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Biographical Note – Lori Andrews

B.A., Yale College, J.D., Yale Law School. Lori Andrews has been involved in setting policies for genetic and reproductive technologies both in the U.S. and abroad. She has been an advisor on genetics, nanotechnology, and reproductive technologies to United States Congress, the World Health Organization, the National Institutes of Health, the Centers for Disease Control, the federal Department of Health and Human Services, the Institute of Medicine of the National Academy of Sciences, and several nations including the emirate of Dubai and the French National Assembly. Andrews is the author of ten non-fiction books and three novels. She uses her fiction to discuss the policy issues she addresses as a lawyer and scholar. Currently, Andrews is a Distinguished Professor of Law at IIT Chicago-Kent College of Law and Director of the Institute for Science, Law & Technology (ISLAT).

Assessing Values to Set Policies for Consent, Storage, and Use of Tissue and Information in Biobanks

By Lori Andrews, J.D.¹

The range of human tissue sources available to researchers is extraordinary. There are brain tissue banks, breast tissue banks, blood banks, umbilical cord banks, sperm banks, and tissue repositories for studying AIDS, Alzheimer’s, other mental illnesses, and aging. Over 282 million archived and identifiable pathological specimens from more than 178 million individuals are being stored in the United States alone.² At least 20 million new specimens are added each year. Some specimens are unlinked from names; others carry patient names or codes that allow
personal identification. Yet patients and research participants frequently do not know that their tissue and medical information is being compiled, stored, shared, or used. Between newborn screening, routine medical visits, specialized research biobanks, forensic DNA banks, and so forth, virtually everyone in an industrialized nation has their tissue on file somewhere. Thus, everyone has a stake in the policies that are created about tissue and data use in research. On the other hand, with new genetic research strategies and the possibility of linking electronic medical records, the opportunities for important research to be undertaken are unparalleled.

Research institutions, biotech companies, and government research agencies are increasingly utilizing large databases containing individuals’ tissue, genomic information and associated medical records and phenotypic information. The amount of information associated with each sample is increasing, and pressures to keep the samples linked (even if coded) to the patient’s identity rest on the alluring potentials for research. As noted by Garrath Williams and Doris Schroeder (2004), “in both pharmacogenomics and population genetics, the integration of genetic and clinical data is deemed essential, and donors’ health care and/or lifestyle data is to be input into the bank on an on-going basis.” The promise of genomics has been described as being restricted only by the “rate-limited step” of access to samples with associated clinical information (Hakimian and Korn 2004, 2500).

Initially, it was believed that privacy concerns could be met by de-identifying the data and tissue. But recent scientific developments indicate that it is possible to identify tissue sources using as few as 30 single nucleotide polymorphisms (Lin, Owen and Altman 2004; McGuire and Gibbs 2006; Homer et al. 2008).

The goal of this chapter is to evaluate the individual and societal values that should be considered when researchers, institutions, government agencies, advocacy groups and
policymakers determine consent, storage, and use policies with respect to biobank data and tissue samples. The chapter analyzes 1) individual level data from existing attitudinal studies to discern the factors that influence people’s decisions about participation in research and use of their data and samples and 2) social level data from legislation and court cases.

**Legal and Ethical Issues**

With the evolution of genetic research, institutions and researchers are calling for greater access to a larger number of tissue samples and related medical records and are collaborating with researchers at other institutions and in industry (GAIN Collaborative Research Group 2007). As a result, research institutions, medical and scientific organizations, and government agencies are struggling to develop appropriate informed consent and data access policies (Hakimian and Korn 2004; Ness 2007; Greely 2007). In the United States, the issue has attracted the attention of state legislatures and courts. Individuals have sued researchers, asserting that their rights of privacy and self-determination have been infringed when researchers compile or access tissue samples and information without their consent.

The key ethical and legal issues around biobanks involve the initial collection of tissue, the subsequent decisions about uses, and the linking of an individual’s medical information to his or her samples. The areas of privacy and informed consent are especially sensitive policy issues. The norms of science over the past century sometimes have assumed that scientific progress has required that patients or their tissue be used in research endeavors without informed consent. In many instances, when the research protocol was later publicized, trust in science has been diminished. In some instances, scandals have resulted, and the researchers involved have been subjected to civil lawsuits or even criminal prosecution. Court actions have been filed not only in the famously egregious cases, but in cases where the research involved an early use of a new
technology without sufficient information\textsuperscript{9} or even researchers’ access to tissue samples.\textsuperscript{10} It is thus crucially important that now, as researchers seek increased access to biobanks and related medical data, appropriate policies be developed. This will forestall later scandals, loss of trust, loss of funding, and possible prosecution.

Under standards for both informed consent to medical care and informed consent to research, information that is \textit{material} to the person’s decision-making must be disclosed in advance. Various studies, statutes, and cases provide information about what factors are material to individuals and therefore what information should be disclosed to research subjects in connection with biobanking. The studies also provide guidance for the development of storage and use policies.

Over 40 published studies provide data about how people feel about the use of their tissue in research and about participation in research studies in general. Some studies analyze people’s preferences about the type of research they will participate in. Other studies analyze the factors that people consider when they decide whether or not their tissue should be used in research. The type of data contained in the studies consists of the results of surveys, questionnaires, focus groups, and analysis of existing or recently-obtained informed consent forms containing tiered or blanket consent. The study subjects include patients, participants in research, potential participants in research, and members of the general public from various countries.

These studies provide individual level data—descriptions of what factors people take into consideration in determining whether to participate in research and whether to allow their tissue or data to be used in research. How do we know, though, that the rationales for potential decision-making about biobanks that people give in these studies illustrate their underlying values? We can put the data into context by analyzing social level data—international treaties,
legislation, and court cases that indicate what values people consider important when determining policies in analogous areas, such as access to health information, genetic information, private facts, or commercialization of medical information or private facts.

**Analysis of Studies of People’s Attitudes Towards Participation In Research, Use of Their Medical Information In Research, and Use of Their Tissue In Research**

Using this individual and social level data, my colleagues at the Institute for Science, Law & Technology and I identified certain factors that are relevant to people’s decisions about whether to participate in research (or to have their tissue or data used in research).

The ability to choose the type of research their sample or data will be used in. Numerous studies indicate that agreement to permit use of one’s tissue in one type of research project does not indicate that the person would be willing to participate in another type of project (Mezuk, Eaton and Zandi 2008; Kettis-Lindblad et al. 2005). For example, in one survey, 92.5% of people said that they had a positive attitude toward research on tissue for the development of treatments, but fewer (77.2%) had a positive attitude toward genetic mapping research (Kettis-Lindblad et al. 2005, 434). In another study, researchers found that 82% of survey respondents would be willing to donate tissue samples for cancer research; 65% would be willing to donate tissue samples for research on genetic disorders; 59% would be willing to donate tissue samples for research on general knowledge of tissues or for testing different medicines; and only 26% would be willing to donate tissue samples for research on genetic cloning (Goodson and Vernon 2004, 137).11 In another study, nearly 90% of respondents were willing to consent to genetic research on preventable medical illnesses (i.e., heart disease) and mental illnesses (i.e., schizophrenia) (Schwartz et al. 2001, 339).12 On the other hand, approximately 70% of respondents were willing to participate in genetic research on homosexuality, and only
approximately 60% of respondents were willing to participate in genetic research related to the character trait of frugality (Schwartz et al. 2001, 339).

On the legislative level in the United States, states have enacted laws protecting their residents who might participate in human research studies. In explaining the purpose of its statute, the California legislature noted that past research abuses lead to the Nuremberg Code and the Declaration of Helsinki which set forth ethical principles governing research, but are not codified in American law. At least four states have enacted laws that provide comprehensive requirements for human subjects research; others focus on protecting specific populations, such as people with disabilities. For example, California enacted a statute to protect human subjects that includes an “experimental subject’s bill of rights,” which provides that people must be told the nature and purpose of the experiment, that they have the right to withdraw from participation, and the identity of the entity funding the research.

In the United States, there are at least 11 states that have laws preventing genetic testing of people without their consent. South Dakota and Florida require informed consent, even when the testing is done in a research context.

At the federal level, research regulations require that, in federally-funded research, extensive disclosures must be made to the proposed research subject and subjects must be told that they can withdraw at any time. Yet the federal office enforcing these regulations presumed that, if the research was undertaken on a de-identified tissue sample, consent would not be necessary. There are two difficulties with that approach. Many people do care what is done with their tissue samples. And, it is no longer possible to de-identify the samples.

Assurances about anonymity, privacy and the linking of associated information. In one tissue banking study, over one third (37%) of the people were concerned about privacy issues
(Helft et al. 2007, 18), compared to 40.3% who were not at all concerned (Helft et al. 2007, 18). Promises of anonymity and privacy are important to a small but significant proportion of potential participants. The type of information (such as medical records or demographic data) that will be associated with a person’s tissue affects their willingness to participate in research.

One survey found that 86% of respondents would contribute an extra linked blood sample for genetic research (Kettis-Lindblad et al. 2005, 435). However, among patients who were undecided or responded that they would not provide a blood sample that would be linked to their medical records, 28.3% would contribute if the sample was anonymous (Kettis-Lindblad et al. 2005, 435). Respondents in another tissue banking study were slightly more likely to prefer that their sample be de-identified if it is to be used in research on diseases other than their own type of cancer (Helft et al. 2007, 19). However, far fewer people expressed a willingness to consent to donating a linked sample obtained from their newborn child (Davey et al. 2005, 47). In a newborn screening study, anonymity was considered very important, with 90% of parents indicating that de-identification of the newborns’ samples was a priority (Davey et al. 2005, 47).

Fewer people are willing to contribute tissue specimens if their samples will be linked to medical records. In one study, 61.8% of those surveyed would not want researchers to look at their medical records without first obtaining permission, 4.3% stated that their medical records should never be used in research, and only 33.9% said that researchers could look at their records without prior consent (Hoeyer et al. 2004, 226). Since genetic research often involves access to medical records, more people may be unwilling to participate in genetic research if they are aware that their medical records will be accessed (Hoeyer et al. 2004, 228).
This value is in keeping with the legislative enactments and cases that protect people’s medical, genetic, and other private information. Nearly every state has enacted some type of medical privacy laws that provide different degrees of protection for people’s information.\textsuperscript{21}

The applicability of the research study to them or to their loved ones. People are more likely to participate in research and allow the use of their samples in research if the study involves a disease that affects them, their family, or people close to them. For example, in a study which asked people about their willingness to participate in biomedical research, of those surveyed who had a close family member or friend with an illness, 58\% were willing to participate in medical research studies. Only 39\% of those who did not have a family member or friend with a serious illness were willing to participate in medical research studies. Even among people who said they would not participate in research, a significant number said they would change their mind if they had the disease being studied (Trauth et al. 2000, 31-32).

Similarly, statutes recognize the unique nature of a family relationship. The medical privacy laws of some states have exceptions for disclosures to family members.\textsuperscript{22} We can take from that an indication that, generally, people would want their tissue used in ways that help relatives.

Whether their sample will be stored. Preliminary analysis of studies demonstrates that some people want information about whether their sample will be stored and potentially used in the future. In one study, 42\% of respondents wanted to be informed if their tissues were to be stored beyond the time required for diagnosis, and 35\% wanted to be consulted if additional research was to be undertaken on stored tissue in the future (Goodson and Vernon 2004, 136).

People have initiated lawsuits when researchers or health care professionals have stored samples without their consent. For example, in Minnesota, blood samples were taken from
newborn babies, without the consent of their parents, to be tested for various disorders, stored, and used for research.\textsuperscript{23} A group of families filed a lawsuit against the state’s Department of Health, claiming that the department violated Minnesota’s genetic privacy statute (which includes an informed consent provision for collecting genetic information) by permitting research on blood samples from their newborn babies without the parents’ consent.\textsuperscript{24}

In California, the state has set up a system to conduct research towards understanding and preventing birth defects which includes collecting and storing pregnancy blood samples for future use in research.\textsuperscript{25} Informed consent is required.\textsuperscript{26} A New Mexico statute prohibits the retention of genetic information without the individual’s informed written consent.\textsuperscript{27}

Whether their samples and data will be shared with other researchers. Participants in research, especially people of color, have opinions as to whether they want their samples and data to be shared with other researchers. In one study examining the genetic causes of heart disease, 29\% of African Americans indicated they did not want their tissue shared beyond the confines of the specific research protocol they were agreeing to participate in.\textsuperscript{28} Particular groups of patients are already mistrustful of established medical institutions. Certain members of minority groups, as well as women, have been shown to be less likely to participate in human research in general, and genetics research in particular (McQuillan et al. 2003). It is even possible that people will not seek out 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 members of minority groups, who have 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 (Rapp 1998).

**Trust in the researcher or research institution.** Potential research subjects will be less willing to participate if they do not trust the researcher or institution. Already, one university has
had to return a major grant from the United States government to study an Indian tribe because another university had used tissue from a different tribe without specific consent. Decades after the Tuskegee syphilis study ended, where the natural course of the disease was studied by not giving African Americans penicillin to cure their disease, the effects of the researchers’ malfeasance is still negatively impacting minorities’ decisions about whether or not to participate in research (Freimuth 2001; Corbie-Smith et al. 1999). In one study about their views of research protocols, some African-American participants said that their distrust of researchers was linked to the Tuskegee Syphilis Study and that patients should “expect dishonesty and nondisclosure of research risk from investigators” (Corbie-Smith et al. 1999, 541). A study conducted by the Institute of Medicine found that of people who have been asked to have their personal medical information used in research and decided not to participate, 22% declined because they did not trust the people or organization conducting the research.29

Some states have enacted legislation to allow a potential research participant to determine if he or she trusts an entity before he or she consents to participate in research. For example, California’s medical research statute requires that participants are told the identity of the entity funding the research.30

Whether other entities will have access to the tissue samples and data. To some people, it makes a difference whether their tissue and data will be shared with other researchers. Over a quarter of African Americans in one study indicated they did not want their tissue shared beyond the confines of the specific research protocol they consented to.31 Other studies have shown that some people are also concerned with the types of social institutions that will have access to the banks of tissue and data. Some people do not want to provide their tissue to research biobanks if the tissue will be accessible to forensics investigators (Bexelius, Hoeyer and Lynöe 2007, 443).
This is in keeping with a report of the Institute of Medicine in the U.S. which recommended that DNA banks created for medical and research purposes not be used for forensic purposes (Andrews et al. 1994, 46).

**Commercialization of the research.** Whether the research will be done for commercial purposes is a factor for some people in decisions about use of their tissue. A significant minority of people surveyed in one tissue banking survey did not think it was “all right” for researchers to use tissue samples for the purposes of developing new tools and treatments for profit (Helft et al. 2007, 19). However, 62.6% believed it was “all right” for their tissue samples to be used in profit-motivated research (Helft et al. 2007, 19). Overall, respondents were less willing to allow their tissues to be used in research conducted by national or international groups unaffiliated with their local institution (Helft et al. 2007, 18).

In a Swedish study, 68.2% of the respondents were indifferent to the source of financial funding for the research project and would delegate judgment regarding financial funding to a research ethics committee while a significant minority (18.7%) said that their decision to participate would be affected by whether funding was provided by a private company versus a public or independent source (Kettis-Lindblad et al. 2005, 435). In contrast, 54.9% of Swedish respondents to another survey of prior tissue donors considered corporate interests in the research an important issue, while 14.1% ranked this as the most important issue (Hoeyer et al. 2005, 98).

Courts have recognized a cause of action when physicians or psychiatrists use a patient’s medical information or tissue without permission for commercial gain. For example, a woman gave birth through a Caesarean section operation and consented orally to having a filming of the operation to be presented to medical societies. She successfully sued for privacy violations when
her Caesarean section was made part of a commercial film entitled “Birth.” In another case, a patient undergoing hairy cell leukemia treatment continued to supply his physician with tissue samples but was unaware that the additional tissues would be used for profit by the physician, as the physician obtained a patent on the patient’s cell line. The Supreme Court of California held that a physician must disclose to a patient an intent to do research on or commercialize the patient’s tissue.

Under statutes, commercialization is also a concern. In California, participants in research must be told if the investigator or research institution has a financial interest that exceeds $10,000 in the outcome of the experiment. Rhode Island’s medical privacy statute prohibits managed care entities from giving or selling patients’ personal information to any international, national, regional or local medical data base unless it is necessary to compiling statistical data related to the enrollees.

Commercialization without consent could even lead to criminal action. In the United States, researchers at the National Institutes of Health convinced Alzheimer’s patients and healthy volunteers to provide tissue samples, including spinal fluid collected through spinal taps, for research on Alzheimer’s disease.

But when one of the researchers went to the freezer, the samples were gone. Her boss, Dr. Pearson (“Trey”) Sunderland III, the Chief of NIMH’s Geriatric Psychiatry Branch, told her that 95% of the samples had been destroyed when a freezer malfunctioned. A Congressional investigation, however, discovered that Dr. Sunderland had provided the pharmaceutical company Pfizer with over 3,000 tissue samples and associated clinical data. Between 1998 and 2003, Pfizer paid Sunderland a total of $285,000 in consultation fees and $311,000 in lecture fees and travel expenses.
Sunderland was ultimately charged with violations of a federal law which acts to prevent conflicts of interest—18 U.S.C. § 208(a), which carried with it a potential 5-year prison sentence if his actions were willful. Sunderland was allowed to plead guilty to a misdemeanor charge with two years of probation and 400 hours of community service at a geriatric psychology service (Willman 2006). He also agreed to pay the government $300,000 (Willman 2006).

Conclusion

Researchers, their institutions and funders are struggling with questions about the rights of the individuals whose tissue and information is stored in biobanks. Various professional organizations, and even some biotechnology companies, require that, when the tissue is first extracted from people, they be given information about potential research and commercial uses on their tissue and a chance to refuse to allow the use of their tissue for such purposes (American Society of Human Genetics 1996). The American Medical Association’s Code of Ethics provides that “[p]otential commercial applications must be disclosed to the patient before a profit is realized on products developed from biological materials” and “[h]uman tissue and its products may not be used for commercial purposes without the informed consent of the patient who provided the original cellular material.”

An analysis of the existing studies, statutes, and cases has identified factors that are material to patients whose tissue and information might be used in research and to potential participants in research. These factors can be used by researchers, institutional review boards, research institutions, companies, health care professionals, and advocacy groups. These factors can help guide informed consent by identifying material information that must be disclosed and assessing what uses of the tissue and information should be permitted.
Reference List


Endnotes

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2 According to a 1999 study conducted by RAND, there are samples from at least 2.8 million individuals (referred to as “cases”) held in large tissue banks, repositories and core facilities. If the scope of the repository is expanded to include pathology specimens, newborn screen laboratories, and other repositories that store tissue, the number of cases held reaches over 178 million. Elisa Eiseman & Susanne Hage, *Handbook of Human Tissue Sources: A National Resource of Human Tissue Samples*, 141 (RAND: 1999).


11 This study surveyed one hundred healthy adult volunteers that were recruited from a United Kingdom National Health Service dental practice.

12 Researchers conducted telephone surveys of 273 Jewish individuals in the Baltimore-Washington, D.C. metropolitan area.


18 S.D. Codified Laws §§ 34-14-21 to 34-14-25; Fla. Stat. § 760.40.

19 45 C.F.R. § 46.116.


31 National Heart, Lung, and Blood Institute, “Executive Summary: Request for Information Modifications to the NHLBI Policy for Distribution of Data from Clinical Trials and Epidemiology Studies,” (August 2006), available

33 Moore v. Regents of the University of California, 793 P.2d 479, 481 (Cal. 1990).
34 Moore v. Regents of the University of California, 793 P.2d 479, 483 (Cal. 1990).