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WHAT IS OWED PARTICIPANTS IN BIOTECHNOLOGY RESEARCH?

JULIE A. BURGER*

INTRODUCTION

Recent changes in methods and techniques used in genetics-based research have resulted in a call by researchers for large scale biobanks and increased access to existing biobanks. These changes necessitate a reanalysis of duties owed to human subjects of research. In the past, genetics research usually involved examining the genes of people with a particular disease and their families. It required tissue samples from people with a disease and people likely to develop that disease. The participants tended to be people affected by the disease, and they frequently developed relationships with or felt connections to the principal investigator.

Now, improvements in sequencing technology make it possible to compare the entire genomes of tens of thousands of people in order to locate genetic differences between people with specific illnesses and people without those illnesses. Mutations that are associated with heart disease, breast cancer, diabetes and other diseases with a multi-factorial basis have been located using these genome-wide association studies. In addition to a very large number of samples to ensure statistical accuracy, these studies require gathering more than participants’ genetic information and noting whether they have one particular disease or not. Much more information must be collected about each sample from the many thousands of participants because the more information that is gathered about participants’ samples, the more relationships between diseases can be examined and the more types of research can be performed. Many entities, including universities, private companies, and governmental agencies such as the National Institutes of Health, are initiating or expanding their support of large scale genomics-based initiatives. Included in these efforts is a call for the in-

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creased collection of clinical and phenotypic information for each sample, and an increased sharing of the samples.

However, when more information is known about the person who provided a tissue sample, the potential for secondary uses of that sample increases. It also increases the chances that research will be performed beyond the scope of the participant’s consent or that his or her confidential health information will be divulged, especially as samples and information are increasingly shared. When these breakdowns occur, participants may lose trust in researchers and institutions. But participation in research depends on trust; people will not participate in research if they do not trust the researchers, institutions or companies conducting the research.

A longstanding ethical principle governing any research on human beings has been that consent to participate in research must be voluntary. People have the right to not be researched upon without their consent. They have the right to be told that they are participating in research, and to be given any material information about the research that would affect their initial willingness to participate and their willingness to continue their participation in the research. They also have the right to withdraw from further participation in research without penalty. In the past, these principles were based on the protection of bodily integrity and the right to be free from unwanted touching. Applying these principles to non-genetics research appears to be straightforward in certain circumstances. In the testing of pharmaceuticals, for example, a potential research participant must be told the nature of the study, that it is experimental, whether it is a placebo trial and the implications of that type of research, that she can stop participating in the trial at any time, and what the ramifications would be if she stopped participating; if she discontinued her participation, the drug company could no longer force her to ingest the drug.

But what do these principles mean when the research is performed on blood or other tissue that has been removed from the body? Such samples are most valuable if they are linked to identities and clinical information, including whether a person has a certain disease, environmental exposures, and other personal health information. The participants’ tissue contains their genes which can always be linked to a specific individual and the information used to his or her detriment. Yet increasingly policymakers and

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2. E.g., 45 C.F.R. § 46.116(a)(8).
researchers argue that specific consent is not necessary in genetics research or that the use of tissue that does not have a person's name or other information associated with it is exempt from the regulations governing human research. If this is the standard in ethical and research communities, it perhaps is not known to the people who provided the tissue.

The trend in medical research to use large collections of tissue samples and associated information raises questions: What are the duties and responsibilities of investigators and institutions to the people who participate in biomedical research studies? How well do existing laws, regulations and federal agencies protect research subjects when compared to long-standing ethical principles guiding human subjects research? What is likely to be the effect on research if the rights, interests and preferences of people who participate in research are not protected?

I. ETHICAL AND LEGAL PRINCIPLES GOVERNING HUMAN SUBJECTS RESEARCH

A. The Importance of Voluntary Participation in Research

The paramount ethical principle governing any research on human beings is that participation in research must be voluntary. The ethical guidelines governing human subjects research are set forth in the Nuremberg Code, the Declaration of Helsinki, and the Belmont Report. The first principle of the Nuremberg Code, an international standard for research that was developed after Nazi physicians were convicted of research abuses, is that the "voluntary consent of the human subject is absolutely essential." The World Medical Association provides the Declaration of Helsinki to guide physicians and other researchers conducting medical research. It similarly recognizes that human subjects of research must be volunteers. In 1979, a Presidential Commission issued the Belmont Re-

5. See infra Part II.C.
6. NUREMBERG CODE, supra note 1, at 181-82.
9. NUREMBERG CODE, supra note 1, at 181.
10. DECLARATION OF HELSINKI, supra note 7, § 20. The Declaration of Helsinki states that medi-
port, setting forth ethical principles that must underlie biomedical researchers’ conduct, including respecting people as autonomous agents who choose what shall or shall not happen to them.11

The U.S. Congress has deemed it important to provide protections to human research subjects.12 Regulations governing the protection of participants in human research studies have been codified at 45 C.F.R. part 46 (known as the “Common Rule”).13 The regulations provide “minimum” standards of protection for research participants.14 Though the regulations apply only to federally funded research, many research institutions have agreed to comply with the regulations in their non-federally funded research.15 Under the federal regulations, researchers and research institutions must comply not only with the federal regulations, but also with state laws that provide additional protections for research participants.16

Federal research regulations codify the principle that participation in research must be voluntary.17 Participants have a right to be told their participation is voluntary, that they do not have to participate, and that they

11. BELMONT REPORT, supra note 8, §§ B.1, C.1. The National Commission set forth three commonly repeated ethical principles of human subjects research: (1) Respect for Persons (which became informed consent under the federal regulations); (2) Beneficence (that is, risk-benefit assessment); and (3) Justice (addressing equitable selection of subjects). See id. § B.1–3.

The Secretary [of Health and Human Services] shall by regulation require that each entity which applies for a grant . . . for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit . . . assurances satisfactory to the Secretary that it has established (in accordance with regulations which the Secretary shall prescribe) a board (to be known as an ‘Institutional Review Board’) to review biomedical and behavioral research involving human subjects conducted at or supported by such entity in order to protect the rights of the human subjects of such research.

14. 45 C.F.R. § 46.103(b).
15. All institutions that seek to participate in HHS-supported human subjects research must complete a Federal Wide Assurance (FWA) application stating that they will conduct the research in compliance with HHS guidelines and policies. Office for Human Research Protecs., U.S. Dep't of Health and Human Servs., Assurances (Oct. 25, 2006), http://www.hhs.gov/ohrp/assurances/assurances_index.html; see also 45 C.F.R. § 46.103(a). The OHRP maintains a publicly searchable database for approved FWAs and registered institutions. Office for Human Research Protecs., U.S. Dep't of Health and Human Servs., Search the Office for Human Research Protections Database (Current Data), http://ohrp.cit.nih.gov/search/search.asp (last visited Jan. 23, 2009). This database is comprehensive and allows users to search for specific domestic and international institutions, id., but the way the search engine is designed makes it impractical to compile a detailed list of institutions that have an approved FWA.
16. 45 C.F.R. § 46.101(f) (providing that the existence of the federal regulations “does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects”).
17. 45 C.F.R. § 46.116.
can withdraw from the study at any time.\textsuperscript{18} Participation should not be coerced; the potential subjects must also be told that declining to participate will entail no loss of benefits to which they are otherwise entitled.\textsuperscript{19}

Not all people who participate in research are protected by federal or state regulation. There are many private biotechnology firms that conduct non-federally supported genetics and other research that are not required to follow the federal regulations.\textsuperscript{20} Moreover, some private foundations also support a substantial amount of biomedical research.\textsuperscript{21} Only a very small minority of individual states have laws governing human subjects research. This may leave many research participants without federal protection.

Biomedical research nears the $100 billion mark in the United States.\textsuperscript{22} Driving its growth, however, is not just know-how and stick-toitiveness. Research depends on people and their tissue. These people provide pieces of themselves, literally. Their tissue may lead to the next big medical breakthrough and may be worth millions or even billions of dollars. Given such compelling factors, the most important protection to the participants is the ethical mandate and the legal assurance that they cannot be forced to participate in research. Individuals—and their tissue—should not be used for research unless they consent.

When this standard is violated, controversy is likely to follow. Disputes over tissue, the secondary use of tissue provided for another purpose, and sharing samples between researchers are decades old. In the late 1960's, geneticist James Neel and a group of researchers ventured into the Amazon to collect blood from members of the Yanomami Tribe, a secluded group of indigenous peoples living at the border of Brazil and Venezuela.\textsuperscript{23} Like many isolated groups, the Yanomami Tribe is an attractive target for researchers seeking to track genetic markers for certain diseases or study genetic mutation rates.\textsuperscript{24} In Neel's study, researchers told the Yanomami that they would use these samples for a brief medical study on genetic markers of diseases, as well as to study the diseases present in the Ama-

\textsuperscript{18} Id. § 46.116(a)(8).
\textsuperscript{19} Id.
\textsuperscript{22} Between 1994 and 2003, funding for biomedical research nearly doubled (when adjusted for inflation) to reach $94.3 billion. Moses et al., \textit{supra} note 21, at 1336.
According to the Yanomami, researchers said that after the study was complete, the samples would be destroyed or returned. However, over forty years later, the samples collected by Neel's research group are now circulating among several laboratories, even though the original experiments have been completed. Yet the Yanomami tribe never consented to have their blood given to other researchers for other projects. They seek the return of the samples for destruction in accord with their cultural and spiritual beliefs. Similar disputes between researchers and other indigenous people, such as the Karitiana and the Surui peoples of Brazil, have resulted in opposition to the research and created a distrust of researchers.

B. The Importance of Informed Consent to Participate in Research

For consent to be truly voluntary, people must be given sufficient information to make a reasoned decision about whether or not to participate in the study. Consent must be "informed" and the decision must be autonomous. Most genetics studies are not designed to benefit the participant directly, and participating in studies is not necessary for a patient's care. Many researchers even expressly inform participants that they will not provide the participant with clinically significant information they might discover as a result of the research. It is possible, or even likely, that a participant will receive no benefit for participating in the study, and, in fact, may not be able to afford diagnostics or therapeutics (drugs or devices) developed as a result of clinical trials.

25. See Glenn, supra note 24, at A-16.
26. See id. at A-14. In exchange for their participation in the study, tribes such as the Karitiana and the Yanomami were promised medical benefits, including the measles vaccination. Larry Rohter, In the Amazon, Giving Blood but Getting Nothing, N.Y TIMES, June 20, 2007, at A1. However, the vaccinations only exacerbated the measles epidemic in the area because the Yanomami were given a cheap, outdated vaccine. Mann, supra note 23, at 419.
28. See id.
29. Researchers not only discarded the original plan without obtaining the consent of the Yanomami, but they also disregarded the religious and cultural values of the tribe. For example, the Yanomami believe that all parts of a person, including blood, must be destroyed once that person passes away. Id. The Yanomami are now horrified to think that parts of their deceased ancestors are frozen in laboratories across the world. Id. For further discussion of this controversy and ethics in the field of anthropology, see ROBERT BOROFSKY, YANOMAMI: THE FIERCE CONTROVERSY AND WHAT WE CAN LEARN FROM IT (2005).
Informed consent is required even if there is no physical risk to a participant, and even if there is no physical touching. There are risks inherent in participating in genetics research, including psychological harm (for example, if a person finds out she or a family member has a propensity to develop a certain disease). Participants might discover new information about family relationships, such as a different paternity or sibling relationship that is contrary to what they had previously believed. There is the risk that research participants might be discriminated against by employers, educational institutions, and insurers. People have lost their insurance merely by participating in research protocols investigating a particular genetic disease, even if they do not have the genes that cause the disease, let alone the disease itself. Once tissue is removed from a person, the risk exists that research beyond the scope of their consent will be carried out. The risk also exists that a medical professional has an incentive to perform unnecessary procedures to obtain additional tissue for research.

A committee of the National Academy of Sciences on genetics research noted that, because research on tissue presents risks, “It is not ethically or legally acceptable to ask research participants to ‘consent’ to future but yet-unknown uses of their identifiable DNA samples.” Currently, we


34. For example, a physician in California convinced a patient he needed to undergo medical procedures to harvest bone marrow, blood and other tissue from the patient even though his cancer had been cured. Moore v. Regents of the Univ. of Cal., 793 P.2d 479, 481 (Cal. 1990).

35. COMM. ON HUMAN GENOME DIVERSITY, NAT’L RESEARCH COUNCIL, EVALUATING HUMAN GENETIC DIVERSITY 65 (1997).
cannot fully predict research that may one day be possible. Years ago we lacked the technology to undertake many types of genetics research that are common today. For these reasons, a research participant should be provided with even more information about the research than a person consenting to a routine medical procedure or intervention necessary for his or her care. But how the increased call for large numbers of samples can be balanced with participants' right to voluntary and informed consent has yet to be fully determined. Asking for blanket consent to all future uses of the tissue when we do not know what the research will entail and what the risks and benefits are initially seems inadequate.

The federal research regulations preclude research on an individual and on an individual’s tissue without that individual’s informed consent. To protect participants in federally funded research, “[a] human subject is entitled to all material information.” Material information is that which is required for a participant to make a reasoned and informed decision whether to incur certain risks by participating in the research. Information that would affect a potential participant’s willingness to participate is de facto “material,” as it affects the decision-making process. Information that must be provided to the potential participant includes: the type of research that will be performed; a description of risks and benefits to the participant or to others; alternative procedures or treatments; the extent to which confidentiality will be maintained; and information about who to contact should the participant have questions or wish to withdraw from research. Depending on the type of research, material information might also include a statement explaining: that the research entails unforeseeable risks; what the consequences are if a participant decides to withdraw; that significant findings impacting the participant’s decision to continue participation will be provided; and the number of subjects involved in the study.

The federal regulations distinguish between two types of tissue: that which is a byproduct of a medical procedure, such as pathological or diagnostic specimens, and that which is collected specifically for research purposes. As the federal regulations are currently written, research conducted on the former category is considered exempt from the informed consent protections otherwise accorded human subjects in federal research if the specimens are: (1) already existing when the research was underta-
WHAT IS OWED PARTICIPANTS IN BIOTECHNOLOGY RESEARCH?

ken; (2) were not collected for research purposes; and (3) are publicly available or are not affiliated with a patient’s identifying information. Tissue from the latter category is not exempt.

The case of Washington University v. Catalona illustrates the difficult issues raised in this new era of biotechnology research. The defendant in the case, Dr. William Catalona, is an internationally renowned prostate cancer surgeon and researcher. Two decades ago, he started asking his patients if they were willing to let him use their tissue removed during their cancer biopsies and surgeries, their blood, and other bodily materials for his research. Thousands of men and their families provided tissue to be used in Dr. Catalona’s research over the years.

Eventually, Dr. Catalona’s then employer, Washington University, began to realize the financial value of the tissue he had collected, ultimately pegging the figure at over one million dollars. A dispute arose as to whether Dr. Catalona could send samples to a biotechnology company for research purposes without the University receiving financial compensation in return. As the relationship with Washington University deteriorated, Dr. Catalona decided to move his research and practice to another university. Six thousand patients sent forms to Washington University, directing it to send their samples to Dr. Catalona at his new institution.

In response, Washington University filed a lawsuit against Dr. Catalona, seeking a declaratory judgment that it was the owner of the research participants’ samples. In February 2005, the federal district court sua

42. Id. Because a patient’s genetic information is the ultimate identifier, this exemption does not make sense when applied to tissue samples.


44. Id. at 988. For a thoughtful discussion of the Washington University v. Catalona case, see Lori Andrews, Who Owns Your Body? A Patient’s Perspective on Washington University v. Catalona, 34 J.L. MED. & ETHICS 398 (2006). Any portions of the discussion used are used with author’s permission.


46. Catalona, 437 F. Supp. 2d at 988–89.


48. See Transcript of Hearing Vol. 3 at 32–33, Wash. Univ. v. Catalona, 437 F. Supp. 3d 985 (E.D. Mo. 2006) (No. 4:03CV01065SNL). Internal communication revealed that Washington University was unwilling to share the samples for free; it believed the samples Dr. Catalona wanted to share were worth nearly $100,000. Id. at 30–33 (discussing an e-mail from Jon Kratochvil, Business Development Director, Washington University, to Theodore Cicero, Vice-Chancellor for Research, Washington University).

49. See Opening Brief for Defendant-Appellant, William J. Catalona, M.D., supra note 45, at 11.

50. Id. at 12. The forms had been sent to the patients by Dr. Catalona.

51. Complaint for Declaratory Judgment, supra note 47, at 1.
sponte ordered a hearing to be held to determine the sole issue of "[w]ho owns the . . . [b]iorepository materials at issue in this case?" Shortly before the hearing, the judge joined eight research participants as necessary parties over Washington University's objections. At the hearing, the research participants testified that when they agreed to participate in research, they intended to allow Dr. Catalona to use their tissue for his prostate cancer research. They also pointed to the informed consent documents given to them by the University which referred to "the use of your tissue for research" and reiterated the patient's rights to his tissue: the forms used phrases such as "your tissue" and "your blood sample and pathologic specimen," repeatedly acknowledging the men's retention of rights in their own tissue. The informed consent documents promised the men that if they changed their mind about participating in research, they could withdraw from the research and even direct Washington University to destroy their sample.

Washington University countered that the men had given it a gift of their tissue and it, therefore, had acquired ownership of the tissue. Yet not one of the consent forms stated that the research participant was making a gift to the University or that the University would become the owner of the tissue. The University argued that it had the "sole discretion" to use the participants' samples as it wished, in spite of provisions in the contracts to the contrary. However, if Washington University intended to claim it owned the tissue and could use it in any manner, this was material informa-

52. Wash. Univ. v. Catalona, No. 4:03CV01065SNL (E.D. Mo. Feb. 11, 2005) (order setting permanent injunction hearing to commence on April 11, 2005).
53. See Wash. Univ. v. Catalona, No. 4:03CV01065SNL (E.D. Mo. Mar. 14, 2005) (order joining patients as necessary parties). No party seemed to know that the hearing that was to be held less than one month before the research participants were added to the case would be case dispositive. Plaintiff's Memorandum in Opposition to Interveners' Expedited Application for Leave to Intervene at 8, Wash. Univ. v. Catalona, 437 F. Supp. 985 (E.D. Mo. 2006) (No. 4:03CV01065). In fact, when Washington University objected to the research participants' motion to intervene, it suggested that they should be added after the hearing, if at all, to prevent any delay to the hearing. Id. This unusual procedural posture effectively deprived the research participants of their right to conduct discovery—Washington University would not have had to answer any discovery they propounded until after the hearing. Additionally, the research participants were given little time to prepare for the hearing—preparation which would entail reviewing the record and documents already produced by each side during the nineteen months that the case had been pending. Their attorneys also had to schedule and prepare witnesses for the hearing, and prepare cross examination, opening and closing statements, and exhibits.
54. Transcript of Hearing, supra note 48, at vol. 2, 71-72 (testimony of Richard Ward); id. at vol. 1, 158-59 (testimony of James Ellis); id. at vol. 1, 211 (testimony of Thomas McGurk).
55. Appendix of Appellee Volume 4 Trial Exhibits at 812–37, 907, 937, Wash. Univ. v. Catalona, 490 F.3d 667 (8th Cir. 2007) (Nos. 06-2286 & 06-2301); Joint Exhibit Appendix of Appellants at 1, Wash. Univ. v. Catalona, 490 F.3d 667 (8th Cir. 2007) (Nos. 06-2286 & 06-2301).
57. Id. at 994.
58. Complaint for Declaratory Judgment, supra note 47, at 53.
tion that it was required to tell potential participants. It is information that would have affected the participants’ willingness to participate, and the lack of this information hindered their ability to make an informed decision about whether to participate.

After the hearing, the trial judge ruled that the informed consent documents were “inconsequential” and declared that Washington University is the owner of the tissue.59 The United States Court of Appeals for the Eighth Circuit upheld the trial court’s decision without considering the applicable federal regulations.60 It did hold, however, that the research participants retained the right to direct the University to destroy or stop using their tissue.61

What are the implications of the Catalona case for biomedical research and the standards of voluntary and informed consent in research studies? The decision that Washington University is the owner of the tissue provided by the men allows the University to perform stigmatizing or ethically objectionable research on the participants’ tissue, or sell it to a biotech company for profit. This is not what the research participants intended. The patients agreed to participate in Dr. Catalona’s research studies because they wanted to contribute to research that could help their families and future generations avoid the same disease that afflicted them.62

This is exactly the type of altruistic actions that medical research has depended on in the past—people providing tissue to be used for a specific purpose to which they agreed and for which they were promised it would be used. If people learn that they have no right to support the research of their choice, that promises made to them about the research are “inconsequential,” that their tissue can be sold to the highest bidder, and that they cannot stop research on themselves at their discretion, they will not participate in research studies. The negative effects on the institution are obvious: litigation, distrust of researchers, an inability to recruit research participants, bad publicity, and a loss of funding. Clearly this is a lose-lose situation for both individuals and researchers.

59. Catalona, 437 F. Supp. 2d at 998, 1002.
60. Wash. Univ. v. Catalona, 490 F.3d 667, 677 (8th Cir. 2007).
61. Id. at 675 (“The [research participants’] subsequent rights to their biological materials were expressly limited to the option to discontinue participation in the study to avoid answering additional questions, donating more biological materials, or allowing their biological materials to be used for further research.”).
62. All testifying research participants stated that they did not intend to give their tissues to Washington University as a gift; rather, they merely intended to allow Dr. Catalona to use their tissues as part of his research on prostate cancer. Transcript of Hearing, supra note 48, at vol. 2, 71–73 (testimony of Richard Ward); id. at vol. 1, 157–58 (testimony of James Ellis); id. at vol. 1, 211 (testimony of Thomas McGurk).
C. Participants Must Be Allowed to Withdraw from Research

Hand-in-hand with the axiom that participation in research must be voluntary is the principle that research participants must be able to stop their participation in research on their own tissue at their discretion. If research is continued after consent is withdrawn, participation is no longer voluntary. The Nuremberg Code mandates that the human subject must be allowed to bring the experiment to an end. The federal regulations require that the participant must be told that he or she may discontinue participation at any time without penalty, and must be told the consequences of discontinuing the research. In genetics research, continuing research upon participants' samples without their consent is not only inconsistent with the principle of informed consent, but it also could be harmful to the participants' interests or contrary to their religious or other beliefs. The right to withdraw should continue even if the samples or information have been shared with researchers at other institutions or with biotechnology companies. But if the right to withdraw does not mean this, it is material information that must be told to potential participants.

Some organizations have argued that when a research participant exercises his or her right to withdraw from biomedical research, the researchers can take the person's name off the tissue sample and continue to use it. In Catalona, for example, the participants were promised that they could withdraw their consent at any time. The trial court held that this meant if a participant changed his mind about participating in research, Washington University retained the right to strip his name off his sample and continue to use it. But the participants argued this is contrary to the letter and the spirit of voluntary and informed consent. On appeal, the court of appeals recognized the research participants' option of disallowing their biological materials to be used for future research.

64. 45 C.F.R. § 46.116(a)(8) (2007).
65. Id. § 46.116(b)(4).
66. See, e.g., Brief for Amici Curiae Cornell University et al. as Supporting Plaintiff-Appellee at 6, 25, Wash. Univ. v. Catalona, 490 F.3d 667 (8th Cir. 2007) (Nos. 06-2286 & 06-2301).
69. Wash. Univ. v. Catalona, 490 F.3d 667, 675 (8th Cir. 2007).
People's attitudes regarding the storage of their tissue and the possibility of future research being undertaken on their samples reflects the importance of informing potential participants what will be done with their tissue should they choose to withdraw from the study. Potential research participants are concerned about what is done with their tissue after the research they consented to is completed. A survey conducted of 100 healthy adults found that 42% said they would want to be informed if their tissues were going to be stored after donation. Thirty-five percent of respondents expressed a desire to be consulted if future research was to be undertaken on stored their tissue samples.

Another study queried participants in a long-term research project tracking mental disease in the general population regarding their willingness to participate in an additional phase of the research by contributing a blood or buccal (cheek swab) sample. Since these individuals were willing to participate in such a long-term project regarding a sensitive medical diagnosis (mental illness), one might expect that this group would be more willing to provide samples for research. Yet, over one-quarter of the total participants either refused to provide a sample or would not consent to unlimited use of their genetic specimens.

Consent forms given to research participants frequently offer different options for the uses of their tissue—for example, whether the institution can share the tissue with other institutions, whether it can use the tissue in future research without additional consent, or whether the person would like to be recontacted for permission. In a study analyzing the responses on different variations of National Institutes of Health consent forms between 2000 and 2002, almost one-fifth of participants given the option between being recontacted before their tissue was used in the future or authorizing all future research chose to be recontacted. When participants were given the option between refusing all future research, authorizing all future research, or being recontacted before future use, 26% chose to be recontacted. These figures are even higher for people who had not already

71. Id.
72. Briana Mezuk et al., Participant Characteristics That Influence Consent for Genetic Research in a Population-Based Survey: The Baltimore Epidemiologic Catchment Area Follow-up, 11 COMMUNITY GENETICS 171, 171–72 (2008). In that study, 83% of participants consented to provide either a blood or buccal (cheek swab) sample. Id. at 172–74.
73. Id. at 173–74. The genetic tests specified in the consent forms were associated with dementia, diabetes, depression, and cardiovascular disease. Id. at 173.
75. Id. at 654.
agreed to participate in research on tissue but were being asked about their potential participation. This indicates that even a sizable number of people who are willing to participate in future research still want to retain both control over their tissue and the ability to make a contemporaneous choice.

D. Participants Cannot Be Made to Waive Certain Rights

Waivers of liability are common in consent forms for medical procedures. But for certain economic, ethical, moral, financial, and other public policy reasons, people cannot be forced to—and indeed are not allowed to—give up certain rights. Research participants similarly cannot be required—or even asked—to give up certain rights. The federal regulations recognize this by prohibiting research subjects from waiving either their legal rights to redress for negligence or their legal rights to their tissue. 45 C.F.R. § 46.116 provides:

No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

As interpreted by government agencies, “legal rights” include the participants’ rights in their tissue, such as property rights or the right to stop others from using it. A plain reading of this section, giving due import to the comma after “legal rights” which separates that phrase from “negligence,” supports a conclusion that it was meant to prohibit more than just waivers of negligence.

The Office for Human Research Protection (OHRP), the agency charged with enforcing the federal regulations and protecting participants in federally supported research, has provided research institutions with examples of forbidden exculpatory language, including: “By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.” In contrast, acceptable language under 45 C.F.R. § 46.116 includes: “By con-

76. Id.
78. 45 C.F.R. § 46.116 (2007).
79. “[T]he right to exclude others [is] ‘one of the most essential sticks in the bundle of rights that are commonly characterized as property.’” Dolan v. City of Tigard, 512 U.S. 374, 384 (1994) (quoting Kaiser Aetna v. United States., 444 U.S. 164, 176 (1979)).
senting to participate, you authorize the *use* of your bodily fluids and tissue samples for the research described above." The interpretation of the exculpatory language prohibition by the OHRP comports with the U.S. Food and Drug Administration's (FDA) interpretation of the exact same language. The FDA has stated that the term "donation" is prohibited in informed consent form language (and even in accompanying informational brochures) because it impermissibly suggests that the research participant is waiving a legal property right in the tissue. Many institutions have agreed to abide by the OHRP and the FDA's interpretation of this prohibition on exculpatory language.

Subsequent to the *Catalona* decision, the University asked the OHRP to review the trial and appellate courts' opinions and the language used in the University's informed consent documents. The OHRP confirmed that language in informed consent documents requesting individuals waive legal rights they have in their tissue is exculpatory.

Although institutions have no need to own participants' tissue, one reason they might prefer to do so is because it gives them more latitude with the samples. If this is forbidden by the federal regulations and by ethical standards, institutions and researchers owe participants a duty to not assert ownership claims or to ask participants for more than the *use* of their tissue.

82. *Id.* (emphasis added). The OHRP has enforced this regulation against universities who use forbidden language, such as language requiring participants to "give up your property rights that you may have in your bodily fluids, substances, or tissues." Letter from Carol J. Weil, Compliance Oversight Coordinator, Div. of Human Subject Prot.s., Office of Human Research Protections, to John C. McDonald, Chancellor/Dean, La. State Univ. Health Sci. Ctr. Shreveport (Jan. 25, 2006), http://www.hhs.gov/ohrp/ohrpltr/yr06/jan06a.pdf. In deciding the *Catalona* appeal, the Eighth Circuit ignored this rule and declined to review the University's use of improper language in its informed consent documents. See Wash. Univ. v. Catalona, 490 F.3d 667, 675-76 n.7 (8th Cir. 2007).


85. Letter from Ivor A. Pritchard, Acting Dir., Office for Human Research Protections, to Samuel L. Stanley, Jr., Vice Chancellor for Research, Wash. Univ. Sch. of Med. 2a, 5a (Nov. 29, 2007) (on file with the author). The University tried to use the letter as a concession on the OHRP's part that examples it has given as exculpatory language are just examples and not actually binding. See Brief for the Respondent in Opposition at 23-24 n.5, Catalona v. Wash. Univ., 128 S.Ct. 1122 (2008) (Nos. 07-521 & 07-525). In doing so, the University glossed over the fact that the OHRP had unequivocally stated that the language was forbidden, that it would enforce the prohibition against such language in the future, and that it had ordered the University to remove such language from any forms it might currently be using. See Letter from Ivor A. Pritchard to Samuel L. Stanley, Jr., *supra*, at 5a.
tissue. If it is not forbidden, then a consensus should be reached and potential participants must be given this material information before agreeing to participate.

E. Participants Must Be Given the Right to Choose the Studies in Which They Will Participate

As part of informed consent, people must be told that they are participating in a research study and about the nature of the research that will be undertaken.\textsuperscript{86} People have strong attitudes towards the research they will participate in and what can be done with their body parts and tissue. For example, some people oppose embryonic stem cell research and would not provide their tissue to be used in such research. Other people oppose the patenting of human genes for religious, moral or other reasons, and would not participate in research that would lead to this result. In a survey of 100 healthy adults in the United Kingdom, 82% of respondents indicated they would be willing to donate tissues samples for cancer research; 65% would be willing to donate tissues for research on genetic disorders; 59% would consent to research on general knowledge of tissues or for testing different medicines; and only 26% would be willing to donate tissues for research on genetic cloning.\textsuperscript{87} A survey of Jewish persons found that the participants were the most likely to be willing to have their stored DNA samples used in research into preventable medical illnesses (87%), mental illnesses (87%), and alcoholism (85%), and the least likely to agree to studies about frugality (60%) and homosexuality (72%).\textsuperscript{88} If people cannot choose what research studies are performed on them and on their body parts, and if they cannot stop research, they will simply stop joining research studies.

Pure common sense, as well as ethical and legal standards, tells us that just because a person consents to one type of research or research by a particular researcher, the person would not necessarily consent to a different type of research, or to research undertaken by a different researcher, at a different institution, or at a company. In a study examining the genetic causes of heart disease, 29% of African American participants indicated that they did not want their tissue shared beyond the confines of the specific research protocol to which they consented.\textsuperscript{89} One obvious solution might

\textsuperscript{86} 45 C.F.R. § 46.116(a)(1) (2007).
\textsuperscript{87} Goodson & Vernon, supra note 70, at 136.
\textsuperscript{88} Marc D. Schwartz et al., Consent to the Use of Stored DNA for Genetics Research: A Survey of Attitudes in the Jewish Population, 98 AM. J. MED. GENET. 336, 336 (2001). The authors noted that the sample size was small and cautioned against making broad generalizations based on the results of the survey which had been conducted years earlier.
\textsuperscript{89} NATIONAL HEART, LUNG, AND BLOOD INSTITUTE, NATIONAL INSTITUTES OF HEALTH,
seem to be to simply exclude people who do not agree to the unfettered sharing of their tissue. However, excluding these individuals could lead to skewed or biased results. Additionally, it could be coercive to decline to enroll people who want to participate in studies but will not consent to the sharing of their tissue in outside research. Consent must be sought under circumstances that “minimize the possibility of coercion or undue influence.”  

Telling people they can only participate if they agree to tissue and data sharing may place an undue and improper influence on their autonomous decision making.

It is likely that people participate in studies of diseases that are important to them; for example, the family of a person who has diabetes may agree to participate in diabetes studies, just as they may choose to donate money to the American Diabetes Association, instead of to some other cause. People may choose to participate in studies they believe will help them, their families, or others afflicted with the same disease. A study undertaken to examine breast cancer patients’ views and interest in receiving information about research studies found that, while “a few” participants expressed hope that the research undertaken on their tissue samples would benefit them, “more” participants responded that they donated their tissue in order to help others—either women in general or their family members—suffering from breast cancer. Biotechnology research depends on the altruistic intent of people who provide their time and their tissue to be used in research. Taking away their right to choose their causes could reduce participation in studies.

Another reason a participant may want to consent only to certain studies is that certain types of research may be stigmatizing to a person or to

90. 45 C.F.R. § 46.116.

91. A group of African Americans surveyed identified three main reasons for participating in a medical research study: (1) to help themselves or a loved one; (2) altruism; and (3) financial compensation. Vicki S. Freimuth et al., African Americans’ Views on Research and the Tuskegee Syphilis Study, 52 SOC. SCI. & MED. 797, 797, 803–04 (2001). A group of parents considering enrolling their children in a genetics research study identified three main reasons for allowing their children to participate in the genetic study: (1) to help their own child; (2) to help others; and (3) to contribute to scientific knowledge. Lynn Gillam et al., Enhancing the Ethical Conduct of Genetic Research: Investigating Views of Parents on Including Their Healthy Children in a Study on Mild Hearing Loss, 32 J. MED. ETHICS 537, 537, 539 (2006).

92. Kimberly A. Kaphingst et al., Views of Female Breast Cancer Patients Who Donated Biologic Samples Regarding Storage and Use of Samples for Genetic Research, 69 CLINICAL GENETICS 393, 394–95 (2006). The study does not quantify the data “a few” and “more.” The twenty-six participants in the study were female breast cancer patients who had previously consented to donate blood or tissue samples for breast cancer research at the Dana-Farber Cancer Institute in Boston. Id. at 394.
the particular group to which the person belongs. Recent studies have tried to link genetics to race or ethnic groups, thus creating the possibility that some groups will become known as a greater insurance risk, less healthy, or more expensive to treat. Research studying the genetic causes of mental illness, alcoholism, or criminal propensities are other examples of such studies. In 2006, a researcher made the controversial claim that he had discovered a “warrior” gene in the Maori Tribe, which allegedly makes them more aggressive, more violent, and more likely to be criminals. The Maori and others protested this claim as stigmatizing and scientifically questionable.

Particular groups of patients are already mistrustful of established medical institutions. Certain minority groups, as well as women, whose rights have been abused or ignored for years, or who have not been given the opportunity to benefit from research, have been shown to be less likely to participate in human research in general, and genetics research in particular. Taking this one step further, it is even possible that people will not seek medical care if they cannot trust that their tissue will not be taken and used in medical research against their will. This is especially a concern for individuals in minority groups, who have already been shown to be less likely to seek medical care for existing conditions due to apprehension about what an institution will do with their tissue.

In a survey of over 1000 Vanderbilt patients, only 76% of African American respondents (as compared to 93% of Caucasian respondents) felt that leftover blood and tissues taken during routine medical procedures should be used in anonymous medical research. African American par-

94. Bennetts & McLean, supra note 93; Maori ‘Warrior’ Gene Linked to Aggression, supra note 93.
95. E.g., Giselle Corbie-Smith et al., Attitudes and Beliefs of African Americans Toward Participation in Medical Research, 14 J. GEN. INTERNAL MED. 537, 541 (1999).
96. ANDREWS, supra note 33, at 77–79, 90–92.
97. Corbie-Smith et al., supra note 95, at 540; Freimuth et al., supra note 91, at 803.
100. Jill M. Pulley et al., Attitudes and Perceptions of Patients Towards Methods of Establishing a DNA Biobank, 9 CELL TISSUE BANKING 55, 55, 59 (2008). In spite of the fact that over a quarter of the African American survey participants did not agree that blood samples drawn during routine clinical care should be retained and used for research that is linked to medical records that have had certain identifiers removed, Vanderbilt has implemented a plan to amass 300,000 blood samples in five years for genetic research. Id. at 55. Vanderbilt will not seek individual patient consent for the collection;
participants in the long-term mental health study were 50% less likely to consent to storage of their sample in a biobank for use in unspecified future genetic research.\(^{101}\) A study that surveyed cancer patients in Indiana produced similar results, with members of minority groups less likely to allow tissue samples to be used in unspecified future research, especially if that research investigated other diseases or other types of cancer than their own.\(^{102}\)

There are also groups that will not consent to certain types of research.\(^{103}\) In one case, a researcher collected blood samples from members of the Havasupai Tribe, a Native American group that lives an isolated existence in the Grand Canyon.\(^{104}\) According to members of the tribe, the researcher told the tribal elders she was undertaking diabetes research on the samples, a disease that affects the tribe in a much higher percentage than in the general population.\(^{105}\) But the researcher had already filed grant applications for schizophrenia research when she allegedly made this representation.\(^{106}\) The samples were shared with researchers at other universities and were used not only for schizophrenia research, but also for origins and migration studies, which conflicted with the tribe’s religious beliefs.\(^{107}\) The tribe and its members filed a lawsuit against the researcher and her university.\(^{108}\) Other Native American groups have indicated their support for the

rather, it will "widely publicize" the project and patients must affirmatively opt-out. Id. Overall, almost 5% of those surveyed were decisively opposed to the research, and 16% were skeptical. Id. at 61. A survey conducted by Vanderbilt researchers prior to implementation of the DNA Databanking project found that only 32% of patients recalled seeing informational posters that were placed in phlebotomy areas to provide information about the program and how to opt out. Jill M. Pulley et al., Evaluation of the Effectiveness of Posters to Provide Information to Patients About a DNA Database and Their Opportunity to Opt Out, 8 CELI TISSUE BANKING 233, 235–36 (2007).

101. Mezuk, supra note 72, at 173.


103. For a discussion of the need for group consent see Debra Harry, Indigenous Peoples and Gene Disputes, 84 CHI-KENT L. REV. 147 (2009).

104. See Rex Dalton, When Two Tribes Go to War, 430 NATURE 500, 500 (2004).

105. Id. at 500–01.

106. Id. at 501.


Havasupai people, and one tribe has declined to participate in a study for which federal funds had already been approved because of the Havasupai situation. It could take decades to rebuild trust and reestablish relationships with groups such as this, if at all possible. Thirty years after the Tuskegee Syphilis Study, some African Americans link a distrust of researchers to the infamous study, saying research participants should expect dishonesty and nondisclosure from investigators.

Federal agencies, in an attempt to address these complex issues, have created plans that might not completely take people's opinions about their tissue and the use of it in research into consideration.

II. SHARING OF INFORMATION, DATA AND SAMPLES: TWO FEDERAL PLANS

The National Institutes of Health (NIH) and the National Cancer Institute (NCI) have each created plans for data, information, or sample sharing in research they support. Analyzing how these policies evolved, the public response to the proposed policies, and the duties potentially owed to research participants in the context of these federal policies illustrates the extent to which the rights of participants are protected; where shortcomings might exist; and where protections might go beyond those which are required, serving as an example for other research projects.

A. NIH GWAS Data Sharing

In the spring of 2006, the NIH released its proposed policy for data sharing in genome-wide association studies (GWAS). GWAS involve searching for genetic variation across the entire human genome and attempting to link genetic traits with observable traits (such as weight) or a disease. It varies from non-GWAS research, which typically looks at a

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110. Giselle Corbie-Smith et al., Attitudes and Beliefs of African Americans Toward Participation in Medical Research, 14 J. GEN. INTERN. MED. 537 (1999).


112. Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Associa-
WHAT IS OWED PARTICIPANTS IN BIOTECHNOLOGY RESEARCH?

small portion of the genome. Tissue samples are not all that is needed for GWAS studies; researchers also need clinical and phenotypic data about the person who provided the sample to find associations between genetic variation and a physical characteristic or disease manifestation.\textsuperscript{113} The NIH solicited comments from the public, policy organizations, and investigators, and held a public town hall meeting in November 2006.\textsuperscript{114} The final policy\textsuperscript{115} was issued on August 28, 2007, and became effective on January 25, 2008.\textsuperscript{116}

The NIH has stated that one of the main goals of its GWAS data sharing policy is to facilitate broad and consistent access to data through the creation of a centralized data repository.\textsuperscript{117} The agency views increased access to data used in gene studies as a means to identify common genetic factors that influence health and disease, to improve predictability of disease, and, ultimately, to advance personalized medicine.\textsuperscript{118} Under the final policy, all investigators who are funded by the NIH to conduct analyses of genetic variation are expected to submit descriptive information about their studies to a centralized repository at the NIH.\textsuperscript{119} Although the data repository will not include actual physical specimens (those will be maintained by the original researchers), it will include the resulting analyses of thousands of single nucleotide polymorphisms and related data.\textsuperscript{120}

General information about the studies, including the protocol, questionnaires, study manuals, variables measured, and any other supporting documentation, will be available to the public and other researchers through the GWAS data repository.\textsuperscript{121} Genotypic and phenotypic data...
(such as blood pressure, weight, and psychiatric information); exposure information (such as drug use and environmental factors); pedigree information (including information about familial relationships); and analyses of such data, including genetic associations with observable traits, will be made available to researchers and investigators at both domestic and foreign academic and commercial institutions through a controlled access process. Some of the information in the database will be available online.

The NIH acknowledged that during the public comment period, many respondents expressed concern over the highly sensitive nature of the information that the data repository will contain and the potential for this data to be used to identify people or to create social stigmatization or discrimination. Respondents noted that it is becoming increasingly possible to connect genetic information with individual observable traits (such as height and weight), with the risk of developing certain diseases, or even with certain behaviors. In its final policy, the NIH attempted to address these concerns by providing detailed information about how submitted data is to be anonymized. Under the initial proposed policy, the submitting institution was required to remove the names and other “identifying information” from the data, replacing it with a random, unique code that was to be held by the submitting institution. Under the final policy, this requirement is described as “de-identifying” all data submissions. “De-identified” means: (1) the identities of research participants cannot be easily ascertained or associated with the data by the repository staff or by secondary users; (2) the eighteen identifiers stated in the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule are removed;
and (3) the institution submitting the data has no knowledge that the remaining information could be used to identify the research participant.¹³⁰

1. Voluntary and Informed Consent to Participate

By setting up the GWAS data sharing paradigm so that the collecting institution codes the information before submitting it, institutions can take the position that explicit informed consent is not necessary. The OHRP has endorsed this position, determining that the GWAS repository does not constitute human subjects research under 45 C.F.R. part 46 because the information would be de-identified and used in research studies other than that for which it was originally collected.¹³¹ This means that, according to the OHRP and its interpretation of 45 C.F.R. part 46, IRB review or certification and informed consent considerations would not have been required for the GWAS studies.¹³²

Yet the attempted de-identification of information raises problems. Because genetic information is inextricably linked to the person from whom it came, it is never possible to completely anonymize or de-identify genetic data.¹³³ For example, I could fairly easily obtain a DNA sample from someone by offering him or her a cup of coffee or by picking up a piece of gum he or she threw out. The DNA contained in the person’s saliva on the cup or in the gum could be sequenced for very little money and then compared to research results. Or I could have my own genes analyzed and compare them to sequences available on the Internet to determine information about any of my relatives who had participated in genetics research, and my relatives (known or unknown) could do the same to me.

¹³⁰ Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), 72 Fed. Reg. at 49,295 & n.6.

¹³¹ NAT’L INSTS. OF HEALTH, supra note 122, at l n.1. The NIH has stated that a data set of genetic information and limited phenotype information is not “identifying” information because the data set is only limited information and there is hardly any risk that someone can look at it and discern the identity of the research participant, especially without a comparison sample. Nat’l Insts. of Health, Town Hall Meeting on a Proposed Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), (NIH video broadcast Dec. 14, 2006). This may be a distinction without a difference. Without a comparison list or database, my health plan number, medical record number, or even Social Security number cannot be used to track me down. And other information, such as my address, is not even uniquely mine. No one, however, has my exact genes.

¹³² NAT’L INSTS. OF HEALTH, supra note 122, at 1 n.1.

¹³³ Zhen Lin et al., Genomic Research and Human Subject Privacy, 305 SCIENCE (SPECIAL ISSUE) 183, 183 (2004).
When the research subjects are members of a small group, or when data includes pedigree information, it is possible to trace the data back to individuals. Even if a person’s name is not included, information such as date, birth location, or zip code, can be used to find a person’s name. It might one day be possible to predict the last name of the man a genetic sample came from by looking at the Y chromosome. And databases and records are not immune to attacks from hackers. The broader the access to data and information, the more likely a security breach can occur. Information contained in databases may reveal the presence or absence of disease, the likelihood of developing a disease, environmental exposure, and medical history that could be used to discriminate and could reveal harmful information about family relationships (for example, paternity) or health status.

While the NIH has stated that “the GWAS database does not currently involve human subjects research,” and although it recognizes that the OHRP does not classify the research as human subjects research, the NIH still requires some level of consent and IRB review. According to the NIH policy, submitted data should be accompanied by a certification from the submitting institution, stating that it has reviewed and approved the submission to the GWAS. The final policy states that data submitted to the repository must be accompanied by a certification from the responsible IRB or other Institutional Officials certifying that the identities of the re-

135. Frequent incidences of theft, carelessness, computer hacking, and inadvertent disclosures make it difficult to ensure that private information is truly secure. See Privacy Rights Clearinghouse, A Chronology of Data Breaches, http://www.privacyrights.org/ar/ChronDataBreaches.htm#Total (last visited Jan. 29, 2009) (reporting data breaches involving sensitive personal information since January 2005, with over 200 million records maintained by government and private entities accessed by unauthorized persons during that time period). Breaches have occurred not only at banks, universities, health care entities, and private companies, but also at government agencies such as the U.S. Department of Veteran’s Affairs, the National Institutes of Health, the Internal Revenue Service, and the Department of Transportation. See Larry Greenemeier, Security Breach: Feds Lose Laptop Containing Sensitive Data—Again, SCI. AM., Mar. 25, 2008, http://www.sciam.com/article.cfm?id=security-breach-lost-laptop (describing security breaches at General Electric, Fidelity Investments, the VA, the IRS, and the DOT, as well as a March 2008 incident in which an NIH employee’s laptop containing the names and personal information of 2500 research participants was stolen).
136. NAT’L INSTS. OF HEALTH, supra note 122, at 11; see also Nat’l Insts. of Health, Town Hall Meeting on a Proposed Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), (NIH video broadcast Dec. 14, 2006). (indicating that GWAS data-sharing does not constitute human research because the data that will be submitted is coded by the submitting investigator and, therefore, is a “secondary use” of the data).
137. NAT’L INSTS. OF HEALTH, supra note 122, at 1 n.1.
138. Request for Information (RFI): Proposed Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), 71 Fed. Reg. 51,629, 51,630 (proposed Aug. 30, 2006). Under the initial guidelines, an IRB would have provided a certificate to the NIH, specifically noting that inclusion of the data in the GWAS repository is consistent with the research participant’s initial informed consent and identifying any uses of the data that are specifically excluded in the informed consent. Id.
search participants will not be disclosed. Moreover, under the final policy, the certification must assure that an IRB reviewed and verified that submission to the data repository is consistent with the informed consent of the research participants; that the researcher’s plan for de-identifying the data is consistent with the standards outlined by the final policy; that it has considered risks to individuals, their families, and groups or populations associated with the submitted data; and that genotype and phenotype data were collected in a manner consistent with the Common Rule.

In the final policy, the NIH acknowledges that there are informed consent concerns regarding submitting data to the repository from both studies undertaken after the policy was implemented ("prospective studies") and studies which collected samples and data or conducted research before the policy was implemented ("retrospective studies"). The NIH expects that for prospective studies in which GWAS are conceived within the design of the study at the time the research participants provide informed consent, researchers will disclose to the participants that their genotype and phenotype information "will be" shared with other researchers through the data repository.

For retrospective studies in which data that has been previously collected is to be provided to the data repository, the NIH expects that the institution submitting the information to the data repository will ensure that the study materials are "appropriate for submission," and gives individual IRBs broad discretion in determining whether submitting data is "consistent with" the terms in the original consent documents signed by the participants. It is up to the submitting institution and its IRB to determine if additional informed consent is required from research participants before the information is submitted to the data repository.

In determining whether data submission to the NIH central repository

139. Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), 72 Fed. Reg. 49,290, 49,295 (proposed Aug. 28, 2007).


141. See Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), 72 Fed. Reg. at 49,293.

142. Id.; see also Nat’l Insts. of Health, supra note 122, at 10.

143. Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), 72 Fed. Reg. at 49,293.


145. Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), 72 Fed. Reg. at 49,293.
is "consistent with" an original consent form, the IRB must consider the scope of the consent form. Submission may be considered appropriate if: the consent form discusses the broad benefits of the research, rather than benefits to the specific individual; it discusses the risks associated with genetic research and risks consistent with data-sharing in GWAS; representations in the consent form are consistent with GWAS policies on returning research results to individual patients; it discusses methods of privacy protection that are consistent with NIH GWAS policies; and it discusses whether a subject may withdraw consent in language that is consistent with NIH GWAS policies. If data is acceptable for submission, the certification to the NIH must list the types of research the data may be used for according to the consent given by the participant. The NIH recognizes that submitting pre-existing data or samples may require seeking additional consent from research participants, and it may consider requests for funding to obtain this additional consent.

In this way, the NIH has provided admirable steps towards addressing certain consent issues. Yet for retrospective studies, the policy might not provide enough guidance to IRBs to determine if additional informed consent is required. And, it is unlikely that any previous research contemplated the broad data sharing now required by the NIH, so material information—such as the risks associated with having a participant’s data shared in this manner—probably was not disclosed. Therefore, it is possible that no retrospective study obtained informed consent for the sharing of data and for future studies using the information.

Additionally, it does not appear that institutions will necessarily give potential participants the option of participating in research but not having their data and information shared beyond the study confines. The NIH may decline to fund projects for which broad consent for data-sharing has been refused by participants. In this way, the policy might effectively be both overinclusive and underinclusive, because participants might be prevented from participating in research if they do not want their samples shared. On the other hand, they might be involuntarily participating in research for which they gave no specific consent.

147. Id. at 12.
148. Id. at 10.
149. Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), 72 Fed. Reg. 49,290, 49,293 (proposed Aug. 28, 2007).
151. See id. at 1.
2. The Rights to Withdraw from Research and to Choose What Studies to Participate or Not Participate In

Under the final policy, people might not have the option of withdrawing their data and information from the studies. The policy allows submitting investigators and their institutions to request removal of data on individual participants from the data repository if research participants decide to withdraw their consent.\(^\text{152}\) Data that has already been distributed to other investigators for approved research, however, will not be retrieved, even if a research participant withdraws his or her consent.\(^\text{153}\) In this way, people cannot effectively withdraw from research. This is consistent with the OHRP's opinion that the data sharing is not human subjects research.

Similarly, it appears that it would not be required that participants be given the option of choosing which types of research they participate in, although it has been suggested that a form of tiered consent be utilized. Perhaps participants would choose to participate in a study searching for genetic causes of obesity, but would not participate in a study of the genetic causes of bipolar disease.

For retrospective studies, the submitting institution is given the responsibility of ensuring that consent is "consistent with" the scope of the consent originally provided by the person. The IRB must consider whether information sharing was precluded; whether certain types of research were specifically excluded; whether research was limited to a certain location or type of disease, and whether the consent specified how long data could be stored, or who could conduct the research.\(^\text{154}\) In making determinations, the IRB must also consider whether commercial uses are precluded, whether there are cultural concerns with sharing information, whether the information was obtained from a child, or whether consent was obtained by proxy.\(^\text{155}\) If data is acceptable for submission, the certification to the NIH must list the types of research the data may be used for according to the consent given by the participant.\(^\text{156}\) Each of these factors will certainly be relevant to determining if the sharing is consistent with the original consent. Nevertheless, "consistent with" is a vague term that could easily be interpreted too loosely or too stringently, and it is not clear how much weight each of these considerations should be given.

\(^{152}\) Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), 72 Fed. Reg. at 49,293; NAT'L INSTS. OF HEALTH, supra note 122, at 8.

\(^{153}\) Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS), 72 Fed. Reg. at 49,293; NAT'L INSTS. OF HEALTH, supra note 122, at 8.

\(^{154}\) NAT'L INSTS. OF HEALTH, supra note 122, at 11–12.

\(^{155}\) Id. at 13.

\(^{156}\) Id. at 12.
Some individuals will likely feel that these types of data sharing policies are acceptable, while other people may object. In a study of seeking to determine peoples' preferences towards differing levels of consent by interviewing individuals who recently participated in an epilepsy gene study, eleven of fifteen respondents stated that it was "very or extremely important that they be informed" when their information was shared with other researchers. Furthermore, thirteen of fifteen participants felt that it was very or extremely important to have "general control over who could access and use their DNA." 

Yet people do not necessarily object to genetics research, and may in fact view it very positively, especially depending on the nature of the study. In a Swedish study, of those surveyed, 77.2% had a positive attitude toward genetic research regarding the mapping of the genome, 85.3% had a positive attitude toward research designed to develop disease risk assessment tools, 91.0% had a positive attitude toward research into diagnostic tools and 92.5% had a positive attitude toward genetic research for the development of new treatments. The proportion of respondents who were undecided ranged between 6.6% and 18.9% depending on the purpose of the research, and those who held negative views ranged from 0.9% (regarding new treatments) and 3.9% (regarding genome mapping).

Another study found a difference between U.S. individuals' general support for a large scale genetic study and their willingness to actually participate in the study. Eighty-four percent of those surveyed felt that the study either definitely (25%) or probably (59%) should be done but willingness to actually participate varied from 51% to 73% depending on the details of the proposed study. A survey that aggregated the data from thirty studies conducted in the U.S and abroad came to conclusion that "people want to control whether their samples are used for research and that most are willing to contribute samples." With such widely diverse views and statistics, the main certainty is that these studies present issues

158. Id.
160. Id.
162. Id.
that are difficult to address.

3. Epilogue

Eight months after its data sharing policy went into effect the NIH removed genetic information from internet databases available to the public.\textsuperscript{164} Recently released research had demonstrated that new DNA analysis methods could be used to determine whether an individual’s genetic sample were present in a sample that might contain DNA from as many as one thousand people.\textsuperscript{165} Previously, it had been widely accepted that it would not be possible to identify a person when a sample contained DNA from many people or when data that resulted from analyzing the genetic makeup of many people were pooled or presented in a summary-level fashion.\textsuperscript{166} The new research laid that theory to rest, and fortunately the NIH reacted quickly by pulling aggregate genetic data from its publicly available databases.\textsuperscript{167}

B. NCI Best Practices for Biospecimen Resources

With an annual budget of several billion dollars, the National Cancer Institute is the agency responsible for the federal government’s cancer research initiatives. In 2004, a report for the National Cancer Advisory Board showed substantial differences in the way biorepositories are managed across the NCI.\textsuperscript{168} The study revealed that “NCI-supported biorepositories are not optimized in terms of operational, legal, and ethical policies and procedures, nor are they coordinated to provide a unique resource value.”\textsuperscript{169} In response to these findings, the NCI established a committee to


\textsuperscript{166} Id. at 9.

\textsuperscript{167} NAT’L INSTS. OF HEALTH, supra note 164, at 1. Before the information was taken down from the NIH’s website, it was downloaded at least 140 times. Jason Felch, DNA Profiles Blocked from Public Access, L.A. TIMES, Aug. 29, 2008, at 31.

\textsuperscript{168} First-Generation Guidelines for NCI-Supported Biorepositories, 71 Fed. Reg. 25,184, 25,184 (proposed Apr. 28, 2006).

\textsuperscript{169} Id.
advise it and to make specific recommendations on policy and operational issues with respect to NCI-supported biorepositories and tissue and data sharing.\footnote{170. NAT’L CANCER INST., BEST PRACTICES FOR BIOSPECIMEN RESOURCES 1 (2007), http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf.}

As a result of the committee’s work, the NCI has released its \textit{Best Practices for Biospecimen Resources} (the “Best Practices”), which is to be followed by NCI-supported biorepositories on a voluntary basis.\footnote{171. \textit{Id.} § A.2.} The Best Practices were released in June 2007, after approval by the National Cancer Advisory Board. Prior to writing the Best Practices, the NCI issued \textit{First-Generation Guidelines for NCI-Supported Biorepositories} (the “Guidelines”), for which it requested public comment.\footnote{172. First-Generation Guidelines for NCI-Supported Biorepositories, 71 Fed. Reg. at 25,184.} The NCI received sixty-one responses from academic institutions, professional societies, private industries, foundations, advocacy groups, and governmental agencies.\footnote{173. NAT’L CANCER INST., BEST PRACTICES FOR BIOSPECIMEN RESOURCES 2 (2007) (unpublished draft, on file with author).} According to the NCI, cancer centers and biorepositories provided the majority of the comments, but because the comments are not publicly available, it is not known how many patient rights groups commented, how many organizations that commented had commercial interests in the way biorepositories are run, or what the content of the comments was.\footnote{174. \textit{Id.}}

As with the NIH’s plan for data sharing in GWAS studies, in some ways the NCI’s plan might not fully protect the interests of people who participate in research, and yet it has made changes to its proposal that are beneficial to research participants.

1. Voluntary and Informed Consent to Participate

As with its predecessor document (the Guidelines), NCI’s Best Practices addresses\footnote{175. \textit{Id.}} the need for voluntary and informed consent for participation in research. Yet, unlike in the Guidelines, the Best Practices states that informed consent might not be necessary, even for human subjects research, if the research is exempt under 45 C.F.R. § 46.101(b), or if an institutional review board grants the research a waiver under § 46.116(c)–(d).\footnote{176. \textit{Id.}} Thus, after the commentary period, it appears as though the NCI might be adopting a view that certain research is exempt from the regulations governing human subjects research, or that informed consent can be
waived. However, neither of the regulatory provisions cited by the NCI are applicable to tissue that is collected for research protocols. 45 C.F.R. § 46.101(b)(4) creates an exemption to the informed consent regulations for research that is conducted on existing pathological or diagnostic specimens if the specimens are not linked to the patients' identities.\textsuperscript{177} Samples collected for research purposes are not already “existing,” at least with respect to the study for which they were collected. They also were not collected for the detection of disease, so they do not satisfy the latter part of the exception. 45 C.F.R. § 46.116(c) is inapplicable because it covers research regarding public benefits (such as welfare),\textsuperscript{178} and § 46.116(d) only applies when the risk to the participant is minimal,\textsuperscript{179} which is not the case in genetics research.\textsuperscript{180}

Although when it had originally drafted the standards, the NCI had contemplated providing biorepositories with a sample consent template, which could have been adapted to conform to relevant state laws and policies and for approval by the appropriate IRB,\textsuperscript{181} the Best Practices does not contain a sample consent form. The NCI suggests that, as part of informed consent, research participants should be able to select general types of research for which their biospecimens may be used, including future studies.\textsuperscript{182} Both in the model informed consent attached to the Guidelines\textsuperscript{183} and under the Best Practices (which does not have a sample informed consent document, but which does give examples of consent options),\textsuperscript{184} participants would be given tiered options for their participation; for example, the consent form could first ask whether the participants' tissue could be used in unspecified cancer research, and second, whether their tissue could be used in studies of other diseases, such as “diabetes, Alzheimer's disease or heart disease.”

But both the Guidelines and the Best Practices seem to ignore a third category of research—research that is potentially objectionable to some people, such as research into mental illness, addictive tendencies, or criminal behavior. A participant may not want to provide tissue for research that

\begin{footnotes}
\item[178] Id. § 46.116(c).
\item[179] Id. § 46.116(d).
\item[182] Id. at 25,184; NAT’L CANCER INST., supra note 170, § C.2.2.7.
\item[184] NAT’L CANCER INST., supra note 170, § C.2.2.7.
\end{footnotes}
offends his or her religious or moral beliefs, as has happened with indigenous people, religious sects, and certain minority groups. Such was the situation for the Havasupai. The tribal members consented to providing their tissue for use in diabetes studies, but objected to the unfettered use of their tissue in research on mental illness and research that contradicted their beliefs about their origins. Similarly, many people object to the patenting of human genes. They would choose not to participate in research that leads to gene patents.

Participants may find the tiered consent for future or non-specified research suggested by the NCI to be inadequate to ensure informed consent to research because it is broadly worded; asks people to give away their rights; and asks people to consent to future research, the risks of which are unknown. Both the prior NCI Guidelines and its subsequent Best Practices note that obtaining informed consent from human research subjects for the collection and storage of biospecimens and for their use in future studies is difficult because the specifics of future research may be unknown when the specimen is collected. Not only is the exact nature of future research difficult to contemplate because it is not known what technology will exist in the future, but the exact risks of participating in this research are unknown and impossible to predict. This is one reason participants must be allowed to effectively withdraw from research in which they no longer wish to participate.

2. Withdrawal of Consent and Discontinuation of Participation

Both the NCI Guidelines and the subsequent NCI Best Practices recognize participants’ right to withdraw from research. The Guidelines discuss the participants’ retention of the power to withdraw their consent during the “analysis phase of identifiable private information.” Under the NCI’s earlier Guidelines, if a research participant did, in fact, withdraw his or her consent, then the individual biospecimen contained in the biorepository would be withdrawn from the biorepository and attempts would

185. Dalton, supra note 104, at 500–01.
187. First-Generation Guidelines for NCI-Supported Biorepositories, 71 Fed. Reg. at 25,194; see also NAT’L CANCER INST., supra note 170, § C.2.2.7.
be made to retrieve any sample of that specimen that has already been distributed. The NCI recommended that once consent was withdrawn, the biospecimen samples should be destroyed or stripped of all direct and indirect identifying information.\textsuperscript{190} It stated that this latter option should be included in the initial informed consent form.\textsuperscript{191}

As with the NCI Guidelines, the subsequent NCI Best Practices states that the “[i]nformed consent documents should highlight the human subject’s ability to discontinue participation and describe what will take place should this occur.”\textsuperscript{192} But the Best Practices appears to handle the recall of already disseminated samples differently. Under the Best Practices, if a participant discontinues participation, samples that have been transferred need not be recalled.\textsuperscript{193} However, the biorepository is “ethically obligated” to notify recipients of the tissue that the participant withdrew consent.\textsuperscript{194} Then, the recipient investigator would be required to withdraw the participant’s tissue from research if the biospecimen were individually identifiable.\textsuperscript{195} The collecting institution and the recipient investigator are given three options: (1) stop using the individually identifiable specimens and private information (which includes medical record information); (2) remove the individually identifiable information and eliminate private information; or (3) destroy the sample and information.\textsuperscript{196} The NCI Best Practices contains a provision similar to the Guidelines reminding investigators to be aware of cultural issues and to return the sample to the person it came from or properly destroy it as appropriate.\textsuperscript{197}

The final Best Practices thus has standards in place that would allow research to continue on a participant’s tissue even after a participant specifies that she is discontinuing participation. First, the NCI does not require that samples be recalled from recipient investigators, even if the collecting institution knows which coded sample belongs to the participant. It makes sense that a participant’s sample cannot be withdrawn from research if his or her name has been irretrievably unlinked from the sample and there is no way to locate it; coded samples, however, are a different story. Regardless of whether the recipient investigator has the code, the information in the

\textsuperscript{190} Id. at 25,194.
\textsuperscript{191} Id.
\textsuperscript{192} NAT’L CANCER INST., supra note 170, § C.2.2.9.
\textsuperscript{193} Id.
\textsuperscript{194} Id.
\textsuperscript{195} Id.
\textsuperscript{196} Id.
\textsuperscript{197} Id.; NAT’L CANCER INST. FIRST-GENERATION GUIDELINES FOR NCI-SUPPORTED BIOREPOSITORIES 24, (2006).
code can be readily ascertained by the collecting institution. Next, the NCI’s Best Practices allows the receiving researcher to remove the participant’s identity and continue to use the sample. Tissue contains uniquely identifiable DNA, so it is never possible to completely de-identify it.\(^{198}\) And, allowing tissue to be used after a person withdraws consent means that tissue from the person is being used in research without his or her consent. The participant might not realize he or she can never effectively withdraw from research.

The NCI Best Practices illustrates how even governmental agencies have interpreted the regulations designed to protect the rights of individuals in a manner that may not comport with what the individuals might prefer, while at the same time providing important protections that courts and other institutions have overlooked.

**CONCLUSION**

Evidence demonstrates that people do have strong preferences about what is done with their tissue after it is removed from their body. They care about who conducts the research, what type of research is undertaken, whether their samples are going to be shared with other institutions or biotech companies, and the length of time their sample will be stored. People also tend to be interested in knowing what the financial incentives for conducting the research are, whether their physician or the person collecting the tissue has a personal financial stake in their participation, and whether the study is funded by a company or pharmaceutical company.\(^{199}\) But disclosing this information need not make researchers fret that participation will decrease; disclosing this information may actually make people more likely to agree to participate because they feel they can make a reasoned decision about whether the particular potential conflict of interest worries

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199. In a study of Swedish participants, a significant minority (18.7%), said that their decision to participate in research would be affected by whether funding was provided by a private company versus a public or independent source. Kettis-Lindblad et al., *supra* note 159, at 435. But this information does not necessarily prevent people from participating. In a survey of Americans with chronic illnesses, results revealed that most potential research participants wanted to be informed about potential conflict of interest even though they still would want to participate. S.Y.H. Kim et al., *Potential Research Participants’ Views Regarding Researcher and Institutional Financial Conflicts of Interest*, 30 J. MED. ETHICS 73, 76 (2004). For example, 81% of potential research participants with heart disease would want to know if the study received funding from the company that manufactures the drug being studied but only 2% of respondents indicated that they would not participate in the study. *Id.* at 76. In fact, 46% of respondents indicated that they would be more likely to participate in the trial, citing reasons such as, “I would feel better about it if it was a well known company funding the project.” *Id.* at 76, 78.
them. Yet there is a value to asking people even if the answer is “yes.”

Allowing individuals to make decisions about research will help maintain trust in researchers and research institutions. Trust is an important factor affecting a person’s willingness to participate in research. Some patients are more willing to consent to tissue banking and unspecified future research if the institution enrolling the patient is a community hospital or private practice rather than a large academic research institution. Other people may decide to participate in research based on the recommendation of a trusted physician. A recent study found that respondents who indicated that they trusted medical researchers were significantly more likely to agree that they felt “very positive” about genetic research. But levels of trust can vary depending on the reputation of the institution or individual researchers. Potential participants who are less trusting of medical researchers are more likely to want their permission sought for future research on their tissue samples.

Genetics-based research holds many promises for the future—the detection of genetic propensities to certain diseases, and the better prevention and treatment of diseases. Research depends on people willing to participate in research studies. There is a recent trend to find ways to argue that ethical and legal protections that were created to protect people who participate in research should be interpreted in a way that might ultimately undermine the research enterprise. If this trend continues, and if institutions and governmental agencies decide to ignore evidence about how people feel about the use of their tissue in research, research may suffer as people become increasingly unwilling to participate or demand that their tissue not be used in future studies. True transparency in the research system and adherence to the legal and ethical principles that underlie the research system should be encouraged as a means for greater participation in research.

201. Thomas Malone et al., High Rate of Consent to Bank Biologic Samples for Future Research: The Eastern Cooperative Oncology Group Experience, 94 J. NAT’L CANCER INST. 769, 770 (2002).
204. Malone et al., supra note 201, at 770.