

# Harnessing the Benefits of Biobanks

Lori B. Andrews

We have a thriving biotechnology industry in the United States. There are over 1,450 biotechnology companies developing diagnostic and treatment technologies in medicine, creating more nutritional foods, and innovating new industrial processes.<sup>1</sup> Yet this \$28.5 billion sector of the economy is not without controversy.<sup>2</sup> The “bio” in biotechnology comes from living, biological entities – people, plants, animals, and even bacteria. In the realm of biobanking, people are the source of the raw material for the discovery of genes for research, diagnosis, and therapy, raising a host of issues about rights and responsibilities, fiduciary duties and societal obligations.

When I was growing up, it was said that the chemicals in the body were worth 89 cents. Today, though, like a bullish stock market, the price tags on body parts have soared. The value of a human egg can be tens of thousands of dollars. A single cadaver can be mined for medical and research uses – its skin worth \$36,522, its bones \$80,000, its tendons \$21,400, and so forth. The value of a particularly interesting human gene – or even snippets of human genetic material – can be billions.

New uses for human tissue are constantly being discovered. Researchers funded by the biotech company Geron used leftover embryos that had been created by *in vitro* fertilization (IVF) patients to create the most coveted of human cells: embryonic stem cells, which are primitive cells that can grow into every type of body tissue, including nerves, bones, and muscles.<sup>3</sup> In the future, biotech companies could use stem cells to produce marketable treatments – such as new heart cells to inject into an ailing heart, which would then repair itself.

And it is not just the medical sector that finds human tissue useful. Tissue such as blood, hair, and DNA – and even human corpses – are used as a medium by artists. In the United States, artist Marc Quinn created *Self*, a sculpted model of his head using nine liters of his own frozen, congealed blood.<sup>4</sup> In Great Britain, Canadian artist Richard Gibson was fined for outraging public decency when he sculpted a head of a woman and then used actual aborted human fetuses as earrings.<sup>5</sup> German pathologist Gunther von Hagens has outraged and entertained people around the world with his controversial *Körperwelten* exhibit featuring real human corpses in artistic displays, often in familiar poses such as running, sitting, gesturing, and playing chess.<sup>6</sup>

Due to its multiple uses in the biotechnology age, human tissue is being gathered and stored in repositories known as biobanks. Some biobanks have been created indirectly, when, for example, the pathology de-

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partment of a hospital stores biopsy samples from cancer patients or the criminal justice system keeps blood samples collected from felons for DNA databases. Others have been created directly, such as ones owned by entrepreneurs who solicit hospitals for access to their tissue samples or by families of patients with particular diseases who want to encourage research into their disorder.

The range of human tissue sources available to researchers and biotech companies 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 176 million individuals are being stored in United States repositories.<sup>7</sup> At least 20 million new specimens are added each year. Some specimens are anonymized or coded and not identified with specific individuals; others carry patient names or codes that allow personal identification.<sup>8</sup> Between these pathology samples, forensic samples, public health samples, and samples collected on people associated with the military, virtually everyone has his or her tissue "on file."

Expanding markets have increased the value of this tissue. Hospitals, research laboratories, and the state and federal repositories that store tissue samples find they possess a capital resource. In October 2001, I spoke to the national meeting of the College of American Pathologists and learned that health care institutions were routinely selling their patients' tissue to biotechnology companies, often without consent of the patients involved. Some pathologists in the audience said that adequate diagnosis was being impeded by these sales. Pathologists would attempt to undertake an autopsy, but find that the bones and other tissue had already been removed for sale, preventing them from correctly assessing the medical condition of the individual. One forensic coroner said that he had to put his foot down and require that sales be made after his autopsy because the practice was impeding his ability to investigate crimes. Other attendees suggested that these sales were the death knell for non-commercial research. A geneticist indicated that he had attempted to do a study on leftover placentas in his hospital, but was told that the Obstetrics and Gynecology Department had sold them all to a biotech company.

Biobanks vary in whether the biobank owner is willing to allow access by outside researchers to the tissue samples. In some instances, any researcher can order cell lines of particular types of patients through a catalogue. The entries in American Tissue Culture Catalogue<sup>9</sup> and its foreign counterparts,<sup>10</sup> for example, describe in telegraphic style the people whose tissue is for sale. CRL 5867 – a 49-year-old black female with cancer of the lymph node. JCR B0068 – a 14-week-old Japanese fetus who died of cytomegalovirus. SK-HEP-1 – a 52-year-old German man with liver cancer. Thousands of individuals are listed, but it is doubtful that more than a handful of them or their families realize that they are part of this elite market.<sup>11</sup>

The more recent trend, however, is for most research biobanks to hoard tissue samples, rather than to share them with other researchers. When Jonathan Shestack wanted to fund research on the genetics of autism, each university researcher he visited told him that they did not have enough tissue samples from families with autism to identify the gene responsible for the disease.<sup>12</sup> When Shestack asked why they did not share samples with researchers at other institutions, the researchers described their commercial motives. They each said they wanted to be the one to discover the autism gene and patent it.

Biobanks can be established without oversight, even without the knowledge of people whose tissues are used. Yet the practice of biobanking raises profound ethical and legal questions about the circumstances under which such banks are established and how the benefits of the banks are harnessed. While the concept of battery protects living people from physical interventions, and the Uniform Anatomical Gift Act gives them control over what happens to their body parts after they die, there is no overriding legal concept to govern the relationship between the tissue source and the biobank. Indeed, the principle most commonly applied seems to be that of "finders keepers" where pathologists, physicians, and researchers who have access to patient tissue feel no qualms about keeping it for their own use, beyond the purposes for which the tissue was collected.<sup>13</sup>

Biobanking raises a series of questions, which this issue of the journal seeks to address, such as:

What type of information, if any, should the source

of the tissue be given before tissue is entered into a biobank?

What cultural and personal values might it violate for person's tissue to be used without his or her informed consent?

What should be done with genetic information gleaned from a biobank?

Under what circumstances is commercialization of biobank samples and information appropriate?

How should the fruits of biobanking be distributed?

How can people protect themselves from unauthorized and unwanted use of, or commercialization of, their tissue samples?

What new institutional policies and legal regulations might be necessary to govern the emerging biobank economy?

### **Informed Consent and the Sensibilities of the Tissue Source**

A basic tenet of research law and ethics is that research should not be undertaken without the subject's consent.<sup>14</sup> The research goals of advancing scientific understanding and curing diseases are laudable, but research is not a matter of conscription. People can refuse to participate in research, even if it involves no risk to them and enormous potential benefit to the community. Thus, they could readily refuse to give blood to a biobank in the first place. With respect to federally-funded research, the protections of human subjects, including the right to refuse to participate in research, are codified in federal regulations.<sup>15</sup> But what about research that involves not an intervention on the person, but on a snippet of their tissue in a biobank – or in a facility that proposes to sell the tissue to the biobank?

Some researchers argue that the federal regulations requiring informed consent for human research do not apply to previously-collected tissue samples, such as those in hospital pathology labs. Indeed, 45 C.F.R. § 46.101 of the federal regulations governing human research states that:

(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:...

(4) Research, involving the collection or study of existing data, documents, records, pathologi-

cal specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

This provision was adopted long before the advent of widespread genotyping and genetic sequencing, and before the troubling commercialization that now dominates health care institutions and academic research.<sup>16</sup> “The thirty years since the establishment of the National Commission for the Protection of Human Subjects (NCPHS) have seen changes in the world and in research, both swift and sweeping. The moral landscape and the horizon are no longer recognizable,” note Charles MacKay and Gerald S. Schatz. Among these changes are “(t)he expanded commercialization of the research enterprise.”<sup>17</sup> Consequently, it is inappropriate to use § 46.101(b)(4) to allow research on previously-collected samples, such as those in biobanks, without the specific informed consent of the tissue source. In some instances, the regulation on its face will not apply; for example, the provision does not provide an exception to the requirements of informed consent for samples that are collected initially in situations that do not involve diagnosis or pathology. It does not cover, for example, samples collected initially for research purposes or law enforcement uses. But, more importantly, the exemption only applies to research on samples without identifiers. Now that DNA typing is available which can identify individuals, samples cannot ever be truly anonymized.

Moreover, even if a sample could be anonymized, research on it without consent may still disturb the tissue source. Such research may conflict with the personal preferences or religious beliefs of the tissue source. Albert Einstein said he wanted to be cremated, yet his brain was kept by a young pathologist after Einstein's death without his previous consent, even though the pathologist had many opportunities to talk to Einstein across the months as he drew his blood to monitor his health.<sup>18</sup>

Anonymous research on biobank samples might also lead to discrimination against the tissue source, not because his or her individual identity was revealed, violating traditional notions of privacy, but because of some characteristic revealed about him or her as a member of a group. If research on samples in a biobank shows that a particular ethnic group has a higher incidence of a certain illness or a genetic predisposition to a disfavored behavior, individuals from that ethnic group may face stigmatization and discrimination.

Research on tissue from people from certain ethnic

or religious groups may disturb other members of that group, including relatives of the people whose tissues were used for research. In the Orthodox Jewish community, unauthorized use of body tissue violates religious beliefs because the religion requires that the body be buried whole.<sup>19</sup> If a person's leg is amputated during his or her life, arrangements are made to store that body part for burial with the individual after death.<sup>20</sup> Rabbis apparently asked the pathologist for Einstein's brain so that it could be buried, allowing the scientist to rest in peace.<sup>21</sup> Similar issues are raised by research on Native Americans, when graves of their ancestors were disturbed to acquire bones for research. According to James Riding In, "Many Indians assert that disinterment stops the spiritual journey of the dead, causing the affected spirits to wander aimlessly in limbo. These affected spirits can wreak havoc among the living, bringing sickness, emotional distress, and even death."<sup>22</sup>

Changes in the culture of research since the adoption of the federal regulations also prompt concerns that were not envisioned at the time the informed consent exemption in § 45 C.F.R. 46.101(b)(4) was enacted. The federal human research regulations were adopted at a time when pathologists used existing tissue samples for non-commercial purposes, such as to attempt to improve a test to diagnose a certain disorder. They were adopted before the enactment of the federal technology transfer laws that allowed university researchers and federal researchers using federal funds to personally benefit financially from the research, such as by patenting a gene they identified in a patient's tissue.<sup>23</sup>

Now, however, any tissue sample on the shelf anywhere is potentially in the pipeline toward commercial research. Yet some individuals object to their tissue being patented<sup>24</sup> or their body being used by a for-profit enterprise. In 1951, a 31-year-old African-American woman, Henrietta Lacks, died of ovarian cancer. Without the knowledge or consent of Lacks or her family, her tissue was taken and made into a cell line that has been extremely valuable for research and is still sold today. In an interview in 1994, her husband said, "As far as them selling my wife's cells without my knowledge and making a profit – I do not like that at all. They are exploiting both of us."<sup>25</sup>

For people whose tissue is used without consent, there are concerns that their doctors will view them as "treasure troves" and order unnecessary interventions. This was underscored in the case of *Moore v. Regents of the University of California*<sup>26</sup> when the court recognized that physician/researchers have a fiduciary duty to their patients to disclose their intent to use patient tissue samples for research or commercial purposes. The California Supreme Court pointed out, "A physician

who adds his own research interest to this balance may be tempted to order a scientifically useful procedure or test that offers marginal, or no, benefits to the patient."<sup>27</sup>

Because of the increasing recognition that unauthorized use of previously-collected tissue samples might violate the values of the tissue source, social norms are evolving to recognize that the tissue source should have greater control over the subsequent use of his or her samples. In Florida, for example, a person's genetic material may not be tested without consent, even for important research purposes.<sup>28</sup> Today, 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.<sup>29</sup> 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."<sup>30</sup>

Just as professional guidelines have evolved to evince concern about the wishes of the tissue sources, so have the protocols of particular projects. NUGENE, the biobank established by Northwestern University School of Medicine, has established extensive guidelines for informed consent.<sup>31</sup> The biotechnology company Ardaís, which has deals in place with Harvard and Duke to undertake genetic research on their hospital patients' tissue, also requires informed consent.<sup>32</sup>

Yet none of the professional guidelines, university consent materials, or consents used by biotechnology companies establishing biobanks provide information that could be key to a true informed consent: information about how the research on the patient's tissue or its subsequent commercialization is likely to impact access to diagnostics and treatment technologies and how commercialization might influence the research enterprise overall.

### Commercialization of Biobanks

Much of the current activity of biobanks focuses on the identification – and subsequent patenting – of genes and segments of DNA that might be useful in diagnostic testing, gene therapy, and drug development. With gene patents potentially worth over a billion dollars a year to the patent holder,<sup>33</sup> it is no wonder that companies are willing to pay sums such as \$200 million for access to biobank research on particular disorders.<sup>34</sup> Yet gene patenting poses potential harms to the tissue source, the health care system, and the research enter-

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prise. These problems are sufficiently troubling that the American Society of Human Genetics and the College of American Pathologists oppose gene patents as threatening medical advances and patient care.<sup>35</sup> Consequently, tissue sources should be informed – in advance of any research on their tissue – about whether or not genes discovered in their tissues (or related products created based on this genetic information) will be patented, how the patent will be licensed, and what the impact of the patent is likely to be on health care and research.

This is material information because when a gene is discovered in a biobank tissue sample and patented, the gene patent holder can charge whatever it wants for a diagnostic test for mutations in that gene (or any other use of the gene). The patent holder can prohibit anyone else from performing a diagnostic test for the gene, and instead require all doctors to send the patient's sample for testing to the patent holder's own lab, which may be in another state or even another country. In fact, the tissue source whose gene was patented could find that he cannot afford the test or treatment created with his own gene or that he cannot get access to a genetic diagnostic test for family members because the gene patent holder is restricting who may perform the test.

In the future, a person might want to get a scan of his whole genome, all 30,000 genes. The technology to do so is already technically available, but cannot be implemented due to the financial and practical limitations put in place by gene patent holders. Myriad Genetics, which holds the patent on the BRCA1 gene, charges \$1500 for the test.<sup>36</sup> Multiply that by the 30,000 genes in a person's body and it is clear that a whole genome scan would be unaffordable if every gene was patented and access to it was priced in the Myriad way. Already, one in four laboratories has stopped performing certain genetic tests because of patent restrictions or excessive royalty costs.<sup>37</sup> Half had not developed a test for fear of running afoul of patent law.

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disease that their gene patent covers.<sup>38</sup> The risks of gene patents to health care are much greater than the risks of granting a patent on a drug or medical device. Other researchers can create alternatives to drugs and devices. There are no alternatives to the patented human genes in genetic diagnosis and gene therapy.

Companies now sequence disease-causing bacteria and virus genes and gain patents on the genome of the infectious disease. In fact, in one instance, a company wants to introduce inexpensive, quick public health testing for a common infectious disease – but the company holding the patent on the gene for the infectious disease has forbidden it. Similarly, genetic tests are possible to determine if a drug will be effective on a particular patient. Most drugs only work on a percentage of patients who use them. But what if the holder of the genetic segment for the test also manufactures the drug? There may be an incentive not to employ the test in order to protect the market for the drug. For example, one pharmaceutical company has filed for a patent on a genetic test to determine the effectiveness of one of its asthma drugs. But the company says it will not develop the test – or let anyone else develop it.<sup>39</sup> In trademark law, the holder can lose the trademark if he does not use it for three years<sup>40</sup> and in some European nations, a patent holder must “work” the patent.<sup>41</sup> But in the United States a patent holder can deny society access to a genetic sequence for the term of the patent, twenty years from the date of filing the application.

To the extent that people's tissue is used without their consent or people are asked to donate their tissue for research purposes without being told of the specific problems created by commercialization of tissue via intellectual property rights, tissue sources cannot adequately protect themselves against the harms that gene patents entail for access to health care and for appropriate medical research. For example, knowing of the potential barriers that gene patents pose for accessible health care and widespread research, an individual may wish to donate his tissue to a biobank that will not patent any gene segments discovered – or that will allow access of other researchers and health care providers to the gene.

### **The Moral and Legal Obligations**

## to Tissue Sources

The people whose tissue is used by biobanks for research and commercialization provide the raw material for an important social enterprise. Usually when an entity provides raw material for any business (including health care enterprises), they are compensated. Yet this is not the case with biobanking. The sources of tissue are not only generally unable to reap commercial rewards from the use of their own tissue, they are not even allowed to limit problematic commercial uses of their tissue by others. This manifest unfairness has led professional organizations<sup>42</sup> and courts<sup>43</sup> to question how tissue sources might share in the financial benefits that accrue from discoveries made through biobank research.<sup>44</sup>

The Human Genome Organization (HUGO), an international organization of genetics researchers, has pioneered the discussion of benefit sharing. Yet its recommendations seem paradoxical. It recommends against undue inducement through compensation for individual participants, families, and populations. Although HUGO recommends against financial compensation, it suggests that the communities participating in research receive non-financial benefits through “agreements with individuals, families, groups, communities or populations that foresee technology transfer, local training, joint ventures, provision of health care or of information infrastructures, reimbursement of costs, or the possible use of a percentage of any royalties for humanitarian purposes.”<sup>45</sup>

Because HUGO is an international entity which needs to be concerned about the values of many cultures, perhaps it is understandable that it wants to protect potential research participants from the dangers associated with money.<sup>46</sup> HUGO would not want people in certain indigenous cultures, for example, to run roughshod over their cultural values for pay, particularly when the decision to participate in such research could disturb other members of the group. This could be true, for example, of research on Native Americans or indigenous populations around the world.

In mainstream U.S. culture, however, there are already precedents for payment for tissue and no cultural ban against it. The state laws that ban payment for organs for transplant do not ban payment for replenishable tissue, such as blood, which is the main tissue collected by biobanks. In the United States the purveyors of sperm or eggs usually receive compensation, which can be quite extensive. (One man, for example, markets his sperm over the internet for \$4000 a vial.) One way for the tissue source to capture some of the value of his tissue from the biobank and to control how that tissue is used is through contracts and joint ventures that recognize the contributions from the source.<sup>47</sup>

Already, some patient groups are entering into agreements through which they receive a portion of the royalties attributable to the patent on their gene.

Even when there has not been a specific agreement establishing a joint venture between the tissue source and the biobank, one court has suggested that the individuals who provided tissue to a researcher for the discovery of a particular disease gene, as well as some funding for the research, could maintain a claim of “unjust enrichment” against the researcher and the hospital that patented the gene and charged a fee for use of the genetic sequence in testing.<sup>48</sup> In extreme instances, the biobank that unjustly enriched itself might be required to disgorge all of its profits to the tissue sources.<sup>49</sup>

There is an inherent flaw in the three ways that the problems in biobanking have been dealt with thus far – the HUGO formulation for benefit sharing, the joint venturing with patient groups, and the legal declaration of unjust enrichment. None of these approaches provide protection against commercialization per se, or the problems that can be caused by patents. In fact, the court that recognized the claim for unjust enrichment also held that the tissue sources had no right to be informed about the potential commercialization of their tissue before they provided tissue to the researcher.<sup>50</sup> This could lead to the anomalous situation where a person’s tissue could be used for commercial purposes without his knowledge or consent in ways that violate his personal or religious beliefs, and his only legal remedy would be to get a cut of the action after the offending act takes place. Because of the limits of these three current approaches, innovative new policies may be necessary to assure that both the contributors to biobanks and society at large are sufficiently protected.

## Structuring Biobanks for the Good of Society

Adequate regulation of biobanking requires a focus on the unique aspects of this business: its raw material is derived from people; its “product” is often the genetic information derived from analysis of this raw material; there are conflicts over the legal status of both the raw materials<sup>51</sup> and the product<sup>52</sup>; and the product has no ready substitutes.

For all these reasons, health care providers and researchers establishing biobanks should be viewed as having a fiduciary duty to tissue sources. If people’s samples are entered into a biobank or research is undertaken on samples already in a biobank, the biobank should assure that participation by sources is informed and voluntary. A general blanket consent to all future research should not be considered sufficient to meet the standards of informed consent.<sup>53</sup> People whose tissue samples are solicited or used should be given adequate information upon which to base their decision, includ-

ing whether the use of their present or past tissue samples will lead to patents – and, if so, it should be disclosed that such patents can lead to higher cost diagnostics and treatments. Patient tissue sources should be told that perhaps other researchers would allow them to participate in a joint venture governing the use of their tissue.

Such requirements will protect people against having tissue used in an unauthorized way or in a way that violates their personal and religious beliefs. But those requirements may not be sufficient to protect society as a whole from the effects of biobank commercialization. For that, more radical policies might be needed – such as allowing health care providers and researchers to use the genetic sequences discovered in the people's tissue in biobanks without having to pay a royalty in order to protect access to health care and to encourage research.<sup>54</sup>

Whatever policies we develop, we cannot lose sight of the fact that the bio in biotechnology – the genes in the gene patents – come from people. And the scientific enterprise must have the trust of those people in order to get them to give up their tissue for research into diagnostics and cures. The raw material in the biotech industry is not widgets. It is pieces of my body, and your body, and all of our bodies. The policies that are developed should assure that society harnesses the benefits of biobanks for all of us.

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4. "Incarnate" exhibition in Gagosian Gallery, New York City: Catalog (New York: Gagosian, February, 1998).
5. "Fetus Earrings Made to Promote Debate Says Artist," *Daily Telegraph* (London), February 8, 1989: at 3.
6. "Körperwelten," Catalog of the exhibit at the State Museum of Technology and Labor (Mannheim, October 30, 1997, to February 1, 1998); see also, E.L. Andrews, "Anatomy on Display and It's All Too Human," *New York Times*, January 7, 1998: at A1.
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9. American Tissue Culture Catalogue, at <<http://www.atcc.org>> (last visited December 23, 2004).
10. See, e.g., *World Data Center for Microorganisms*, at <<http://wdcm.nig.ac.jp/DOC/menu3.xml>> (last visited December 23, 2004).
11. John Moore's cells are for sale as CRL-8066; a plasmid containing Moore's DNA sequence that codes for colony stimulating factor is sold as ATCC 39754.
12. E. Marshall, "Whose DNA is it anyway?" *Science* 278 (1997): 564-567.
13. L. Andrews and D. Nelkin, *Body Bazaar* (New York: Crown Publishers, 2001): at 9-11; see also S.F. Witelson, D.L. Kigar, and T. Harvey, "The Exceptional Brain of Albert Einstein," *Lancet* 353 (1999): 2149-2153, at 2150.
14. The Nuremberg Code states that "the voluntary consent of the human subject is absolutely essential."
15. See 45 C.F.R. § 46.101 et seq. (1997).
16. The Code of Federal regulations provisions governing federal research 45 CFR § 46.101 et seq. were adopted in 1974 as 45 C.F.R. 46. The provision that is the current 46.101(b)(4) was adopted in 1981.
17. C. MacKay and G.S. Schatz, "The Unfinished Research Agenda," presentation to the National Institutes of Health Inter-Institute Bioethics Internet Group, June 7, 2004. This has led the Secretary of Health and Human Services to release a new guidance, "Financial Relationships and Interest in Research Involving Human Subjects: Guidance for Human Subjects Participation."
18. Einstein's brain tissue was tested for a genetic propensity to aneurysm. S. McCartney, "Believing Einstein's Brain Matters, Doctors Keep the Remains," *Asian Wall Street Journal*, May 6, 1994. If such a propensity was found, it could have implications for his blood relatives – since their insurers might refuse to insure them based on this genetic flaw. "Einstein's Brain," *The Economist*, April 2, 1994, at 82.
19. Jewish tradition maintains that as man was created in the image of God, in death the body should retain the unity of that image. M. Lamm, *The Jewish Way in Death and Mourning* (New York: Jonathan David Publishers, 1969): at 10. If parts are removed, they must be returned and buried with the body. *Kohn v. United States*, 591 F.Supp. 568 (E.D.N.Y. 1984), citing Fred Rosner, "Autopsy in Jewish Law and the Israeli Autopsy Controversy," in F. Rosner and J.D. Bleich (eds.), *Jewish Bioethics* (New York: Hebrew Publications, 1979): at 332. Court cases have recognized that a patient's religious beliefs should be taken into consideration in determining what is proper handling of their bodies. See, e.g., *Lott v. State of New York*, 32 Misc. 2d 296, 225 N.Y.S.2d 434 (Ct. Cl. 1962).
20. H. Fitzgerald, Jr., "Woman Awarded \$1.25 million in Suit; Funeral Home Must Compensate for Losing Mother's Amputated Legs," *Sun-Sentinel* (Fort Lauderdale), May 16, 1997, at 1B. In fact, when Menorah Gardens and Funeral Chapels lost an amputated leg of an Orthodox Jewish woman, it made a \$1.25 million lawsuit settlement with her daughter. "Orthodox Jews believe that at the end of time, not only will a person's soul be resurrected, but the body as well....It's important that the whole body, including blood, be buried."
21. See S. LaFee, "Einstein's Mind: His Brain Sits on a Shelf, Largely Unsought by the World," *The San Diego Union-Tribune*, May 17, 1995, at E1.
22. J. Riding In, "Without Ethics and Morality: A Historical Overview of Imperial Archaeology and American Indians," *Arizona State Law Journal* 24 (1992): 11-34, at 11, 13.
23. Prior to the 1980s, if a university or federal researcher discovered or invented something using federal funds, that advance belonged to the public. The researchers could not personally profit. But with the passage of the Bayh-Dole Act, and the Stevenson-Wydler Act in 1980, and the Federal Technology Transfer Act, in 1986, the

rules changed completely.

These legal measures were enacted to encourage the commercial development of government-funded research. The Bayh-Dole Act allows universities and non-profit institutions to apply for patents on federally-funded inventions and discoveries and provides significant tax incentives to companies investing in academic research. 35 U.S.C. § 200-211 (2004). The Technology Transfer Act allows researchers in government facilities, including scientists at the National Institute of Health, to patent their inventions, and keep up to \$150,000 of the yearly royalties on top of their government salaries. 15 U.S.C. § 3710c (a) (3) (2004). The law allows government researchers to enter into commercial arrangements (known as CRADAs – cooperation research and development agreements) with for profit companies. 15 U.S.C. § 3701-3714 (2004).

Overnight, behavior that would have sent federally-funded university researchers to the penitentiary in the 1960s and 1970s – personally profiting from research done on taxpayers' expense – was not only legal, but encouraged. See L. Hayflick, "Novel Techniques for Transforming the Theft of Mortal Human Cells Into Praiseworthy Federal Policy," *Experimental Gerontology*, 33 (1998): 191-207, at 204. Largely as a result of these legal changes, NIH patent applications increased nearly 300 percent. See S. Krimsky, "The Profit of Scientific Discovery and its Normative Implications," *Chicago-Kent Law Review* 75 (1999): 15-39, at 22. But not all political leaders were convinced it was a wise move. Then-Congressman Al Gore argued that the arrangement was akin to "selling the tree of knowledge to Wall Street." S. Shulman, *Owning the Future* (New York: Houghton Mifflin Company, 1999): at 114.

24. P.R. Reilly, M.F. Boshar, and S.H. Holtzman, "Ethical Issues in Genetic Research: Disclosure and Informed Consent," *Nature Genetics* 15 (1997): 16-20.
25. H.A. Washington, "Henrietta Lacks – An Unsung Hero," *Emerge*, October 1994, at 29.
26. *Moore v. Regents of University of California*, 51 Cal. 3d 120, 132-133, 793 P.2d 479, 486, 271 Cal. Rptr. 146, 153 (1990) (physician/researcher had a duty of informed consent to disclose that he was undertaking research and that he was commercializing it).
27. *Id.* at 130.
28. Fla. Stat. Ann. § 760.40 (1995).
29. American Society of Human Genetics, "Statement on Informed Consent for Genetic Research," *American Journal of Human Genetics* 59 (1996): 471-474.
30. American Medical Association, *Code of Ethics*, E-2.08, at <<http://www.ama-assn.org/ama/pub/category/2512.html>> (last visited December 23, 2004).
31. See R. Chisholm, "Protocol Title: Gene-Disease Association and Treatment Outcomes," September 18, 2002 (on file with author).
32. In 2002, Ardaís earned over \$4 million in subscription and licensing revenue for the library, with revenue projections set at \$18 million for 2004. A. Connolly, "Ardaís Ambitious With Plans For Clinical Genomics," *Boston Business Journal*, November 22, 2002, available at <<http://boston.bizjournals.com/boston/stories/2002/11/25/story2.html>> (last visited December 23, 2004).
33. S.M. Thomas et al., "Ownership of the Human Genome," *Nature* 380 (1996): 387-388.
34. R. Kunzig, "Blood of the Vikings," *Discover* 19 (1998): 90-99.
35. College of American Pathologists Advocacy, *Gene Patents Detrimental to Care, Training, Research*, at <[www.cap.org/apps/docs/advocacy/advocacy\\_issues/issue\\_genepat.html](http://www.cap.org/apps/docs/advocacy/advocacy_issues/issue_genepat.html)> (last visited December 23, 2004, 2004).
36. Phone conversation with Myriad representative (June 2, 2004).
37. R. Kotulak, "Taking License with Your Genes: Biotech Firms Say They Need Protection," *Chicago Tribune*, September 12, 1999, at 1, citing a survey of 120 labs by University of Pennsylvania bioethicist Jon Merz.
38. K. Blanton, "Corporate Takeover Exploiting the US Patent System," *Boston Globe*, February 24, 2002, at 10.
39. G. Anand, "Big Drug Makers Try to Postpone Custom Regimens," *Wall Street Journal*, June 18, 2001, at B1.
40. 15 USCS § 1127 (2004).
41. N. Macfarlane, "The Tension Between Nation Intellectual Property Rights and Certain Provision of EC Law," *European Intellectual Property Review* 16 (1994): 525-530, at 526. To "work" the patent means to sufficiently commercialize the invention and make it available in order to meet the needs of the particular country.
42. HUGO Ethics Committee, *Statement on Benefit-Sharing*, April 9, 2000, at <<http://www.gene.ucl.ac.uk/hugo/benefit.html>> (last visited December 23, 2004).
43. *Greenberg v. Miami Childrens Hospital*, 264 F. Supp. 2d 1064 (S.D. Fla. 2003).
44. The idea of benefit sharing has been addressed on numerous occasions in the international context. See, e.g., HUGO Ethics Committee, *Statement on Human Genomic Databases*, December 2002, at <[http://www.gene.ucl.ac.uk/hugo/HEC\\_Dec02.html](http://www.gene.ucl.ac.uk/hugo/HEC_Dec02.html)> (last visited December 23, 2004) (recommendation 6: "Researchers, institutions, and commercial entities have a right to a fair return for intellectual and financial contributions to databases." They recommend that there should be "reciprocity and exchange of information with fair return" with fair return mechanisms being "non-exclusive licenses, copyright, monetary, non-monetary (e.g. publication or credits), database pools, and central repositories." They also provide that "any fees should not restrict the free flow of scientific information and equitable access."); HUGO Ethics Committee, *Statement on Benefit-Sharing*, April 9, 2000, at <<http://www.gene.ucl.ac.uk/hugo/benefit.html>> (last visited December 23, 2004) (Recommendation 3: "...there should be prior discussion with groups or communities on the issue of benefit-sharing."); HUGO Ethical, Legal, and Social Issues Committee Report to HUGO Council, *Statement on the Principled Conduct of Genetics Research*, March 21, 1996, at <<http://www.gene.ucl.ac.uk/hugo/conduct.htm>> (last visited December 23, 2004) (Recommendation bullet 9: "That undue inducement through compensation for individual participants, families, and populations should be prohibited. This prohibition, however, does not include agreements with individuals, families, groups, communities or populations that foresee technology transfer, local training, joint ventures, provision of health care or of information infrastructures, reimbursement of costs, or the possible use of a percentage of any royalties for humanitarian purposes."); UNESCO, *International Declaration on Human Genetic Data*, October 16, 2003, at <[http://portal.unesco.org/shs/en/ev.php-URL\\_ID=1882&URL\\_DO=DO\\_TOPIC&URL\\_SECTION=201.html](http://portal.unesco.org/shs/en/ev.php-URL_ID=1882&URL_DO=DO_TOPIC&URL_SECTION=201.html)> (last visited December 23, 2004)(Article 19: *Sharing of Benefits*: "...benefits resulting from the use of human genetic data, human proteomic data or biological samples collected for medical and scientific research should be shared with the society as a whole and the international community." These benefits include "access to medical care," "provision of new diagnostics, facilities for new treatments or drugs stemming from the research," and "support for health services."); UNESCO, *Universal Declaration on the Human Genome and Human Rights*, July 17, 2002 at <<http://www1.umn.edu/humanrts/instree/Udhrhg.htm>> (last visited December 23, 2004)(Article 12(a): "Benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all, with due regard to the dignity and human rights of each individual."); Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, 2002 at <[http://www.cioms.ch/frame\\_guidelines\\_nov\\_2002.htm](http://www.cioms.ch/frame_guidelines_nov_2002.htm)> (last visited June 4, 2004)(Geneva)(Guideline 10: *Research in populations and communities with limited resources*: "Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that: the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.");
45. HUGO Ethical, Legal, and Social Issues Committee Report to

- HUGO Council, *Statement on the Principled Conduct of Genetics Research, Recommendation 9, March 21, 1996*, at <<http://www.gene.ucl.ac.uk/hugo/conduct.htm>> (last visited December 23, 2004).
46. This is especially true since international genetics research tends to target certain isolated populations that have greater genetic homogeneity and thus disease genes can be more readily identified since they stand out. The Pima Indians in Arizona, for example, have had a very high rate of diabetes. The Bedouins in Israel include many people with a congenital form of deafness, and the Amish have a high rate of apparently inherited depression. P.M. Rowe, "Lessons About NIDDM from the Pima Indians," *Lancet* 347 (1996): 1320; P. Salopek, "Genes Offer Sampling of Hope and Fear; Cures Possible, but Groups Worry about Exploitation," *Chicago Tribune*, Apr. 28, 1997, at 1. Other targeted populations have been chosen as research subjects because their genes seem to protect them against specific diseases. People from the village of Limone Sur Gardi in Italy were relatively isolated until the 1950s because the road system was not nearby. They are of scientific interest because of the striking absence of heart disease in the population. Blood samples from the people, taken in 1994, revealed that thirty citizens had a unique gene that protected them from arterio-sclerosis and, therefore, from heart disease. P. Salopek, "Basically, We Are All the Same; Controversial Genetic Quest is Unlocking Secrets of the Human Rainbow," *Chicago Tribune*, Apr. 27, 1997, at 1; S. Goetnick, "Artherosclerosis Prevention a la Milanese," *Harvard Health Letter* (May 1996). The Cherokee of Oklahoma seem resistant to Alzheimers. R.C. Risser, et al., "Genetic Factors for the Development of Alzheimer's Disease in the Cherokee Indians," *Archives of Neurology* 997-1000 (1996); and the Hagahai from Papua, New Guinea are resistant to a leukemia-causing virus, HTLV. G. Taubes, "Scientists Attacked for Patenting Pacific Tribe," *Science* 270 (1995): 1112. Elderly Chinese people are genetically interesting as research subjects because of their unusual longevity. Z. Dang and X. Lei, "Chinese Center Sues over Study Coverage," *Science* 283 (1999): 1990-1992. The genes of all these groups are potentially valuable resources.
  47. When Sharon Terry learned that her two young children had inherited PXE (pseudoxanthoma elasticum), a connective tissue disorder that leads to blindness and potential heart attacks, several groups of researchers called to ask for tissue samples from her children to try to find the gene. M. Fleischer, "Seeking Rights to Crucial Gene," *The National Law Journal*, June 25, 2001, at C1. She inquired as to why they did not get samples from other researchers and was told that scientists would not share the samples. Terry started a bank with tissue samples from her children and began a collaborative project with researchers. When University of Hawaii pathobiologist Charles Boyd isolated the gene, he listed Sharon Terry as a co-inventor on the patent. The PXE patients' group she formed will make the decisions about how to license the rights to the gene. Additionally, the PXE group will give 50% of the resulting royalties to the University. This way the PXE patients' group can keep the price of diagnostic tests down by licensing providers who charge a lower fee.
  48. *Greenberg v. Miami Childrens Hospital*, 264 F. Supp. 2d 1064 (S.D. Fla. 2003).
  49. See *University of Colo. Found. v. American Cyanamid*, 153 F. Supp. 2d 1231, 2001 U.S. Dist LEXIS 10679 (D. Colo., 2001) for disgorgement of patent royalties in an unjust enrichment context.
  50. *Greenberg v. Miami Childrens Hospital*, 264 F. Supp. 2d 1064, 1070 (S.D. Fla. 2003).
  51. For example, there is a question about whether a person can have a property interest in his or her tissue.
  52. For example, some commentators suggest that genes should not be patented in the first place. Patents are not allowed on formulas or products of nature. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). Yet genes seem to be both. Patents are central to drug development and thus appropriate in the pharmaceutical context, but discovery of genes does not require the same incentives as drug development. Molecular biologists were attempting to identify genes long before the U.S. Patent and Trademark Office made clear that genes could be patented. As opposed to the development of drugs, which is undertaken primarily with private funds (for which investors expect a commercial return), the discovery of genes has been undertaken with vast quantities of public funds. Over \$1.8 billion of taxpayer money was spent by the U.S. government and non-profit institutions on genomics in the year 2000 alone. Myriad, the genetics company that first isolated and described BRCA1, utilized over \$5 million from a government agency, the National Institutes of Health. B.W. Jones, "History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing," *Health Law Journal* 10 (2002): 123-146, at 123, 131. Even the private company that made its own efforts to sequence the human genome, Celera, used sequence data from the publicly-funded project in its sequencing.
  - Moreover, no expensive clinical trials are necessary for the transition from a gene discovery and knowledge to the actual use of the gene sequence in clinical diagnostics. In some cases, a disease gene has been identified one day and testing begun almost immediately. Because the Food and Drug Administration ("FDA") does not regulate the clinical services of genetic tests (as opposed to the sale of genetic diagnostic kits or gene therapies), there is no costly FDA approval process. Thus, the need to financially compensate a gene-discoverer is not as great as the need to compensate the developer of a drug that must take it through costly clinical trials, with only a small number of drugs actually becoming commercially-viable products.
  - Gene patents do not seem necessary to encourage technology transfer in the move from gene discovery to the availability of a genetic diagnostic test. As soon as information about the discovery of the hemochromatosis gene was published, laboratories began testing for mutations in the gene. After a patent on the gene was granted seventeen months later, 30% of the 119 U.S. laboratories surveyed reported discontinuing or not developing a genetic test for the disease. The patent holder was asking for an up-front fee of \$25,000 from academic laboratories and as much as \$250,000 from commercial laboratories, plus a fee of \$20 per test. J.F. Merz, A.G. Kriss, D.G.B. Leonard, and M.K. Cho, "Diagnostic Testing Fails the Test," *Nature* 415 (2002): 577-579, at 578. The patent interfered with clinical adoption of the test and potentially compromised the quality of testing by limiting the development of higher quality or lower cost alternative testing methods.
  53. As a report of a committee of the National Academy of Sciences on genetic research notes, "It is not ethically or legally acceptable to ask research participants to 'consent' to future yet unknown uses of their identifiable DNA samples." *Evaluating Human Genetic Diversity* (Washington, D.C.: National Academy Press, 1997): at 65.
  54. U.S. Members of Congress Lynn Rivers and David Weldon introduced such a bill covering health care providers and non-commercial researchers in 2002, the proposed Genome Research and Diagnostic Accessibility Act. L.B. Andrews, "Genes and Patent Policy: Rethinking Intellectual Property Rights," *Nature Reviews Genetics* 3 (2002): 803-808, at 806.