

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

## 1 **Chapter 1** 3 **Overview and Introduction**

---

4  
5 Biomedical researchers have long studied human biological material—such as cells collected in  
6 research projects, biopsy specimens obtained for diagnostic purposes, and organs and tissues  
7 removed during surgery—to increase knowledge about human disease and to provide better  
8 means of prevention, diagnosis, and treatment. Today, new technologies and advances in  
9 biology provide even more effective tools for using such resources to improve medicine's  
10 diagnostic and therapeutic capacities. Human biological materials also constitute an invaluable  
11 source of information for public health planning and programming, through disease surveillance  
12 and studies of disease incidence and prevalence.

13  
14 Yet the very power of the technology raises important and difficult ethical issues. Is it  
15 appropriate to use stored biological material in ways originally contemplated neither by the  
16 people from whom the material came nor by those who collected the material? Does it matter  
17 whether the material is identified, or identifiable, as to its source or is linked, or linkable, to other  
18 medical or personal data about the source? Based on past research with human biological  
19 material, proponents argue that future studies will also benefit millions of people. How should  
20 this prospect be weighed against the risk that the studies could harm or wrong the individuals  
21 whose material is being studied or the families or other groups of which they are members?  
22 Under what circumstances should researchers seek informed consent from people whose

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 biological samples they are studying? How ought consent requirements be adjusted if the  
2 sources of the biological material would be difficult or impossible to locate or if they have died?

3

#### 4 **THE RESEARCH VALUE OF HUMAN BIOLOGICAL MATERIALS**

5

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

18

---

<sup>1</sup> 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. The Commission believes that this distinction becomes important when considering the applicability and adequacy of the existing federal protections for human subjects.

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1           In this report, human biological material is defined to encompass the full range of  
2 specimens, from subcellular structures like DNA, to cells, tissues (e.g. blood, bone, muscle,  
3 connective tissue and skin), organs (e.g., liver, bladder, heart, kidney, placenta), gametes (e.g.,  
4 sperm and ova), embryos, fetal tissues, and waste (e.g., hair, nail clippings, urine, feces, sweat,  
5 and shed skin cells).<sup>2</sup> The most common source of these materials is from diagnostic or  
6 therapeutic interventions in which tissue or other material is taken to determine the nature and  
7 extent of a disease or to remove diseased tissue. Even after the diagnosis or treatment is  
8 complete, it is routine to retain a portion of the specimen for future clinical, research, or legal  
9 purposes. Specimens are also taken during autopsies that are performed to establish the cause of  
10 death. In addition, volunteers donate organs, blood or other tissue for transplantation or research,  
11 and some donate their bodies after death for transplantation of organs or anatomical studies.  
12 Each specimen may be stored in multiple forms, such as slides, paraffin blocks, formalin-fixed,  
13 tissue culture, or extracted DNA. Repositories provide commercial and noncommercial  
14 laboratories with access to specimens for medical and research purposes.  
15

---

<sup>2</sup> Due to the fact that research using embryonic tissue is prohibited from federal funding, the current regulations do not apply to such research, and their use is not specifically discussed in this report. Should the moratorium be lifted, many of the issues addressed in this report would be relevant; additional ethical considerations might apply.

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1           In addition to its future clinical use, a specimen of human biological material can be used  
2 to study basic biology or disease. It can be examined to determine its normal and abnormal  
3 attributes or it can be manipulated to develop a research tool or potentially marketable product  
4 (OTA, 1987). Just as a clinician will choose a biological material appropriate to the medical  
5 situation at hand, a researcher's choice of such materials depends on the goals of the research  
6 project. The selected tissue can be used just once, or alternatively used to generate a renewable  
7 source of material, such as by developing a cell line, a cloned gene, or a gene marker. In  
8 addition, proteins can be extracted, or DNA isolated, from specimens.

9  
10           There is substantial research value both in unidentified material (*i.e.*, not linked to an  
11 individual or his or her on-going medical records) and in material linked to an identifiable person  
12 and his or her continuing medical records. In the former, the value to the researcher of the  
13 human biological material is in the tissue itself and often the attached clinical information about  
14 that individual, without need to know the identity of the person from whom it came. For  
15 example, investigators may be interested in identifying a biological marker in a specific type of  
16 tissue, for example, cells from individuals with Alzheimer disease or specific tumors. In such  
17 cases, beyond knowing the diagnosis of the individual from whom the specimen was obtained,  
18 researchers may not need more detailed medical records, either past or on going.

19  
20           Sometimes, however, it is necessary to identify the source of the research sample,  
21 because the value of the material for research depends on linking findings about the biology of

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 the sample with updated information from medical or other records about its source. For  
2 example, in a longitudinal study to determine the validity of a genetic marker as a predictor of  
3 certain diseases, the researchers would need to be able to link each sample with the on-going  
4 medical records of its source in order to ascertain whether those diseases developed. A recent  
5 study of late-onset Alzheimer Disease linked the presence of the disease with the apolipoprotein-  
6 E allele by studying the stored tissues of 58 families with a history of Alzheimer Disease and  
7 then obtaining autopsy records of those individuals whose tissue revealed the presence of that  
8 allele (Payami, 1996). Already, findings from research on biological materials have produced  
9 tests to diagnose predisposition to conditions such as cancer, heart diseases, and a variety of  
10 familial diseases that affect millions of individuals. In some cases, prevention or treatment is  
11 available once a diagnosis is made; in those cases, knowing the identity of the specimen sources  
12 would permit making them aware of medical information of potential importance to their health.  
13 In other cases, when medical interventions are not available, having one's specimen linked with  
14 a disease predictor is likely to be of less value to the individual.

15

16 Human biological materials also may be used for quality control in healthcare delivery,  
17 particularly in diagnostic and pathologic laboratories. Other uses include identification of an  
18 individual, such as in paternity testing, cases of abduction or soldiers missing in action, and other  
19 forensic purposes where biological evidence is available for comparison. The advent of  
20 technologies that can extract a wide array of information from these materials has generally

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 increased the potential uses, in research and otherwise, of human biological materials that are  
2 unrelated to individual patient care.

3

4 Through the power of new DNA technologies and other new molecular techniques  
5 scientists can potentially turn to millions of stored human biological materials as sources of  
6 valuable scientific, medical, anthropological, and sociological information. Indeed, these  
7 technologies are so powerful—even revolutionary—that they also hold the ability to uncover  
8 knowledge about individuals no longer alive and for those yet to be born. For example, in 1997  
9 scientists at University of Oxford in England announced that they had compared DNA extracted  
10 from the molar cavity of a 9,000-year-old skeleton, known as Cheddar Man, to DNA collected  
11 from 20 individuals currently residing in the village of Cheddar and established a genetic tie  
12 between the skeleton and a schoolteacher who lived just half a mile from the cave where the  
13 bones were found. Similarly, scientists have used enzyme-linked assays to analyze tissues more  
14 than 5,000 years old to track the historic spread of diseases such as malaria and schistosomiasis,  
15 obtaining knowledge that can enlighten current efforts to control infectious disease (Egyptian  
16 Mummy Tissue Bank, 1997). This ability means that human tissue and DNA specimens that  
17 have been sitting in storage banks for years—even a century—could be plumbed for new  
18 information to reveal something not only about the individual from whom the tissue was  
19 obtained, but possibly about entire groups of people who share genes, environmental exposures,  
20 racial, ethnic, or even geographic characteristics. Clearly the same is true for collections of such  
21 material that may be collected in the future. DNA, whether already stored or still to be collected,

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 can be used to study genetic variation among people, to establish relationships between genes  
2 and characteristics, such as single gene disorders, or more generally, to conduct basic studies of  
3 the cause and progression of disease, all with the long-term goal of improving human health.  
4 Providing information towards this goal is the federally funded Human Genome Project, which  
5 expects to map and sequence the entire human genome by 2005 (Collins, 1993).

6

## 7 **GENETIC INFORMATION**

8

9 Genetic information is one form of biological or medical information. Like certain other  
10 types of medical information, genetic analyses can reveal sensitive information about an  
11 individual. Further, genetic information concerning an individual can sometimes reveal similar  
12 information about a person's relatives or entire groups of people (Knoppers, 1997).

13

14 In some instances, genetic and other biological information can indicate a risk for  
15 developing certain diseases (e.g., predisposition to cancer or likelihood of developing heart  
16 disease). This is also true, of course, for other types of medical information. At present,  
17 however, the detailed information contained in a person's genes is largely unknown to that  
18 person. Moreover, because DNA is stable, stored samples can become the source of increasing  
19 amounts of information as new genes are mapped (Annas, 1995). In the words of Francis  
20 Collins, Director of the National Human Genome Research Institute, "we are hurtling towards a  
21 time where individual susceptibilities will be determinable on the basis of technologies that

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 allow your DNA sequence to be sampled and statistical predictions to be made about your future  
2 risk of illness” (NBAC transcript, October 4, 1996, pp. 129-130).

3

4 For these reasons, some observers have concluded that genetic information is a unique  
5 form of biological and medical information. They claim that the major distinguishing  
6 characteristics of genetic information are its predictiveness and its implications for individuals  
7 other than the person from which the information was derived (IOM, 1994). Gostin, for  
8 example, has suggested that “genomic” data are qualitatively different from other health data  
9 because they are inherently linked to one person, that is, one’s DNA is unique except in the case  
10 of identical twins (Gostin, 1995).

11

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

19

20 Nevertheless, public discourse and concern about the potential availability of personal  
21 genetic information has been intense in recent years for a number of reasons, including: 1) its

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 early beginnings in reproductive medicine and family planning; 2) a history of eugenics and  
2 genetic discrimination; 3) because of the unknown power of these new technologies; 4) because  
3 of the rapid pace of the Human Genome Project and its associated spin-offs; and 5) because  
4 people may fear the lack of any protection from the misuse of this information outside the  
5 research context.

6

7       Recently scientific and medical organizations have also dedicated a great deal of attention  
8 to the appropriate protocols for gaining access to the use of genetic information that can be  
9 derived from collections of human biological materials. The growing number of position  
10 statements and recommendations issued by scientific and medical organizations regarding the  
11 use of human biological materials in research reflects this recent focus (see Chapter 4). Their  
12 efforts to work through complex ethical and policy issues have been valuable and have provided  
13 NBAC with an understanding of the range of positions existing among such organizations.

14

#### 15 **GROWING CONCERNS ABOUT THE RESEARCH USE OF HUMAN BIOLOGICAL MATERIAL**

16

17       The increasing use of genetic information about individuals has fueled a recent debate  
18 about genetic privacy and discrimination. While medical research is generally considered a  
19 public good and is vigorously supported by the American public, the power of DNA-based  
20 technologies to find an extraordinary amount of detailed information in a single cell raises the  
21 specter that information about individuals will be discovered and used without their consent and

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 possibly to their detriment. The use of such information may result in potential loss of insurance,  
2 employment, or dramatically affect life choices (Powers, 1994). Although this type of  
3 information might also be obtained through a variety of other means, DNA analysis currently is  
4 the most powerful and increasingly will be the method of choice.

5  
6 The cases at the center of the current debate usually involve single-gene, highly penetrant  
7 disorders of medically severe or socially stigmatizing natures, which are not symptomatically  
8 apparent at the time of the analysis. In the future, however, the majority of cases will deal with  
9 polygenic, multifactorial disease whose genetic status will, at best, provide a probabilistic  
10 estimate of the likelihood of disease manifestation. In recent years these various concerns have  
11 caused consumer, scientific and professional groups to begin to address the issues surrounding  
12 the collection and use of human biological materials. (AAMC, 1997; ASHG, 1987; 1997;  
13 ACMG, 1995; HUGO, 1998; Pathologists, 1997).

14  
15 Media focus on highly contentious cases using biological samples, such as the use of  
16 stored neonatal blood spots for anonymous studies of HIV prevalence in a given population, and  
17 efforts by the military to establish a DNA databank, have made the issue of research use of  
18 human biological materials a matter of increasing public concern. In the course of its  
19 deliberations, NBAC identified several trends that are contributing to the need for the  
20 consideration of a more comprehensive public policy concerning the use of these biological  
21 materials for research purposes:

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

- 1 • increasing public concern that personal genetic and other medical information could be used
- 2 to discriminate against individuals in employment or access to benefits such as health or life
- 3 insurance, or could be stigmatizing in some way;
- 4 • growing public concern about privacy of all medical records;
- 5 • increasing awareness in the medical and scientific communities regarding beliefs about the
- 6 moral status of bodies and their parts;
- 7 • the emergence of new considerations regarding both the nature of consent to participate in
- 8 research protocols and disclosure of results;
- 9 • disagreement among scientific and medical groups about conditions that need to be satisfied
- 10 to ensure ethical research to insure the appropriate use of human biological materials, namely
- 11 requirements for review and the nature of the required consent process.

12

### 13 **Concerns about Discrimination and Stigmatization**

14

15       There is growing recognition that human biological materials can be analyzed to ascertain

16 significant amounts of genetic information about the person from whom the sample was

17 obtained. Thus, there is increasing concern that genetic and other medical information could be

18 used to discriminate against individuals in insurance and employment and could be stigmatizing

19 for individuals and families (Cohen, 1995; Hudson, 1995; NIH-DOE Working Group, 1993). In

20 March 1998, the White House released a report prepared by the U.S. Departments of Labor,

21 Health and Human Services, and the Equal Employment Opportunity Commission, *Genetic*

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 *Information and the Workplace*, which predicted that by the year 2000, 15 percent of employers  
2 plan to check the genetic status of prospective employees and cites a 1995 Harris poll, which  
3 revealed that more than 85 percent of Americans are concerned that insurers and employers may  
4 have access to their genetic information.

5  
6 One particular area of concern centers on whether the information that can be obtained  
7 from the research use of human biological materials places those who are the sources of the  
8 samples at unacceptable risk. Such data might reveal, for example, information about an  
9 individual's disease susceptibility (e.g., carrying a gene that is associated with an increased risk  
10 of colon cancer or breast cancer). When there is an intervention that can be pursued to  
11 counteract the increased health risk, such as regular mammograms, dietary modification, or drug  
12 treatment, some might perceive the information worth receiving and worth the psychological and  
13 financial risks associated with the information. If, however, the analysis reveals information for  
14 which no intervention is currently available (e.g., susceptibility to Huntington's disease or  
15 Alzheimer's disease), many individuals might perceive the risks of uncovering such information  
16 as outweighing the benefits. In any case, concern may arise when an individual did not consent,  
17 in advance, or show any interest in receiving such information. Many would agree that finding  
18 out about an adverse health status should be done knowingly and willingly since it can provoke  
19 anxiety and disrupt families, particularly if nothing can be done about it and the finding has  
20 potential implications for other family members (Wilcke, 1998).

21

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1           Concern about insurers and employers having access to genetic information has a basis in  
2 fact. In the 1970s several insurance companies and employers discriminated against sickle cell  
3 carriers, even though their carrier status did not and would not affect their health (Holtzman,  
4 1989). In the absence of guaranteed access to health care or laws that prevent discrimination on  
5 the basis of health status there persists a real concern that medical information may be used to  
6 deny individuals insurance or jobs (OTA, 1990; NCHGR, 1993). In addition to these possible  
7 financial harms, research findings about one's future medical status can, in some cases, inflict  
8 psychological or social harms (Davison, 1994).

## 10 **Privacy of Medical Records**

11  
12           Health care systems increasingly rely on information technology, such as electronic  
13 records, to manage and facilitate the flow of sensitive health information. This has had positive  
14 effects in clinical practice, but these trends also magnify concerns about privacy of certain  
15 genetic and other medical information. Recent debates about privacy of medical records and  
16 attempts to protect privacy through legislation are evidence of the growing public concern about  
17 these issues.

18  
19           An ongoing concern in medical care and in the protection of research subjects is the  
20 potential invasion of privacy or compromise of confidentiality. Measures to provide appropriate  
21 protections to both individual privacy and for the confidentiality of clinical and research data are

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 important if research is to continue. When research samples are identifiable, that is, linked to the  
2 person who provides them, steps must be taken to ensure protections in the collection, storage,  
3 and use of the data. However, computerized medical records and large informatics databases  
4 raise concerns about who has access to data (i.e., the security of these data bases) and whether or  
5 not these data are linked to individual patient records. Many people distrust computer  
6 technology and large, bureaucratic record keeping systems, and it is widely believed that current  
7 confidentiality practices are insufficient to safeguard medical information. In addition, different  
8 cultural and religious groups may have differing conceptions of what constitutes privacy or  
9 confidentiality (Tri-Council, 1997).

10

11 Many privacy issues can emanate from the research analysis of human biological  
12 materials since the information contained in these samples can affect individuals or groups of  
13 people (Foster, 1997). Moreover many of the privacy concerns arise within the context of  
14 "secondary use" of the samples collected. "Secondary use" means that the samples and the  
15 information derived from them are being used or analyzed for purposes that extend beyond the  
16 purpose for which the specimens were originally collected (Alpert, 1997). For instance, when  
17 materials are collected during surgical procedures and used solely for clinical purposes, the  
18 clinical use of these specimens raise very few privacy concerns (beyond concerns about the  
19 confidentiality of the medical record itself, which are by no means trivial). This is because they  
20 are being examined for the primary purpose of determining appropriate medical care for an  
21 individual, and because the custodian of that biological specimen does not allow others access to

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 it. It is only when the use of such specimens extends beyond the original clinical use that the  
2 majority of these privacy issues are raised. For example, if a sample is used as part of a research  
3 study into familial linkage of a specific disease, and the family pedigree is published as a result  
4 of the study, an individual might be easily identifiable even without any names attached to the  
5 pedigree (Botkin, 1998).

### 7 **Moral Status of Bodies and Body Parts**

8  
9       There is increasing awareness in the medical and scientific communities regarding beliefs  
10 about the moral status of human bodies and their parts (Andrews, 1998). The use of human  
11 biological materials in research can raise ethical and religious issues about the relationships  
12 among body parts, bodies, and self-identity. However, many important ethical and religious  
13 traditions do not provide clear guidance about the ways in which human tissues should be used  
14 or obtained. Although there are variations among them, selected Western religious traditions  
15 offer some insight about the significance of the human body and they generally favor the transfer  
16 of human biological materials as gifts (Campbell, 1997). As such, human tissues would warrant  
17 some measure of respect, which is the basis often expressed for restricting sales of human tissues  
18 and organs. But cultural differences can be significant because of the different symbolic nature  
19 or sacrality they attach to specific body parts or tissues (Campbell, 1997).

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

## 1 **Nature of Consent to Research Participation**

2

3           New considerations have emerged regarding both the nature of the consent to participate  
4 in research protocols and disclosure of results. Informed consent is one mechanism for  
5 protecting individuals from unanticipated medical and research harms. It is widely accepted and  
6 expressed in federal regulations that informed consent must be obtained for research projects that  
7 involve the direct involvement of research subjects. Researchers are required to disclose the  
8 purpose of a study, as well as potential benefits and risks, before enrolling subjects. For research  
9 involving archived human biological materials, the role of informed consent has been much less  
10 clear. The use of genetic and other new technologies to study human biological materials  
11 presents several problems for the consent process—particularly if the material is linked to a  
12 specific individual: 1) the full research uses of the material may be unknown and unanticipated at  
13 the time of collection; 2) the analyses can provide information that may lead to stigmatization,  
14 discrimination, or psychosocial problems for an entire category of persons defined by shared  
15 characteristics (Foster, 1997); and 3) the study may generate ambiguous results, tempting for  
16 clinical use but not really ready for reliable application (Reilly, 1980). In addition, physicians  
17 have not customarily sought patient's explicit, informed consent to permit the use of pathology  
18 specimens for specific research purposes; instead, permission to use stored material for other  
19 than clinical purposes has been general, that is, granted with the understanding that such use is  
20 merely a possibility. Once stored, the materials have been available for research, usually without  
21 the knowledge or consent of the sources, particularly if unidentifiable.

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1           According to the federal regulations governing research with human subjects (45 C.F.R.  
2 46), research with stored DNA and tissue has been exempted from review by Institutional  
3 Review Boards (IRBs) and from requirements for prior informed consent when:

- 4           1) the samples are existing at the time the research is proposed; and
- 5           2) either the sources are publicly available or information is recorded by the investigator  
6           in such a manner that subjects cannot be identified, directly or through identifiers  
7           linked to the subjects

8  
9           Alternatively, research with stored, identifiable samples conducted in a manner such that  
10 the source of the specimen can be identified may be permitted by an IRB with a waiver or  
11 modification of informed consent if *all* of the following conditions are met:

- 12          1) The research presents only minimal risk to subjects;
- 13          2) The waiver of consent will not adversely affect the rights or welfare of subjects;
- 14          3) The research could not practicably be carried out without the waiver; and
- 15          4) That subjects will be provided with information about their participation afterwards,  
16          when appropriate.

17  
18           Contention surrounds the question of who defines and determines what constitutes  
19 “minimal risk.” (Merz, 1996). Some analysts believe that certain genetic research (e.g., on a  
20 stigmatizing genetic predisposition to a disease, such as alcoholism or schizophrenia) surpasses  
21 minimal risk and should, therefore, not qualify for expedited, or be exempt from, IRB review.

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 Because in such cases the perceived risks appear to be significant, many observers, including  
2 some consumer and scientific groups, have called for increased attention to the consent process  
3 pertaining to human DNA and tissues (Clayton, 1996).

4

5 How specific do the consent documents need to be with respect to materials collected in a  
6 clinical context? How detailed should disclosure be about the intended purposes of subsequent  
7 research studies with stored materials? How much information should be provided to patients in  
8 clinical settings about the possibility of post-diagnostic research on stored materials? These  
9 questions are likely to have different answers depending on whether the specimen has already  
10 been collected or if it will be collected in the future, and whether the materials was initially taken  
11 as part of medical treatment or a research protocol. It stands to reason that a person's rights and  
12 interests are only truly protected if that person has some form of control over her/his removed  
13 biological materials, especially if it remains identifiable. That control may be best achieved by  
14 an improved consent process but can rarely be absolute.

15

16 Informed consent is a process, the effectiveness of which has been widely debated, and  
17 many agree can be improved. Discussions about its relative value in clinical and research  
18 settings are by no means unique to genetics or the issue of human biological materials. What  
19 people are told, what they understand, and what they remember when consent is sought is likely  
20 to vary as much when providing DNA or tissue as when consenting to medical interventions.  
21 When human biological material is stored, people may not understand, for example, that it might

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 be used for research unrelated to their own disease status. When told a sample is being kept “for  
2 research,” a patient may believe the samples will be used only for research related to his or her  
3 own condition. Patients may not realize that federal and state regulations require that specimens  
4 be stored for a certain length of time. In most cases, the repositories where specimens are stored  
5 were designed for a particular purpose, and the protocols and procedures might not have  
6 addressed issues regarding access, destruction, or future uses of the materials, such as for  
7 research (Merz, 1997). Finally, the use of human biological materials raises subtle but  
8 significant distinctions in the applicability of federal regulations, the review of research  
9 protocols, and obtaining consent, if the sources of materials can be patients, volunteer research  
10 subjects, or cadavers. In addition, determining whether a person is a patient or research subject  
11 is relevant, for example, in determining the applicability of Federal regulations governing  
12 federally funded research using human biological materials (OTA, 1987).

13

14 Finally, information obtained through research may have implications for families,  
15 groups, and others. For example, because certain genetic research may reveal information about  
16 the family and community of the person whose materials are studied, informed consent becomes  
17 more complex and for some it takes on new and broader meaning. Recently, the concept of  
18 community consultation in research with human subjects has received increasing attention.  
19 NBAC heard testimony from the National Institute of Allergy and Infectious Diseases (NIAID)  
20 about the essential nature of community involvement in NIAID's AIDS clinical trials.<sup>3</sup>

---

<sup>3</sup> Presentation by John Y. Killen, M.D., Director of the NIAID Division of AIDS, to NBAC on December 9, 1997.

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 Representatives of the community of participants in those research studies participated in the  
2 entire research process, from the formulation of ideas through the design of the studies,  
3 recruitment at a community level, and the execution and analysis of the research itself. It was  
4 concluded that such participation provided invaluable benefits to the research.

5  
6 The Centers for Disease Control and Prevention (CDC) has recognized the growing role  
7 of community involvement in public health initiatives, establishing a Committee for Community  
8 Engagement to consider a growing body of literature reflecting the experiences of those involved  
9 in engaging individuals and organizations in communities across the country. While community  
10 engagement increasingly has become a basic element of health promotion, health protection, and  
11 disease prevention, to date the only formalized procedures for seeking community involvement  
12 in research with human subjects exist in federal regulations governing informed consent  
13 procedures when research subjects are enrolled in studies under emergent circumstances. These  
14 regulations pertain to: (1) research subject to regulations codified by the Food and Drug  
15 Administration (FDA) and carried out under an FDA investigational new drug application (IND)  
16 or investigational device exemption (IDE), (see Title 21 C.F.R. Part 50); and (2) research for  
17 which the Secretary of Health and Human Services has waived the general requirements for  
18 informed consent (at 45 C.F.R. 46.116(a), (b), and 46.408). The regulations provide for  
19 consultation (including, where appropriate, consultation carried out by the IRB) with  
20 representatives of the communities in which the research (or clinical investigation, in the case of  
21 the FDA regulations) will be conducted and from which the subjects will be drawn. Moreover,

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 public disclosure of plans for the research and its risks and expected benefits is required of  
2 investigators prior to initiation of the research. Finally, public disclosure of information  
3 regarding the study is required following its completion.

4

### 5 **Conflicting Guidance Regarding Research Use of Human Biological Materials**

6

7 There is disagreement among scientific and medical groups about the conditions that  
8 need to be satisfied to ensure the ethical research use of human biological materials, particularly  
9 with respect to requirements for IRB review, and the nature of the required consent process.

10

11 With the great promise that new scientific developments hold and the increased value and  
12 importance of human biological material comes greater responsibilities for scientists and policy  
13 makers. From available public statements it seems that the scientific community often disagrees  
14 about how to insure the appropriate respect for persons as well as their biological material and  
15 yet to also benefit health and medical research. Within the past few years, many professional  
16 societies have issued policy statements regarding their views on these issues and on the  
17 appropriate use of these materials in the context of genetic research. The sheer variety of  
18 thoughtful approaches suggested is an indication that consensus on how to resolve the difficult  
19 challenges that genetic analysis raises has been difficult to achieve.

20

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1           A stable consensus must strike a balance between the desire to increase knowledge and  
2 the necessity of appropriately protecting individual interests. There need not be a dialectic  
3 between two positions. On the one hand there are those who think that emphasis should be  
4 placed on the distinctive importance of personal and familial information, the right of personal  
5 choice about the use of one's body and the information inherent in the materials taken from it,  
6 and the necessity of being able to exercise a measure of control over the research that can be  
7 done with one's DNA and tissues. On the other hand are those who think that in an era of  
8 increasing professional and legal regulations and emphasis on individual autonomy, renewed  
9 consideration must be given to the invaluable and often irreplaceable research resource, the  
10 inestimable societal and individual benefits that have been gained by means of biomedical  
11 research done with these samples, the responsibility, explicit or implied, that an individual has to  
12 contribute to this common good, and the serious threat posed to the continuation of these  
13 research efforts by unnecessarily restrictive policies.

14

#### 15 **ABOUT THIS REPORT**

16

17           In response to its original charge to consider "issues in the management and use of  
18 genetic information, including but not limited to human gene patenting," NBAC formed a  
19 Genetics Subcommittee to address such issues. The subcommittee met for the first time in  
20 December 1996 to set priorities for the upcoming year and chose initially to pursue three topics:  
21 1) the research use of human biological material; 2) genetic privacy and genetic discrimination;

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 and 3) gene patenting. The research use of human biological material was chosen as the first  
2 topic because the issue is relatively well defined, clearly important, and the focus of a great deal  
3 of current interest.

4

5 There are three basic premises underlying the framework of analysis used by the  
6 Commission in the development of its recommendations:

7  First, research use of human biological materials is essential to the advancement of  
8 science and human health. Therefore, it is crucial that there be permissible and clearly  
9 defined conditions under which such materials can be used.

10  Second, the rapidly advancing Human Genome Project and associated technologies, and  
11 the application of a molecular-based approach to understanding human disease have  
12 raised new issues of autonomy and medical privacy. These issues have relevancy to all  
13 areas of medical research, not solely genetic research, using human biological materials.

14  Third, there is disagreement within the scientific community about the nature of risks to  
15 individuals and levels and types of protections needed to ensure that biological samples  
16 can be used in research with minimal harms for those whose materials are used.

17

## 18 **Framework for Analysis**

19

20 The Commission organized its assessment of the conditions under which research using  
21 human biological materials should be permitted around five considerations: 1) whether the

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 samples were already collected and stored, or are to be collected in the future; 2) the conditions  
2 under which the materials were/are collected (e.g., clinical versus research setting); 3) whether  
3 the research sample used can be linked by anyone (or any combination of people) to the donor;  
4 4) whether the risks posed by the research affect individuals, communities, or both; and 5) the  
5 types of protections that might be employed to protect against harms (specifically, coding  
6 schemes, individual informed consent, community consultation, and prior review and approval  
7 by Institutional Review Boards).

8

## 9 **Organization of the Report**

10

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

17

18 To date, there has been a paucity of information concerning acquisition, use, and storage  
19 of human biological materials; there is no central database that captures information about stored  
20 materials. To assist in its review, NBAC commissioned a study to assess the magnitude and  
21 characteristics of the existing archives of DNA and tissues. Chapter 2 describes what is known

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1 about storage and use of such materials, including where they are stored, the size of collections,  
2 and the sources and uses of the material. It also provides background on the various research  
3 uses of human biological materials and provides a schema for classifying the status of human  
4 biological materials according to their linkage to the source.

5

6 NBAC believes that any set of recommendations in this area must be informed by certain  
7 ethical considerations. Chapter 3 reviews several of these considerations necessary for  
8 deliberations about policy for the research use of biological samples. It aims to articulate in a  
9 systematic way the various kinds of moral considerations that ought to be taken into account  
10 when developing policies about the collection, storage, and use of human biological materials.

11

12 Chapter 4 describes the existing federal regulations governing use of human biological  
13 samples in research. When NBAC began its review of the use of human biological materials in  
14 research, it was aware that a number of scientific and medical organizations had done thoughtful  
15 work on the issue. A number of these organizations have developed position statements and  
16 recommendations that reflected their efforts to work through the many ethical and policy issues  
17 the topic raises. To gain an understanding of the range of positions that exist among  
18 organizations which have carefully considered this subject, NBAC conducted a comparative  
19 analysis of these statements as they applied to the issue of protections for the appropriate use of  
20 human biological materials in research. This analysis is also found in Chapter 4, as is a  
21 description of international activities.

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

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

3

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

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

1   **REFERENCES**

- 2
- 3   1. Alpert, S., "Privacy and the Analysis of Stored Tissues," background paper prepared for the  
4       National Bioethics Advisory Commission, December 1997.
- 5
- 6   2. American Association of Medical Colleges Executive Council, *Medical Records and Genetic*  
7       *Privacy, Health Data Security, Patient Privacy, and the Use of Archival Patient Materials in*  
8       *Research*, 1997.
- 9   3. American Society of Human Genetics. Ad Hoc Committee on DNA Technology. "DNA  
10       Banking and DNA Analysis: Points to Consider." *American Journal of Human Genetics* 42  
11       (No. 5, May 1988): 781-783. Adopted October 9, 1987.
- 12   4. American Society of Human Genetics, "Statement on Informed Consent for Genetic  
13       Research," *American Journal of Human Genetics* 59:471-474, 1996.
- 14   5. American College of Medical Genetics Storage of Genetics Materials Committee, "Statement  
15       on Storage and Use of Genetic Materials," 1995.
- 16   6. Andrews, L. and D. Nelkin, "Whose Body is it Anyway? Disputes over Body Tissue in a  
17       Biotechnology Age," *The Lancet* 351:53-57, January 3, 1998.
- 18   7. Annas, G.J., "Drafting the Genetic Privacy Act: Science, Policy, and Practical  
19       Considerations," *Journal of Law and Medical Ethics* 23:360-366, 1995.
- 20
- 21   8. Botkin, J.R., W.M. McMahon, K.R. Smith and J.E. Nash. "Privacy and Confidentiality in the  
22       Publication of Pedigrees: A Survey of Investigators and Biomedical Journals," *Journal of the*  
23       *American Medical Association* 279(22):1808-1812, June 10, 1998.
- 24
- 25   9. Campbell, C., "Research on Human Tissues: Religious Perspectives," background paper  
26       prepared for the National Bioethics Advisory Commission, October 1997.
- 27
- 28   10. Clayton, E.W., Steinberg, K.K., Khoury, M.J., Thomson, E., Andrews, L., Kahn, M.J.E.,  
29       Kopelman, L.M., and J.O. Weiss, "Informed Consent for Genetic Research on Stored Tissue  
30       Samples," *Journal of the American Medical Association* 274:1786-1792, 1995.
- 31   11. Cohen, M.M., "Genetic Testing and Insurance," *American Journal of Human Genetics*  
32       56:327-331, 1995.
- 33   12. Collins, F.S., and D. Galas, "A New Five-Year Plan for the U.S. Human Genome Program,"  
34       *Science* 262:43-46, 1993.
- 35

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

- 1 13. Davison, C., Macintyre, Smith, G.D., "The Potential Social Impact of Predictive Genetic  
2 Testing for Susceptibility to Common Chronic Disease: A Review and Proposed Research  
3 Agenda," *Soc. Health Illness* 16:540-571, 1994.  
4
- 5 14. Egyptian Mummy Tissue Bank, 1997, [www.mcc.ac.uk/~mellorir/museum/general/mummy](http://www.mcc.ac.uk/~mellorir/museum/general/mummy).  
6
- 7 15. Foster, M.W., Eisenbraun, A.J., Carter, T.H., "Communal Discourse as a Supplement to  
8 Informed Consent for Genetic Research," *Nature Genetics* 17:277-279, 1997.1997.  
9
- 10 16. Gostin, L.O., "Health Information Privacy," 80 *Cornell Law Review* 451, 1995.  
11
- 12 17. Holtzman, N.A., *Proceed with Caution* (Baltimore, MD: Johns Hopkins University Press,  
13 1989).  
14
- 15 18. Hudson, K.L., Rothenberg, K.H., Andrews, L.B., et al., "Genetic Discrimination and Health  
16 Insurance: An Urgent Need for Reform," *Science* 270:391-393, 1995.  
17
- 18 19. Human Genome Organisation Ethics Committee, "Statement on DNA Sampling: Control and  
19 Access," 1998.
- 20 20. Institute of Medicine, *Assessing Genetic Risks* (Washington, D.C.: National Academy Press,  
21 1994).  
22
- 23 21. Knoppers, B.M., Strom, C., Clayton, E.W., et al., "Professional Disclosure of Familial  
24 Genetic Information," *American Journal of Human Genetics* 62:474-483, 1998.  
25
- 26 22. Merz, J.F., "Is Genetics Research "Minimal Risk?" *IRB: A Review of Human Subjects*  
27 *Research* 8(6):7-8, 1996.  
28
- 29 23. Murray, T., "Genetic Exceptionalism and "Future Diaries." Is Genetic Information Different  
30 from Other Medical Information?" in M. Rothstein (ed.) *Genetic Secrets* (New Haven: Yale  
31 University Press, 1997).  
32
- 33 24. NBAC transcript, October 4, 1996.  
34
- 35 25. National Center for Human Genome Research, *Genetic Information and Health Insurance:*  
36 *Report of the Task Force on Genetic Information and Insurance*, NIH Publication No. 93-  
37 3686 (Bethesda, MD: National Center for Human Genome Research, 1993.)  
38

*November 10, 1998: This is a staff draft developed for the National Bioethics Advisory Commission. It does not represent the Commission's conclusions and should not be cited or referenced as such.*

- 1 26. Payami, H., Zarepari, S., Montee, K.R., et al., "Gender Differences in Apolipoprotein E-  
2 Associated Risk for Familial Alzheimer Disease: A Possible Clue to the Higher Incidence of  
3 Alzheimer Disease in Women," *American Journal of Human Genetics* 58(4):803-811, 1996.  
4
- 5 27. Powers, M. 1994.  
6
- 7 28. "Recommended Policies for Uses of Human Tissue in Research, Education, and Quality  
8 Control," Pathologists Consensus Statement, 1997.
- 9 29. Reilly, P. "When Should an Investigator Share Raw Data with the Subjects?" IRB 2 (No. 9,  
10 November 1980): 4-5, 12.  
11
- 12 30. Reilly, P., Boshart, M., and Holtzman, S., "Ethical Issues in Genetic Research: Disclosure and  
13 Informed Consent," *Nature Genetics* 15:16-20, 1997.  
14
- 15 31. Tri-Council Working Group, *Code of Conduct for Research Involving Humans*, 1997.
- 16 32. U.S Congress, Office of Technology Assessment, *New Developments in Biotechnology:  
17 Ownership of Human Tissues and Cells*, OTA-BA-337 (Washington, D.C.: U.S. Government  
18 Printing Office, 1987).
- 19 33. U.S Congress, Office of Technology Assessment, 1990.
- 20 34. Wilcke, J.T.R., "Late Onset Genetic Disease: Where Ignorance is Bliss, is it Folly to Inform  
21 Relatives? *British Medical Journal* 1998;317:744 ( 12 September ).  
22