources. http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf. Accessed January 20, 2008.
27. Duke University Health System Institutional Review Board. Policy on research databases and specimen repositories. http://irb.mc.duke.edu/. Accessed January 20, 2008.
28. Willis G. Cognitive interviewing as a tool for improving the informed consent process. J Empir Res Hum Res Ethics 2006;1: 9–23.
29. Willis GB. Evaluation of cognitive interviewing techniques. In:

Cognitive interviewing. Thousand Oaks (CA): Sage Publications; 2005. p. 207–29.
30. Hall MA, Camacho F, Lawlor JS, Depuy V, Sugarman J, Weinfurt K. Measuring trust in medical researchers. Med Care 2006;44: 1048–53.
31. Maxwell JA. Qualitative research design: an interactive approach. Thousand Oaks (CA): Sage Publications; 2004.
32. Greenhalgh T, Taylor R. Papers that go beyond numbers (qualitative research). BMJ 1997;315:740–3.
33. Pentz RD, Billot L, Wendler D. Research on stored biological samples: views of African American and White American cancer patients. Am J Med Genet A 2006;140:733–9.
34. National Institutes of Health. Policy for sharing of data obtained in NIH supported or conducted Genome-Wide Association Studies (GWAS). http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html. Accessed January 20, 2008.
35. Ness RB. Biospecimen ''ownership'': point. Cancer Epidemiol Biomarkers Prev 2007;16:188–9.
36. Dressler LG. Biospecimen ''ownership'': counterpoint. Cancer Epidemiol Biomarkers Prev 2007;16:190–1.

Informed Consent for Biorepositories: Assessing Prospective Participants' Understanding and Opinions

Laura M. Beskow and Elizabeth Dean

Cancer Epidemiol Biomarkers Prev 2008;17:1440-1451.