Chapter 3
Ethical Perspectives on the Research Use of Human Biological Materials

The retrieval and use of human biological materials for diagnostic, therapeutic, research, and educational purposes represents a further development in the scientific study of the human body as a source of medical information, raising a number of ethical issues for investigators, subjects, their families, and society. This chapter focuses primarily on secular ethical considerations, with a particular emphasis on how various interests can be weighed in considering access to and restrictions on the use of human biological materials in research. [1] The Commission adopted this secular perspective for many reasons, but also because religious perspectives of human organs and tissues has largely focused on donation for therapeutic purposes, with very little direct discussion by religious scholars of non-therapeutic research uses of human biological materials. [2]

As described in chapter 2, more than 282 million human biological samples are currently stored in the United States, chiefly in pathology archives, blood banks, researchers' collections, and state public health department newborn screening facilities. Some materials have been stored for decades, millions more will be gathered and stored in the next year, tens of millions more in

[1] This chapter has been adapted from a commissioned paper prepared for NBAC by Allen Buchanan, An Ethical Framework for Biological Samples Policy. The complete paper is available in Volume II of this report.

[2] It is useful, however, to consider the religious implications of research use of such materials in terms of: 1) religious attitudes to the human body and to organs, tissues, and cells removed from the body; and 2) religious discussion of modes of transfer of body parts, such as donations, offerings, sales, and abandonment. To assist in its deliberations, NBAC commissioned a paper by Courtney Campbell on religious issues, Religion and Tissue Samples. This paper is available in its entirety in Volume II of this report.

the next decade. The individuals who are the sources of the samples are identifiable in some cases, not in others. Some samples were gathered during procedures (such as surgery) in which some form of informed consent was attained, some were not. Even where there was informed consent for the procedure that produced the sample, often there was no consent to some or any possible future uses of the sample. In many, perhaps most cases, individuals had no idea that their sample was being stored, nor any inkling that it might be used for a variety of research purposes, by a variety of individuals.

Gathering information about an individual through the taking of a medical history or by interpreting the inscriptions on an electrocardiogram may have a different significance for the individual or others than biopsying a piece of tissue or drawing blood. But from the standpoint of many of the interests at stake in the way biological samples are used, what is most important is the information the sample can yield, not the physical embodiment of the information.

As technology advances, automated analysis of samples (for genetic and other information) may reduce the need to store samples. Nevertheless, most of the ethical issues would remain, because they are related to the uses of the information derived from the samples, not the sample itself. For this reason, the term "biological sample information" is used to cover both the sample itself and the information that can be extracted from it, noting that in most cases it is the information that matters, once the sample has been taken.

In addition, it is important to recognize that some types of medical research, genetic research in particular, raises certain special concerns because analysis of samples may reveal information about individuals other than the source, such as membership in a family or group. In addition, any sample containing cells from any part of the body can be subjected to genetic analysis because every nucleus of every cell of the body (with the exception of red blood cells and reproductive cells) contains the complete genetic code of the person from whom the sample was taken. As noted in chapter 1, it is in part because of the seemingly limitless uses of genetic analysis—and the concerns that some possible uses evoke—that there is currently much interest in the ethical aspects of the practice of gathering and storing human biological samples that may be used for research.

In the most simple terms, considerations about the ethical use of human biological materials in research entails a balancing of societal interests in the benefits of applied biomedical science (e.g., improved health, economic benefit) and the avoidance of harm to the individuals who provide the material. These goals are not in opposition and do not necessarily pit scientific interests against patient/research participant interests. Scientists have moral (and legal) obligations not to cause harm and individuals often participate in research studies because of feelings of altruism or general social benevolence. Thus, virtually all parties to the discussion acknowledge both the value of scientific research *and,* for example, the right to privacy and confidentiality. Thus, decisions to use human biological materials in research involve a balancing of interests. Moreover, the weights of various interests vary both over time and among cases.

For example, the weight that should be accorded to the societal interest in benefits of applied biomedical science will depend in part upon how widely these benefits are distributed. If there are gross inequalities in the distribution of benefits, it is misleading to speak of the common interest in medical progress. Consequently, the case for tolerating greater risks to the interests of sample sources for the sake of the societal interest in medical progress is weakened if some people, including some who provide samples, lack access to important health care benefits because they cannot afford them. Nevertheless, if the benefits of medical progress accrue to a large number of people, a societal interest is relevant even if not all benefit or not all benefit equally.

NBAC focused on the possible harms that persons can suffer if others gain information from their biological samples or use those samples in various ways. In doing so, the important moral concerns that lie behind the notions of harm, such as violation of privacy and confidentiality, are brought to the fore and policies regarding appropriate protections emerge.

The Commission examined the following potential harms to the individual as worthy of consideration when using human biological materials in research, specifically samples that can be linked to their source.

- insurance and employment discrimination
- stigmatization

- group-based harms
- familial conflict and psychosocial harm
- objectionable, unacceptable, or questionable research
- dignatory harm
- invasion of privacy
- inappropriate disclosure of confidential information
- harms to survivors
- concerns about profits and "commercialization"

Obviously, the easier the linkage between source and sample and the more widely available the information is linking the source and the sample, the greater are the concerns about risks.

Insurance and Employment Discrimination

Given current social and institutional arrangements, persons known to have health problems or susceptibilities to disease may be vulnerable to unfair insurance and employment discrimination. Moreover, being listed in a tumor registry or replying truthfully to questions about one's family medical history may be just as risky as having a positive test for a genetic disorder reported in one's medical records.

The actual extent of insurance and employment discrimination on genetic grounds is a matter of speculation because most of the evidence comes from surveys in which individuals self report discrimination, with little or no independent check on the accuracy of their perceptions (Billings, 1992). Still some evidence has been presented (Lapham, 1996). Moreover, the risk exists only for insurance policies whose issuance is conditional on medical underwriting, and most Americans who have private health insurance obtain it through large group policies in which there is no medical underwriting. Indirect forms of underwriting may effect tens of millions more Americans (Stone, in Murray, 1996). Nevertheless, were insurance and employment discrimination to occur, the results could be devastating for the individual.

The weight that should be accorded to the interest in avoiding insurance or employment discrimination varies with the magnitude of the risk, and hence with the institutional arrangements that either magnify or diminish that risk. For example, if blood were collected from identifiable individuals for use in a study of the basic biological mechanisms of platelet formation, one could argue that the risk of disclosure of that information poses little, if any, risk of discrimination to the individual who donates the blood. If the very same samples, however, were then later used to determine whether trace amounts of illicit substances could be found in the blood, the potential for discrimination, and therefore concern, increases. And, if that blood were collected in the context of the workplace, concerns about the potential for discrimination would become even more pronounced.

It is also important to emphasize that the risk of discrimination is not an inevitable effect of the existence of information about illness or susceptibility: it is an artifact of a particular institution, namely, a private insurance market in which most medical insurance is employment-based and in which private insurers compete in part by attempting to avoid insuring sick (and therefore costly) individuals. If this institution were abolished or modified in certain ways so as to reduce the risk of discrimination, then to that extent the weight of the interest in avoiding discrimination would diminish, and with it the case for restricting access to biological sample information in order to protect the interest in avoiding discrimination. (It is also important to emphasize, however, that discrimination in life insurance and disability insurance also occurs in other countries, which do not rely on private insurance for health care as heavily as does the United States [Knoppers, 1997].)

From this it follows that in a society like ours, in which there is a powerful institution that poses a significant threat of discrimination, greater restrictions on access to biological sample information will be needed, other things being equal, than in a society in which different institutions for financing health care eliminate the possibility of discrimination. If federal and state laws prohibiting insurance and employment discrimination are passed and effectively implemented, the balance between interests that weigh in favor of more restricted access and greater source control and those that weigh in favor of freer access and more permissive uses of biological samples will shift accordingly. Therefore, whatever policy is now developed must be subject to

revision in the future.

Stigmatization

Even if an individual is not denied insurance or employment, he or she may suffer the harm of stigmatization. Although there is an unfortunate tendency to focus only on the stigmatization that results from being identified as having a genetic disorder, other types of illness can be equally or even more stigmatizing (e.g., sexually transmitted diseases, disfiguring diseases, and cancer).

Stigmatization is closely related to discrimination; indeed it can be argued that it is a species of discrimination. Like discrimination, it is a form of exclusion by labeling. In the case of stigmatization, however, there is usually at least an intimation of unwholesomeness, blame, or taint. Some, but not all forms of discrimination include this feature.

Perhaps the most familiar type of stigmatization is that which is imposed on an individual from without, by the judgments and perceptions of other individuals. However, because individuals are so often deeply influenced by the attitudes of their peers, they may internalize stigmatization.

As with discrimination, the weight that should be accorded to the interest in avoiding stigmatization varies among individuals and with cultural attitudes toward disease. For example,

some might find it stigmatizing to learn, as the result of participating in a research study, that they possess a marker that predisposes them to psoriasis, a condition that can be disfiguring. Others might not consider this to be stigmatizing. In some sects of Judaism, it is stigmatizing to be a Tay-Sachs carrier, so much so that some such individuals are considered "unmarriagable" (ref).

To the extent that the public becomes better educated about the nature (and universal prevalence) of genetic susceptibility to disease, the risk of stigmatization on genetic grounds may diminish. And as with insurance and employment discrimination, the actual risk of stigmatization associated with various types of information contained in biological samples, as opposed to the mere possibility of stigmatization, is unknown.

Group Identity-Based Harms

Closely related to discrimination and stigmatization is another potential harm that individuals may suffer because of perceived links between medical information about them contained in a biological sample and what may be called their ascriptive (or group-based) identity. The harm of negative racial stereotyping, for example, is a harm to individuals, but it befalls individuals because of their ascriptive group identity. The term ascriptive here indicates that the identity in question is assigned by others, independent of the choice of the individual thus identified.

Individuals who are vulnerable to ascriptive-identity harms have a special interest in

avoiding situations in which information obtainable from their biological samples may contribute to the reinforcement of harmful group stereotypes, not only because they themselves may be harmed but also because they may wish to avoid harm to other members of their ascriptive group. For instance, genetic information gleaned from biological samples might be used in research on the role of genes in criminal behavior or in intelligence. In the past such research has sometimes both embodied and been taken to validate negative racial stereotypes.

Thus, limiting considerations of potential harms to the individual research subject is arbitrary from an ethical standpoint, especially given the power of new biomedical research technologies. The potential harms that the individual research subject may suffer are harms that other persons can also suffer as a consequence of the research. Research designed to study a group, or which retrospectively implicates a group, may, for example, place the group at risk of being perceived as unusually susceptible to disease. This, in turn, could result in members of the group facing, among other things, stigmatization and discrimination in insurance and employment. What is at issue for both the individual research subject and the group is that the research might expose facts about them – namely, the higher probability of the occurrence of disease – which places them at risk of psychosocial harms.

One might argue that an individual whose identifiable sample reveals her or him to be especially susceptible to a disease is at greater risk of harm than those individuals about whom there does not exist such specific information, and that this fact justifies the special protections

afforded the individual research subject. But there may be circumstances in which the individual research subject faces less risk of harm than other members of a group to which he or she belongs. For example, a socially and economically well-situated research subject will likely be at less risk of suffering the effects of insurance and employment discrimination than less fortunate members of the group. Moreover, the stigma associated with a disease may be far more injurious to a group than to a particular individual, especially where the group is one that is already socially and politically marginalized.

Familial Conflict and Psychosocial Harm

In some instances, biological sample information, like other medical information, may be a source of intra-familial conflict. For example, genetic analysis of a blood sample may reveal that the husband is not the father of the child. Or, in some cultures, if a family finds out that the prospective spouse of one of their members has a genetic disorder or a certain medical condition, they may attempt to prevent the marriage from taking place. Regardless of whether the beliefs on which they are based are rooted in mistaken views about genetics or indefensible assumptions about responsibility for disease, the conflicts they can generate and the resulting harms are quite real.

In addition, finding out that one is, for example, a carrier for a genetic condition, predisposed to heart disease, or infected with the HIV virus, can force families into difficult

situations, emotionally, physically, and economically. The knowledge that one is at elevated risk for disease or may have unwittingly passed on a deleterious genetic trait to one's offspring is sensitive information that should be obtained and delivered with the full knowledge and consent of the individual from whom the sample came.

Objectionable, Unacceptable, or Questionable Research

Individuals and groups can also have an interest in the uses to which the sample itself is put. Some people may find the intended use of the knowledge gained to be objectionable. For example, for religious or other reasons, some people may believe that their human biological material should not be used for contraceptive research or studies aimed at identifying individuals prone to violence or other socially unacceptable behaviors. Or, some individuals might consider it objectionable that their samples were sold by researchers to companies to make money.

It is difficult to know how much weight this interest ought to be given in designing an ethically sound and feasible system for regulating practices concerning the uses of biological samples. First, no one knows at present the full range of possible uses for biological samples in the future; the science of molecular biology and genetic technology is evolving rapidly. Consequently, at some point in the future someone's biological sample might be used in ways that he or she finds inherently wrong. The uncertainty here is not just a function of ignorance of the technical possibilities; future cultural attitudes and regulations (e.g., concerning experiments on

human subjects) could change and constrain possible uses of biological samples, independently of any control that might be exercised by the individual who is the source of the sample. Of course, respect for autonomy may argue for giving some weight to an individual's preferences even when they are based on patently false beliefs or speculation; but nonetheless, the fact that a preference is based on patently false beliefs or speculation should surely reduce its moral weight, other things being equal. What does seem likely is that in some cases what we would now regard as wrong or at least problematic we may regard as acceptable in the future, when society has changed and we have changed with it.

Dignatory Harms

Each person has an interest in being treated as a person, as a moral agent with unique values, preferences, commitments, and conceptions of the good. Part of the moral justification for the requirement of informed consent in research and treatment is to ensure that patients and research subjects are treated respectfully as agents, not as passive objects to be used for the ends of others.

First and foremost, however, the requirement of informed consent protects individuals from nonconsensual invasions of their bodies. Because the right of informed consent, which includes the right to refuse treatment, allows the individual to decide whether the risk of these harms is worth taking, it can also protect individuals from other tangible harms that may result

from the bodily invasion, if the individual chooses not to accept the proposed treatment.

It is important to note that these harms are not restricted to the minimal harms that might occur from techniques such as drawing blood or swabbing cells from the inside of the cheek. The point, rather, is that if one allows others access to one's body for these purposes one is in a position of vulnerability to other unwanted and more dangerous intrusions. For this reason it is somewhat misleading to say that the only physical harm from which one is protected by informed consent and IRB review for a simple procedure such as drawing blood is the extremely remote possibility of harm from the needle stick (beyond the unpleasant momentary sensation of the pricking itself).

A strong case can be made that current practices concerning biological samples often fail to treat persons with due respect because they systematically mislead as to why samples are being taken and to what uses they will be put. It is true that the person who draws the blood sample may not know that the sample will be stored indefinitely and may be used in any number of ways in the future and hence may have no intention to mislead. Nevertheless, the institutionalized practice of storing biological samples for future uses is one for which those who control the practice are responsible, and this practice, as we have seen, often does not inform sample sources about what may happen to the sample. Given the various interests already listed above, a practice that is misleading in this way fails to show proper respect to sample sources.

Invasions of Privacy

People have an interest in not being subjected to unnecessary exposure of the body to the view of others and in not having embarrassing or intimate facts about themselves disclosed, independent of whether such exposure or disclosure threatens other interests they may have or produces other harms. For example, one has an interest in others not knowing certain intimate information about one's reproductive history and in not having one's body unnecessarily exposed to view, even if these breaches of privacy cause no tangible harm.

This interest, which might be called the interest in privacy *per se*, is distinguishable from the various other interests catalogued above that serve to ground a right to privacy. It is closely related to the interest in avoiding dignatory harms, since in most if not all cultures, some modes of exposing the body, in some contexts, are thought to be undignified and demeaning and some intimate information is thought to be embarrassing.

It is this interest in privacy and confidentiality *per se* that is invoked when a patient or subject complains that the setting in which he or she is examined or in which he or she answers questions about his or her personal medical history is "too public" or "lacks privacy." Unlike some of the interests already noted, the interest in privacy *per se*, is at stake as much in the process by which the sample is collected as in what happens to the sample after collection.

Inappropriate Disclosures of Confidential Information

For the most part, once the biological sample is removed from the body, it is the interest in confidentiality, rather than the interest in privacy, that is at issue. The term "confidentiality" means "with trust"; preserving the confidentiality implies keeping confidences, of confiding in those we trust. With some risk of over-simplifying, confidentiality may be thought of as a kind of second best to privacy. In some contexts, medical and otherwise, persons must expose themselves to the gaze of others or divulge sensitive information to them in order to gain certain benefits, and the best they can hope for is that there will be no unnecessary or otherwise inappropriate viewing or disclosure to others, and that those who gain this intimate knowledge of ourselves will not use it to their detriment.

People have an interest in confidentiality, in being able to trust that access to their samples and to the information they contain will be appropriately limited. But what counts as an appropriate limitation will depend upon a complex weighing of conflicting legitimate interests. Thus, simplistic statements about the right to confidentiality (e.g., that access to personal information can be based on a "need to know") are not particularly helpful. To say that there is such a right is simply to assert that the interest in limiting intimate exposures is a high moral priority, and as such warrants special protections.

Harms to Survivors

Many existing biological samples were taken from individuals who are long dead, and if any sample is stored long enough it will outlast its source. It might be thought that once the source is dead, there are no interests to protect; but this is not so, for two reasons. First, the deceased source's family or other loved ones may have an interest in what is done with the sample, or members of the source's ascriptive group may have an interest in what happens to it.

Second, persons can have interests that survive their own deaths. For example, persons ordinarily have an interest in what happens to their children and grandchildren after they themselves die and for this reason plan for the disposition of their estates. Similarly, one can have an interest in the uses to which one's biological sample are put, whether these uses occur before or after one's death. This is especially true if certain uses would be considered impermissible *per se*, from the perspective of one's deepest, life-long religious or ethical values. From this it follows that if a policy of unrestricted access to samples of deceased persons is to be justified, it cannot be justified on the grounds that no interests are at stake. In the same way, this also argues that if a person restricted use of his or her sample while alive, these restrictions should also apply after the person is deceased. (Chapter 4 discusses the regulatory perspective on this issue.)

Concerns about Profits and "Commercialization"

A cluster of interests concern the distribution of the financial gains that may be produced through the uses of samples.

Some individuals and groups have sought to share in the profits that are generated by patentable biologic inventions in whose development the use of their biological samples played a role. Perhaps the most famous case is that of John Moore, who claimed an interest in the cell line that was developed from tissue from his spleen.[3] The California Supreme Court rejected Moore's claim, and hence any claim to a portion of the profits derived from uses of the cell line. However, it did affirm that the physicians who used his spleen tissue to develop the cell line had a duty to disclose to him that they were going to do so.

The two parts of the ruling mark an important distinction between two questions: 1) is the individual entitled to some or all of the profits gained from a product in whose development his biological sample played a role? and 2) is the individual entitled to disclosure of the fact that his biological sample may be used to develop a profitable item and perhaps also allowed to refuse to allow such uses? These questions implicate two distinct interests: the financial interest in profiting from the use of one's sample, and the interest in determining whether one's tissue is used in a profit-generating endeavor. Though less tangible than the financial interest, the second

[3] Moore vs. The Regents of the University of California et al, 793 P.2d 479 (Cal. 1990).

interest may be extremely important for some individuals, for it may be rooted in their most fundamental values about distributive justice.

However, there may be some cases where something profitable can be developed only through the use of a rather rare genetic mutation. (For example, it has been reported that there is a family in Northern Italy that has a mutation that protects against atherosclerosis, an "anti-cholesterol gene." Or, if it turns out that a small minority of the population has a natural immunity to HIV infection, this characteristic might be extremely valuable for the development of an HIV vaccine). Whether or not it would be desirable to recognize a legal property right in such cases will depend upon the proper balancing of a complex array of factors and, above all, upon whether there is reason to believe that individuals with extremely valuable genes will lack sufficient incentive to allow them to be used for producing significant benefits for large numbers of people without the sort of financial reward which such a property right would confer.

At this point it might be objected that it is misleading to talk only of the interest that individuals have in a share of the profits derived from uses of their biological samples and of whether this interest should be recognized by a legal property right: individuals have not only an interest, but a property right, because their tissues, blood, and DNA are their property if anything is. And indeed some moral philosophers have assumed or argued that a person's body is his or her property, in the sense of a moral property right. The model of the body as "property" stems from a claim of self-ownership, and seeks to authorize the individual person with control over the use

and disposition of their body and of body parts (Scott, 1981; Andrews, 1986). This view tends to treat the body as incidental rather than intrinsic to personal identity; the body as a totality is distinct from the self, and body organs and tissues can be transferred or alienated to others without compromising the nature of the self. These features make the property model very conducive to the scientific interest in body tissue; with the proviso that informed consent is obtained from the person. However, conflict can arise when, for example, a patient and a researcher assert competing claims or "property rights" to excised body tissues, as the Moore cases shows. It should be noted as well that there are non-instrumentalist views of the body that are important in prominent cultural and religious traditions in the United States.

CONCLUSIONS

Any ethically sound policy concerning research use of biological samples must reflect a defensible balance of the interests that weigh in favor of greater control over use and stronger protections against harms, on the one hand, and those that weigh in favor of greater access to samples for purposes of research and clinical interventions, on the other hand. These interests vary in weight and impact depending on the extent of identifiability of the sample source and the magnitude of risks and benefits.

The major interests that weigh in favor of greater control by sources and more rigorous safeguards against harms are the interests in avoiding insurance and employment discrimination,

stigmatization, group harms, familial conflicts (including those of survivors of the deceased), and objectionable use on the part of the source.

The major interests that weigh in favor of wider access to samples are: prevention of disease in the present and the future; pursuit of scientific knowledge; freedom of inquiry; and various commercial endeavors.

Given that there are important and morally legitimate interests that weigh in favor of less restricted access to samples, it would be a mistake to assume that policies should be developed that reduces the risks and harms to zero. Not all of the interests that weigh in favor of more stringent restrictions on access are of equal weight, and some are of questionable importance, especially given their low probability of occurring.

The following chapter describes current policies and practices pertaining to the ethical use of human biological materials in research.

REFERENCES

1. Billings, P.R., et al., "Discrimination as a Consequence of Genetic Testing," American. Journal of. Human Genetics 50: 476-482, 1992.
2. Buchanan, A., "Justice and Charity," Ethics, vol.x , no.x , 1987, pp. Xx.
3. Buchanan, A., "Assessing the Communitarian Critique of Liberalism," Ethics, 1989...
4. Buchanan, A., "Liberalism and Group Rights," in In Harm's Way, Jules L. Coleman and Allen

Buchanan (eds.)(Cambridge: Cambridge University Press, 1993).

5. Clayton, E.W., et al, "Consensus Statement: Informed Consent for Genetic Research on Stored Tissue Samples," Journal of the American Medical Association 274(22):1786-1792.

6. Dworkin, G.. "Does Having More Choices Make us Freer?" xxxxxxxxxxx.

7. Edgerton, R.G., Sick Societies: Challenging the Myth of Primitive Harmony (Toronto: The Free Press, 1992).

8. Faden, F. and Tom L. Beauchamp, A History and Theory of Informed Consent. Oxford: Oxford University Press, 1986, pp._____.

9. Feinberg, J., Harm to Others, New York: Oxford University Press, 1984.

10. Knoppers, B, et al, "Control of DNA Samples and Information", Commissioned for NBAC, 1997.

11. Lapham, E., et al, "Genetic Discrimination: Perspectives of Consumers," Science 274: 621-624, 1996.

12. Lawson, S. "The Tyranny of Tradition: Critical Reflections on Nationalist Narratives in the South Pacific," in Narrating the Nation in the Pacific, Nicholas Thomas and Ton Otto (eds.) _____.

13. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, Securing Access to Health Care, Volume One: Report (Washington, D.C.: U.S. Government Printing Office, 1983).