Chapter 1
Overview and Introduction

Biomedical researchers have long studied human biological material—such as cells collected in research projects, biopsy specimens obtained for diagnostic purposes, and organs and tissues removed during surgery—to increase knowledge about human disease and to provide better means of prevention, diagnosis, and treatment. Today, new technologies and advances in biology provide even more effective tools for using such resources to improve medicine's diagnostic and therapeutic potential. Human biological materials also constitute an invaluable source of information for public health planning and programming, through disease surveillance and studies of disease incidence and prevalence.

Yet the very power of these new technologies raises important ethical issues. Is it appropriate to use stored biological material in ways that were never originally contemplated either by the people from whom the material came or by those who collected the material? Does such use harm anyone's interest? Does it matter whether the material is identified, or identifiable, as to its source, or is linked, or linkable, to other medical or personal data about the source?

Based on the many successes of past research with human biological material, it seems highly likely that future studies will also benefit millions of people. How should this prospect be weighed against the chance that the studies could harm or wrong the individuals whose material is being studied, their families, or other groups of which they are members? Under what circumstances should researchers seek the informed consent from people whose biological samples (either existing or to be collected) they propose to study? How ought consent requirements be adjusted if the sources of the existing biological material would be difficult or impossible to locate, or if they have died?

The Research Value of Human Biological Materials

The medical and scientific practice of storing human biological material is more than 100 years old. Human biological collections, which include DNA banks, tissue banks, and repositories, vary considerably, ranging from large collections formally designated as repositories to the informally stored blood or tissue specimens in a researcher's laboratory freezer. Large collections include archived pathology specimens and stored cards containing blood spots from newborn screening tests (Guthrie cards)[1]. Tissue specimens are stored at military facilities, forensic DNA banks, government laboratories, diagnostic pathology and cytology laboratories, university- and hospital-based research laboratories, commercial enterprises, and non-profit organizations.[2] Archives of human biological materials range in size from fewer than 200 specimens to more than 92 million. Conservatively estimated, at least 282 million specimens (from more than 176 million individual cases) are stored in the United States, and the collections are growing at a rate of over 20 million specimens per year (see chapter 2).

In this report, the term *human biological material* is defined to encompass the full range of specimens, from subcellular structures like DNA, to cells, tissues (e.g. blood, bone, muscle, connective tissue and skin), organs (e.g., liver, bladder, heart, kidney, placenta), gametes (e.g., sperm and ova), embryos, fetal tissues, and waste (e.g., hair, nail clippings, urine, feces, and sweat, which often contain shed skin cells). At the present time, research using human embryos is prohibited from federal funding. As such, the current regulations do not apply. The use of human embryos in research raises special ethical concerns, which are addressed in a separate NBAC report.[3] Should the congressional ban on embryo research be lifted, however, many of the

1 Guthrie cards are special filter paper that contain dried blood spots from newborn babies, and contain identifying information, such as the mother's name and address, hospital of birth, baby's medical record number, and baby's doctor's name and address. The cards are used to test newborns for a variety of diseases.

[2] For the purposes of this report, the term "specimen" refers to the human biological material as it is stored in the repository. The term "sample" is used to refer to the material as it used in research. NBAC believes that this distinction becomes important when considering the applicability and adequacy of the existing federal protections for human subjects.

3 Cite title of stem cell report, in press, 1999.

issues addressed in this report would be relevant, although additional ethical considerations might apply.

The most common source of human biological materials is diagnostic or therapeutic interventions in which tissue or other material is obtained to determine the nature and extent of a disease or to remove diseased tissue. Even after the diagnosis or treatment is complete, it is routine to retain a portion of the specimen for future clinical, research, or legal purposes. Specimens are also obtained during autopsies. In addition, volunteers donate organs, blood, or other tissue for transplantation or research, and some donate their bodies after death for transplantation of organs or anatomical studies. Each specimen may be stored in multiple forms, such as slides, paraffin blocks, formalin-fixed, tissue culture, or extracted DNA. Repositories provide qualified commercial and noncommercial laboratories with access to specimens for both clinical and research purposes.

In addition to its future clinical use, a specimen of human biological material can be used to study basic biology or disease (see chapter 2). It can be examined to determine its normal and abnormal attributes or it can be manipulated to develop a research tool or potentially marketable product. Just as a clinician will choose biological materials appropriate to the clinical situation at hand, a researcher's choice of such materials depends on the goals of the research project. The selected tissue can be used just once, or alternatively used to generate a renewable source of material, such as by developing a cell line, a cloned gene, or a gene marker. In addition, proteins can be extracted, or DNA isolated, from particular specimens.

There is substantial research value both in unidentified material (*i.e.*, not linked to an individual or his or her on-going medical record) and in material linked to an identifiable person and his or her continuing medical record. In the former, the value to the researcher of the human biological material is in the tissue itself and often the attached clinical information about that individual, without need to know the identity of the person from whom it came. For example,

investigators may be interested in identifying a biological marker in a specific type of tissue, such as cells from individuals with Alzheimer's disease, or specific tumors from a cancer patient. In such cases, beyond knowing the diagnosis of the individual from whom the specimen was obtained, researchers may not need more detailed medical records, either past or on going.

Sometimes, however, it is necessary to identify the source of the research sample, because the research value of the material depends on linking findings about the biology of the sample with updated information from medical or other records about its source. For instance, in a longitudinal study to determine the validity of a genetic marker as a predictor of certain diseases, the researchers would need to be able to link each sample with the on-going medical record of its source in order to ascertain whether those diseases developed. For example, a recent study of late-onset Alzheimer's disease linked the presence of the disease with the apolipoprotein-E allele by studying the stored tissues of 58 families with a history of Alzheimer's disease and then examining autopsy records for evidence of the disease in those individuals whose tissue revealed the presence of that allele (Payami, 1996).

Already, findings from research on biological materials have produced tests to diagnose predisposition to conditions such as cancer, heart disease, and a variety of familial diseases that affect millions of individuals. In some cases, prevention or treatment is available once a diagnosis is made; in those cases, knowing the identity of the specimen source would permit communication of relevant medical information to the sources that may be of importance to their health. In other cases, when medical interventions are not available, having one's specimen linked with a disease predictor is likely to be of less clinical value to the individual, and might even be troubling.

Human biological materials also may be used for quality control in healthcare delivery, particularly in diagnostic and pathology laboratories. Other uses include identification of an individual, such as in paternity testing, cases of abduction or soldiers missing in action, and other

forensic purposes where biological evidence is available for comparison. The advent of technologies that can extract a wide array of information from these materials has generally increased the potential uses—in research and otherwise—of human biological materials that are unrelated to individual patient care.

By using the power of new DNA technologies and other molecular techniques scientists can potentially turn to millions of stored human biological materials as sources of valuable scientific, medical, anthropological, and sociological information. Indeed, these technologies are so powerful—even revolutionary—that they also hold the ability to uncover knowledge about individuals no longer alive and about those yet to be born. Three interesting cases were reported in recent years.

- In 1997 scientists at the University of Oxford announced that they had compared DNA extracted from the molar cavity of a 9,000-year-old skeleton, known as Cheddar Man, to DNA collected from 20 individuals currently residing in the village of Cheddar and established a genetic tie between the skeleton and a schoolteacher who lived just half a mile from the cave where the bones were found (add ref.).

- Scientists used enzyme-linked assays to analyze tissues more than 5,000 years old to track the historic spread of diseases such as malaria and schistosomiasis, obtaining knowledge that can enlighten current efforts to control infectious disease (Egyptian Mummy Tissue Bank, 1997).

- In early 1999, a U.S. pathologist and a group of European molecular biologists announced that they had found DNA sequences in the Y chromosome of the descendents of Thomas Jefferson that matched DNA from the descendents of Sally Hemings, a slave at Monticello. The data establish only that Thomas Jefferson was one of several candidates for the paternity of Eston Hemings, Sally's fifth child but also raised a storm of controversy (Foster, 1998).

The demonstrated use of these technical capabilities suggest that human tissue and DNA specimens that have been sitting in storage banks for years—even a century—could be plumbed for new information to reveal something not only about the individual from whom the tissue was obtained, but possibly about entire groups of people who share genes, environmental exposures, ethnic, or even geographic characteristics. Clearly the same is true for materials that may be collected in the future. DNA, whether already stored or still to be collected, can be used to study genetic variation among people, to establish relationships between genes and characteristics, such as single gene disorders, or more generally, to conduct basic studies of the cause and progression of disease, all with the long-term goal of improving human health. One of the many initiatives providing information towards this goal is the federally funded Human Genome Project, which expects to map and sequence the entire human genome by 2003 (Collins, 1998).

Is Genetic Information Different from Other Medical Information?

In the past few decades, concern about the misuse of genetic information has often spurred debate about misapplication of medical information in general. Public discourse and concern about the potential availability of personal genetic information has been intense in recent years for a number of reasons, including: 1) people fear the lack of any protection from the misuse of this information (e.g., employment discrimination) outside the research context; 2) its early beginnings in the often contentious public policy areas of reproductive medicine and family planning; 3) a difficult history of and continuing concerns with relation to eugenics and genetic discrimination; and 4) the rapid pace of the Human Genome Project and other developments in human biology.

Genetic information is one form of biological or medical information. Like certain other types of medical information, genetic analyses can reveal sensitive information about an individual. There are, however, some aspects of genetic information that distinguish it from other types of medical information. For example, genetic information concerning an individual can sometimes reveal similar information about a person's relatives or entire groups of people

(Knoppers, 1997). In addition, the detailed information contained in a person's genes is largely unknown to that person. Moreover, because DNA is stable, stored samples can become the source of increasing amounts of information as new genes are mapped (Annas, 1995). In the words of Francis Collins, Director of the National Human Genome Research Institute, "we are hurtling towards a time where individual susceptibilities will be determinable on the basis of technologies that allow your DNA sequence to be sampled and statistical predictions to be made about your future risk of illness" (NBAC transcript, October 4, 1996, pp. 129-130).

Some claim that the major distinguishing characteristics of genetic information are its predictiveness and its implications for individuals other than the person from whom the information was derived (IOM, 1994). Gostin, for example, has suggested that "genomic" data are qualitatively different from other health data because they are inherently linked to one person, that is, one's DNA is unique except in the case of identical twins (Gostin, 1995). In addition, genetic information does not change over time. While other pieces of medical information about an individual might change over the course of a person's lifetime, except in the case of mutations, DNA does not.

Others argue, however, that genetic information is not inherently distinct from other types of medical information (Murray, 1997). First, other types of medical information may be strongly correlated with particular diseases. Moreover, infection with a virus has implications for people other than the person actually infected. Likewise, the health status of a person living in a toxic environment, such as near the Chernobyl nuclear accident site, has implications for others living in that same environment. Clearly, many of the concerns that pertain to the misuse of personal genetic information apply equally to certain other types of personal medical information.

Increasing Discussion about the Appropriate Research Use of Human Biological Material

Increasing concerns about the use of medical information has fueled general debate about medical privacy and discrimination. Because medical research can reveal clinically relevant information about individuals, scientists must ensure that those who participate in research are adequately protected from unnecessary harms resulting from the inadvertent release of such information. Although protection of human subjects in research is of primary concern in the U.S. biomedical research system, research that uses biological materials—which are often distanced in time and space from the persons from which they came—raises unique challenges regarding the appropriate protection of research subjects. While medical research is generally considered a public good and is vigorously supported by the American public, the power of technologies to find an extraordinary amount of detailed information in a single cell raises the specter that information about individuals will be discovered and used without their consent and possibly to their detriment. Although this type of information might also be obtained through a variety of other means, DNA analysis currently is the most powerful means and increasingly will be the method of choice.

In recent years these various concerns have caused consumer, scientific and professional groups to begin to address the issues surrounding the collection and use of human biological materials. (AAMC, 1997; ASHG, 1987; 1996; ACMG, 1995; Clayton, 1995; HUGO, 1998; Pathologists, 1997). In addition, media focus on highly contentious cases using biological samples—such as the storage and research use of stored neonatal blood spots for anonymous studies of HIV prevalence in a given population, and the military's establishment of a DNA bank—has made the issue of research use of human biological materials a matter of increasing public concern.

In the course of its deliberations, NBAC identified several trends that are contributing to the need for a comprehensive public policy concerning the use of these biological materials for research purposes:

- increasing public perceptions that personal genetic and other medical information could be used to discriminate against individuals in employment or access to benefits such as health or life insurance, or could be stigmatizing in some way;
- growing public concern about privacy of medical records;
- the emergence of new considerations regarding both the nature of consent to participate in research protocols and disclosure of results;
- disagreement among scientific and medical groups about conditions that need to be satisfied to ensure that appropriate ethical standards are incorporated into all research protocols using human biological materials, primarily the requirements for review and the nature of the required consent process.

One particular area of concern centers on whether the information that can be obtained from the research use of human biological materials places those who are the sources of the samples at unacceptable risk. Such data might reveal, for example, information about an individual's disease susceptibility (e.g., carrying a gene that is associated with an increased risk of colon cancer or breast cancer). When there is an intervention that can be pursued to counteract the increased health risk, such as regular mammograms, dietary modification, or drug treatment, some might judge the information worth receiving and worth the psychological and financial risks associated with the information. If, however, the analysis reveals information for which no intervention is currently available (e.g., susceptibility to Huntington's disease or Alzheimer's disease), many individuals might perceive the risks of uncovering such information as outweighing the benefits. In any case, concern may arise when an individual did not consent in advance, or show any interest in receiving such information. Some would agree that finding out about an adverse health status should be done knowingly and willingly since it can provoke anxiety and disrupt families, particularly if nothing can be done about it and the finding has potential implications for other family members (Wilcke, 1998).

Potential for Discrimination and Stigmatization

There is growing recognition that human biological materials can be analyzed to ascertain significant amounts of genetic and other medical information about the person from whom the sample was obtained. In particular, there is increasing concern that this information could be used to discriminate against individuals in insurance and employment or could be stigmatizing for individuals and families (Cohen, 1995; Hudson, 1995; NCHGR, 1993; Rothenberg, 1997). In January 1998, the White House released a report prepared by the U.S. Departments of Labor, Health and Human Services, and the Equal Employment Opportunity Commission, *Genetic Information and the Workplace*[4], which predicted that by the year 2000, 15 percent of employers plan to check the genetic status of prospective employees and cites a 1995 Harris poll, which revealed that more than 85 percent of Americans are concerned that insurers and employers may have access to their genetic information (Harris Poll, 1995).

Concern about insurers and employers having access to genetic information has a basis in fact. In the 1970s several insurance companies and employers discriminated against sickle cell carriers, even though their carrier status did not and would not affect their health (Holtzman, 1989). In the absence of universal access to health care or laws that prevent discrimination on the basis of health status, there is a history of concern that medical information may be used to deny individuals insurance or jobs (Gostin, 1991; U.S. Congress, OTA, 1992; NCHGR, 1993). In addition to these possible financial harms, research findings about one's future medical status can, in some cases, inflict psychological or social harms (Davison, 1994). It should be noted, however, that there is little empirical evidence to date documenting extensive employment or insurance discrimination based on genetic status (Wertz, 1997).

Concerns about Privacy of Medical Records

Health care systems increasingly rely on information technology, such as electronic records, to manage and facilitate the flow of sensitive and clinically relevant health information.

4 The report is available on the World Wide Web at www.dol.gov/dol/_sec/public/media/reports/genetics.htm

This has had positive effects in clinical practice, but these trends also magnify concerns about privacy of certain genetic and other medical information. Recent commentary about privacy of medical records and attempts to protect privacy through legislation are evidence of the growing public concern about these issues. Currently, Congress and the Department of Health and Human Services have been discussing legislative and regulatory approaches to protect patient privacy (U.S. GAO, 1999).

An ongoing concern in medical care and in the protection of research subjects is the potential invasion of privacy or compromise of confidentiality. Measures to provide appropriate protections to both individual privacy and for the confidentiality of clinical and research data are important if research using this information is to enjoy broad support. When research samples are identifiable, that is, linked or linkable to the person who provides them, special steps must be taken to ensure protections in the collection, storage, and use of the data. However, computerized medical records and databases raise concerns about who has access to data (i.e., the security of these data bases) and whether or not these data are linked to individual patient records. It is widely believed that current confidentiality practices are insufficient to safeguard medical information. In addition, different cultural and religious groups may have differing concerns of what constitutes privacy or confidentiality (Medical Research Council, 1998).

Privacy concerns can arise within the context of "secondary use" of the samples collected. "Secondary use" means that the samples and the information derived from them are being used or analyzed for purposes that extend beyond the purpose for which the specimens were originally collected (Alpert, 1997). For instance, when materials are collected during surgical procedures and used solely for clinical purposes, the clinical use of these specimens raise few privacy concerns beyond those about the confidentiality of the medical record itself. This is because they are being used for the direct diagnostic or therapeutic benefit of an individual, and because the custodian of that biological specimen does not allow others access to it. Only when the use of such materials extends beyond the original clinical use do privacy issues

arise. For example, if a sample is used as part of a research study into familial linkage of a specific disease, and the family pedigree is published as a result of the study, an individual might be easily identifiable even without any names attached to the pedigree (Botkin, 1998).

Moral Significance of the Relationship between a Person and His or Her Body or Body Parts

There is increasing awareness in the medical and scientific communities regarding a spectrum of beliefs about the moral status of the relationship between a person and his or her body or body parts (Andrews, 1998). The use of human biological materials in research can raise ethical, cultural, and religious issues about the relationships among body parts, bodies, and self-identity. However, ethical and religious traditions do not always provide clear guidance about the ways in which human tissues should be used or obtained. Although there are variations among them, selected Western religious traditions offer some insight about the significance of the human body, and they generally favor the transfer of human biological materials as "gifts" (Campbell, 1997). As such, human tissues would warrant some measure of respect, which is the basis often expressed for restricting sales of human tissues and organs. But cultural differences can be significant because of the different symbolic nature or status cultures attach to specific body parts or tissues (Campbell, 1997).

Nature of Consent to Research Participation when Human Biological Materials are Used

Informed consent is a key foundation of the ethical use of persons as subjects in medical experiments. It is widely accepted and explicit in federal regulations that the informed consent of potential subjects must be obtained before enrolling them in particular research protocols. For research involving human biological materials, the role of informed consent has been much less clear and new considerations have emerged regarding both the nature of the required consent in these cases and the guidelines that should apply regarding the disclosure of results. In particular, the use of new genetic and other technologies to study human biological materials presents several challenges to the consent process—particularly if the material is linked to a specific individual: 1) the use of the material does not pose a physical harm to the subject, thus potential

harms become more speculative; 2) the complete research uses of the material may have been unknown and unanticipated at the time of collection; 3) the analyses might provide information that may lead to stigmatization, discrimination, or psychosocial problems for groups of individuals who share certain characteristics (Foster, 1997); and 4) there is greater awareness that the study may generate ambiguous results, tempting for clinical use but not really ready for reliable application (Reilly, 1980; 1997).

In addition, physicians and hospitals have not customarily sought a patient's explicit, informed consent to permit the use of pathology specimens for specific research purposes; instead, permission to use stored material for other than clinical purposes has been general, that is, granted with the understanding that such use is merely a possibility. In a recent study of general hospital consent forms, for example, it was found that 17 percent of large hospitals disclose potential research uses of records, and 15 percent mentioned research use of tissue samples (Merz, 1998). Once stored, human biological materials have been available for research, usually without the knowledge or consent of the sources, particularly if the sample is unidentifiable.

Federal regulations govern research with human subjects (45 C.F.R. 46), including research with human biological materials. (See Appendix A, Code of Federal Regulations, Title 46, Public Welfare, Part, 46 Protection of Human Subjects.).[5] This system of federal protections involves review of the proposed research by an Institutional Review Board (IRB) and a determination of the need for informed consent of the research subject. In situations for which informed consent is required, the identifiability of the source of the material and the risks posed

5 The Federal Policy (or "Common Rule" as it is sometimes called) was promulgated by 17 federal agencies that conduct, support, or otherwise regulate human subjects research; the Food and Drug Administration also adopted certain provisions of the Common Rule. The Federal Policy is designed to make uniform the human subjects protection system in all relevant federal departments and agencies. The Common Rule and other human subjects regulations are codified at Title 45 Part 46 of the Code of Federal Regulations, and it is the NIH Office for Protection from Research Risks (OPRR) that has taken the lead within the Federal Government on the task of harmonizing human subjects protections across agencies.

by the research are central to determining the breadth and depth of the consent requirement. (See chapter 3 for further discussion.)

The use of human biological materials raises subtle but significant distinctions in the applicability of federal regulations, the review of research protocols, and obtaining consent since the sources of materials can be patients, volunteer research subjects, or cadavers. Contention continues to surround a number of issues regarding the conditions for informed consent and/or IRB review. First there is the question of who defines and determines what constitutes "minimal risk," an important concept in the language of the federal regulations (Merz, 1996). Others believe that certain genetic research (e.g., on a stigmatizing genetic predisposition to a disease, such as alcoholism or schizophrenia) is greater than minimal risk and should, therefore, always receive a thorough IRB review. Because of these ongoing concerns many observers, including some health advocacy and scientific groups, have called for increased attention to the consent process pertaining to the research use of stored and yet to be collected human DNA and tissues (Clayton, 1996).

Informed consent is a process, the effectiveness of which has been widely debated, and which many agree can be improved. Discussions about its relative value in clinical and research settings are by no means unique to genetics or the issue of human biological materials. What people are told, what they understand, and what they remember when consent is sought is likely to vary as much when providing DNA or tissue as when consenting to medical interventions. When human biological material is stored, people may not understand, for example, that it might be used for research unrelated to their own disease status. When told a specimen is being kept "for research," a patient may believe the material will be used only for research related to his or her own condition. Patients may not realize that federal and state regulations require that specimens be stored for a certain length of time. In most cases, the repositories where specimens are stored were designed for a particular purpose, and the protocols and procedures that are followed in collecting and disseminating samples might not have addressed issues regarding

access, destruction, or future uses of the materials, such as for research (Merz, 1996).

Other familiar issues arise with respect to informed consent. How specific, for example, do the consent documents need to be for materials collected in a clinical context? How detailed should disclosure be about the intended purposes of subsequent research studies with stored materials? How much information should be provided to patients in clinical settings about the possibility of post-diagnostic research on stored materials? These questions are likely to have different answers depending on whether the specimen has already been collected or if it will be collected in the future, and whether the material was initially obtained as part of medical treatment or a research protocol. It stands to reason that a person's rights and interests are better protected if that person has some form of control over his or her removed biological material, especially if it remains identifiable. That control may be best achieved by a comprehensive consent process.

Group Concerns

Information obtained through research may have implications for families, groups, and others (Foster, 1997). Recently, the concept of community consultation in research with human subjects has received increasing attention. For example, NBAC heard testimony from the National Institute of Allergy and Infectious Diseases (NIAID) about the essential nature of community involvement in NIAID's AIDS clinical trials.[6] Representatives of the community of participants in those research studies worked together with investigators in the research process, from the formulation of clinical questions to be addressed, through the design of the studies, recruitment at a community level, and the execution and analysis of the research itself. It was concluded that such participation provided invaluable benefits to the research.

The Centers for Disease Control and Prevention (CDC) also has recognized the growing role of community involvement in public health initiatives, establishing a Workgroup for

Community Engagement to consider a growing body of literature reflecting the experiences of those involved in engaging individuals and organizations in communities across the country (CDC, 1997). While community engagement increasingly has become a basic element of health promotion, health protection, and disease prevention, to date there are few formalized procedures for seeking community involvement in research with human subjects.

To date, two sets of federal regulations govern informed consent procedures by requiring a form of community consultation. The first involves research in which subjects are enrolled in studies under emergency circumstances. These regulations pertain to: (1) research subject to regulations codified by the Food and Drug Administration (FDA) and carried out under an FDA investigational new drug application (IND) or investigational device exemption (IDE), (see Title 21 C.F.R. Part 50); and (2) research for which the Secretary of Health and Human Services has waived the general requirements for informed consent (at 45 C.F.R. 46.116(a), (b), and 46.408). The regulations provide for consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research (or clinical investigation, in the case of the FDA regulations) will be conducted and from which the subjects will be drawn. Moreover, public disclosure of plans for the research and its risks and expected benefits is required of investigators prior to initiation of the research. Finally, public disclosure of the results of the study is required following its completion. The second set of requirements have been effect since the 1970s, in which the Indian Health Service has had a policy of requiring approval of the research by the Tribal Government[s] with legal jurisdiction before research can begin (Indian Health Service, 1987).

Differing Opinion Regarding the Ethical Research Use of Human Biological Materials

Recent scientific developments have increased the scientific value and importance of human biological material. There can be expected to be, therefore, increased demand for the use of such material. This generates a greater level of responsibility for scientists and policy makers.

[6] Presentation by John Y. Killen, M.D., Director of the National Institute of Allergy and Infectious Diseases,

From available public statements, however, it seems that the scientific community often disagrees about how to ensure the appropriate respect for persons as well as their biological material and yet facilitate important health and medical research. Within the past few years many professional groups have issued policy statements describing their views on these issues. The sheer variety of thoughtful approaches suggested is an indication that consensus on how to resolve the difficult challenges that the use of human biological materials raises has been difficult to achieve, particularly with respect to requirements for IRB review and the nature of the consent process.

A stable consensus must strike the right balance between the desire to increase knowledge and the necessity of appropriately protecting individual interests. On the one hand there are those who think that emphasis should be placed on the distinctive nature of personal and familial medical information, the right of personal choice about the continual use of one's body or its parts, and, therefore, the information inherent in the materials taken from it, and the necessity of being able to exercise a measure of control over the research that can be done with one's DNA and tissues. On the other hand are those who think that in an era of increasing professional and legal regulations and emphasis on individual autonomy, renewed consideration must be given to: 1) the more extensive use of this invaluable and often irreplaceable research resource; 2) the inestimable societal and individual benefits that have been gained and will continue to be gained via research use of these materials; 3) the responsibility, explicit or implicit, that an individual has to contribute to this common good, especially if risks are minimal; and 4) the serious threat posed to the continuation of these critical research efforts by unnecessarily restrictive policies.

About this Report

In response to its original charge to consider "issues in the management and use of genetic information, including but not limited to human gene patenting," NBAC chose to first

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Division of AIDS, to NBAC on December 9, 1997.

consider the research use of human biological materials because the issue is relatively well defined, clearly important, and the focus of a great deal of current interest. There are four basic premises underlying the framework of analysis used by NBAC in the development of its recommendations:

- First, the people who provide for research human biological materials should be protected and respected.
- Second, research use of human biological materials is essential to the advancement of science and human health, therefore it is crucial that there be permissible and clearly defined conditions under which such materials can be used.
- Third, the rapidly advancing Human Genome Project and associated technologies, and the application of a molecular-based approach to understanding human disease have raised issues of autonomy and medical privacy. These issues have relevancy to all areas of medical research, not solely genetic research, using human biological materials.
- Fourth, there is disagreement within the scientific community about the nature of risks to individuals and levels and types of protections needed to ensure that biological samples can be used in research with minimal risks to those whose materials are used.

NBAC organized its assessment of the conditions under which research using human biological materials should be permitted around five considerations: 1) whether the materials were already collected and stored, or are to be collected in the future; 2) the conditions under which the materials were/are collected (e.g., clinical versus research setting); 3) whether the research sample used can be linked by anyone (or any combination of people) to the donor; 4) whether the risks posed by the research affect individuals, communities, or both; and 5) the types of protections that might be employed to protect against harms (specifically, measures to protect against invasions of privacy or discrimination, such as coding schemes, individual informed consent, community consultation, and prior review and approval by an IRB).

In reviewing these issues, NBAC relied on the existing regulatory framework governing federally sponsored research involving human subjects, 45 CFR 46, or the "Common Rule." It was felt that because the large and diverse community of biomedical scientists are already familiar with these regulations and because NBAC is also more generally charged with the task of reviewing the adequacy of the federal system of protections for research involving human subjects, the Common Rule serves as a useful framework under which to construct an analysis.

Organization of the Report

To assist it in its deliberations NBAC reviewed relevant scientific, ethical, religious, legal, and policy literature, commissioned scholarly papers on several topics relevant to its tasks, and invited members of the public and representatives of professional and consumer organizations to provide written and verbal testimony (see Appendix D). In addition, NBAC posted staff drafts of this report on its website (www.bioethics.gov) and solicited public comments.

To date, there has been a paucity of information concerning acquisition, use, and storage of human biological materials. There is, for example, no central database that captures information about stored materials. To assist in its review, NBAC commissioned a study to assess the magnitude and characteristics of the existing collections of human biological materials. Chapter 2 and Appendix B summarize what is known about storage and use of such materials, including where they are stored, the size of collections, and the sources and uses of the material. It also provides background on the various research uses of human biological materials and provides a schema for classifying the status of human biological materials according to their linkage to the source of these materials.

Chapter 3 summarizes the existing federal regulations governing use of human biological samples in research. (The regulations are also presented in their entirety in Appendix A.) When NBAC began its review of the use of human biological materials in research, it was aware that a

number of scientific and medical organizations had done thoughtful work on the issue. Several of these organizations have developed position statements and recommendations reflecting their efforts to work through the many ethical and policy issues the topic raises. To gain an understanding of the range of positions that exist among organizations that have carefully considered this subject, NBAC conducted a comparative analysis of these statements as they applied to the issue of protections for the appropriate use of human biological materials in research. This analysis is also found in Chapter 3, as is a description of efforts in other countries to address these issues.

NBAC believes that any set of recommendations in this area must be informed by ethical considerations. Chapter 4 reviews the central considerations for policy on the research use of biological materials. It aims to articulate in a systematic way the moral considerations that ought to be taken into account when developing policies about the collection, storage, and use of human biological materials.

Chapter 5 synthesizes the various policy issues that emerge from the preceding chapters and offers recommendations for the future.

Finally, the Commission valued the input from members of the American public, those who are not clinicians, medical researchers, or ethical experts, regarding the use of human biological materials. In addition to hearing public testimony at each of its meetings on this topic, NBAC convened seven discussion fora held across the country to obtain a sense of what Americans believe and feel about uses of such materials, about the ethical obligations of those who may learn significant health risk information from the research use of such samples, and about privacy protections. Input from all these sources assisted the Commission as it deliberated. Findings from the forums are summarized in Appendix C.

Chapter 1 References

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