

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1

2 **Chapter 3**

3 **Collection and Storage of Human Biological Materials**

4 **In The United States**

5

6

7 As part of its analysis, the National Bioethics Commission sought to understand and describe the
8 magnitude and diversity of human biological material collections in the United States. To date,
9 there has been a paucity of information concerning acquisition, use, and storage of such materials;
10 there is no central database that captures information about stored samples. To assist in its
11 review, NBAC commissioned a study to assess the size and characteristics of the existing archives
12 of tissues.¹

13

14 **SOURCES AND USES OF HUMAN BIOLOGICAL MATERIALS**

15

16 The most common source of human biological material is from patients following
17 diagnostic or therapeutic procedures. Tissue specimens may also be taken during autopsies that
18 are performed to establish the cause of death. In addition, volunteers may donate blood or other

¹ These data were collected by Elisa Eiseman, Ph.D. at RAND's Critical Technologies Institute in response to a request by the NBAC Genetics Subcommittee. The report, *Stored Tissue Samples: An Inventory of Sources in the United States* (available under separate cover), is not meant to be a comprehensive inventory, however it does identify the major sources of stored tissue.

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 tissue for transplantation or research, organs for transplantation, or their bodies for anatomical
2 studies after death. Each specimen of human tissue may be stored in multiple forms, such as
3 slides, paraffin blocks, formalin fixed, frozen, tissue culture, or extracted DNA.

4
5 Once removed, human tissue may serve many beneficial purposes. The most familiar and
6 widespread use of human tissues is in the diagnosis and treatment of illness. Another common use
7 of human tissues is for quality control purposes in diagnostic and pathologic laboratories. Human
8 tissue is also used for medical and biological research, and for medical education and training.
9 Other uses of human tissue include identification of a person, such as in paternity testing, cases of
10 abduction or soldiers missing in action, and forensic purposes in crime cases where biological
11 evidence is available for comparison.

12 13 **TOTAL NUMBER OF SAMPLES**

14
15 NBAC estimates that there are over 282 million specimens from more than 176.5 million
16 cases of stored human biological materials in the United States, now accumulating at a rate of
17 over 20 million samples per year.² The size and detail of collections varies considerably, ranging
18 from formal, highly organized repositories to the informal storage of blood or tissue specimens in
19 a researcher's laboratory freezer. Archives of human biological materials range in size from less

² This report attempts to count both the numbers of cases from which stored tissues are derived as well as the number of specimens generated from each case. For example, when a patient enters the hospital for a biopsy, the resulting tissue is accessioned in the pathology department as a single case. However, that single biopsy may generate several specimens including a number of slides, a paraffin block, and a frozen sample.

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 than 200 specimens to more than 92 million.

2
3 Large collections include archived pathology samples taken during diagnostic and surgical
4 procedures, or at autopsy, and stored cards containing blood spots from newborn screening tests
5 (Guthrie cards). These samples are stored at military facilities, forensic and other DNA banks,³
6 government laboratories, diagnostic pathology and cytology laboratories, university- and hospital-
7 based research laboratories, commercial enterprises, and non-profit organizations.

8
9 The collections of these materials generally fall into the following categories:

- 10
11 • large tissue banks, repositories and core facilities;
12 • samples collected as part of longitudinal studies;
13 • research studies requiring unique tissue collections;
14 • pathology specimens;
15 • newborn screening laboratories;
16 • forensic DNA banks;
17 • umbilical cord blood banks;
18 • organ banks;

³ The term “DNA bank” refers to a facility that stores extracted DNA, transformed cell lines, frozen blood or tissue, or biological samples for future DNA analysis. Specimens are usually stored with some form of individual identification for later retrieval. DNA data banks are repositories of genetic information obtained from the analysis of DNA samples, sometimes referred to as “DNA profiles.” The genetic information is usually

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

- 1 • blood banks; and
- 2 • sperm, ovum and embryo banks.⁴

3

4 Two of the largest tissue repositories in the world, the National Pathology Repository and

5 the DNA Specimen Repository for Remains Identification, are housed within a single institution,

6 the Armed Forces Institute of Pathology (AFIP). These two repositories alone store more than

7 94 million specimens. State newborn screening laboratories collectively have archives totaling

8 more than 13 million. Finally, the pathology departments at Graduate Medical Education (GME)

9 teaching institutions collectively constitute the largest and oldest stores of tissue samples in the

10 United States, with some specimens over 100 years old.⁵ Three of these sourcesXthe AFIP

11 National Pathology Repository, GME teaching institution pathology departments, and newborn

12 screening laboratoriesXrepresent more than 265.5 million diagnostic and therapeutic specimens

13 from over 176 million cases. Although the tissue repositories supported by the National Institutes

14 of Health (NIH) are not as large as those of AFIP, NIH is one of the largest funders of tissue

15 repositories, providing over \$53 million in FY 1996.

16

stored in computerized form with individual identifiers

⁴ Due to the unique and ethically complex nature of research on gametes and embryos, their use in research is not addressed in this report.

⁵ Graduate Medical Education (GME) programs are the primary means of medical education beyond the four-year medical school training received by all physicians. Usually called residency programs, they are based in hospitals or other health care institutions, some of which do and some of which do not have formal relationships with medical schools. GME teaching institutions include medical schools, the Armed Forces hospitals, Veterans Affairs medical centers, the Public Health Service, state, county and city hospitals, non-profit

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 The vast majority of samples currently in storage were originally collected for diagnostic
2 or therapeutic reasons. Although a small percentage of these samples may be used for research,
3 educational, and quality control purposes, the vast majority is not. These collections are generally
4 referred to as “pathology samples” and have been the primary source of specimens used to date in
5 research. However, samples collected specifically for research are increasingly in demand, as they
6 are more narrowly defined, are often provided with useful clinical data, and were more likely to
7 have been collected with explicit consent to use for research purposes.

8
9 Several repositories have been established specifically for use in research. In addition,
10 several large longitudinal studies collect and bank samples from study participants. Likewise, a
11 fair amount of research simultaneously creates collections or contributes to existing banks.
12 Collectively, these special research collections contain more than 2.3 million specimens.

13
14 Other than for diagnostic, therapeutic, or research purposes, samples are collected and
15 stored for a variety of other reasons. Blood banks collect approximately 12 million units of blood
16 a year, but only about 20,000 to 40,000 units are stored at any one time. Also, most of the blood
17 collected is used for transfusions, and very little is used for other purposes, such as research and
18 quality control. Organ banks do not collect the same volume of tissue as do blood banks, but are
19 similar in that most of the organs and tissues collected are used for transplants, and very little is
20 available for research purposes. Forensic DNA banks collect and store tissues for use in criminal
21 investigations. The Department of Defense (DOD) DNA Specimen Repository and some

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 commercial DNA banks store DNA samples for remains identification. Sperm, ovum and embryo
2 banks store specimens for anonymous donation or for later use by the individual storing the
3 material. Umbilical cord blood banks also store blood for anonymous donation and later use by
4 families banking their newborn's cord blood. Table 1 summarizes sources of stored samples in the
5 United States. Descriptions of representative collections appear below.

7 **LARGE TISSUE BANKS, REPOSITORIES, AND CORE FACILITIES**

8
9 Large tissue banks and repositories exist in almost every sector of the scientific and
10 medical communities, including the military, the Federal Government, universities and academic
11 medical centers, commercial enterprises, and non-profit organizations. In addition, several
12 universities have established core banking facilities to support both their own research as well as
13 collaborations with other universities. These large tissue banks, repositories, and core facilities
14 are a major source of human biological materials for biomedical research. Representative
15 collections are described below.⁶

17 **Military Facilities**

18
19 The military maintains two of the largest tissue repositories in the world. As mentioned
20 previously, the National Pathology Repository and the DOD DNA Specimen Repository for

⁶ The complete text of the inventory appears in the commissioned paper.

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 Remains Identification are housed in the Armed Forces Institute of Pathology (AFIP)⁷. The AFIP
2 is responsible for maintaining a central laboratory of pathology for consultation and diagnosis of
3 pathologic tissue for DOD, other federal agencies, and civilian pathologists. AFIP also conducts
4 research in pathology, trains enlisted personnel in histopathology and related techniques, and
5 offers over 50 pathology education courses for medical, dental, and veterinary personnel.

6

7 The National Pathology Repository⁸, located at AFIP, is the largest and most
8 comprehensive collection of pathology material in the world. Since 1917, the Pathology
9 Repository has collected over 2.5 million cases comprising over 50 million microscopic slides, 30
10 million paraffin tissue blocks, 12 million preserved wet tissue specimens, and associated written
11 records. The Pathology Repository logs in approximately 50,000 cases annually, with 53,384
12 cases accessioned in FY 1996, and 51,908 in FY 1997. In addition, approximately 40,000
13 cytology cases are sent for primary diagnosis annually, but are not deposited in the repository.
14 During 1993, approximately 10,000 of the cases were cancers and 8,000 were benign neoplasms,
15 with the balance representing the entire spectrum of human disease. Material is stored
16 permanently unless there is a specific request by the contributor or other authorized individual to
17 return or release the material.

18

⁷ Armed Forces Institute of Pathology (AFIP), <http://www.afip.mil/default.html>

⁸ National Pathology Repository , <http://www.afip.mil/repository/welcome.html>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 Cases are sent to AFIP for a variety of reasons. The majority of cases are submitted
2 because the contributor wants a second opinion on a diagnosis. Some are forwarded as part of
3 established peer-review and quality assurance programs. Some military cases are forwarded by
4 DOD regulation, such as forensic cases and those subject to litigation. Other cases are submitted
5 because they are unusual or rare and may be useful to AFIP in its research and education
6 missions. Pathologic specimens stored at the Pathology Repository can be used to study unusual
7 tumors, or as part of a public health surveillance system to study emerging infectious diseases or
8 trends in disease progression. For example, samples in the Repository have been used to identify
9 and date tissues harboring genomic material of the Human Immunodeficiency Virus (HIV) that
10 were obtained before the availability of HIV testing and before the spread of the HIV infection.
11 In addition, cases have been submitted over the years for specific purposes, such as to study a
12 particular disease, or to answer current and future research questions (for example, illnesses of
13 Gulf War veterans).

14
15 All submitted case material is coded by pathological diagnosis, and is identified by an
16 AFIP accession number. The source name, social security number, date of birth, age, sex, and
17 race are stored if provided by the contributing pathologist. Any medical history provided is stored
18 in the case folder and on an optical disk imaging system. The source address is not routinely
19 provided or stored but is obtained on occasion for follow-up studies. Likewise, the original
20 consent is a matter between the patient and the clinician and is not routinely provided to AFIP by
21 the contributing pathologist. The submitting pathologist's name and address, and the source's

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 surgical identification numbers are also stored.

2
3 The Pathology Repository loans pathologic material for patient treatment, research, or
4 litigation. Requests for loan of material or provision of data for research purposes requires
5 submission and approval of a research protocol. All research protocols using stored materials or
6 data are reviewed by the AFIP's IRB. Requests from individuals or organizations other than the
7 original contributor must be accompanied by a properly executed authorization signed by the
8 patient or designated representative. Research involving patient follow-up, and thus requiring
9 identifying information, is reviewed at a full meeting of the IRB prior to approval. Other than for
10 research involving follow-up, original sources of material are not notified of research results. If
11 an unexpected disease or abnormality is discovered, the contributing pathologist is notified, and it
12 is then up to the pathologist to contact the patient. Otherwise, current AFIP policy requires that
13 material be stripped of identifiers before release to outside investigators.

14
15 The DOD DNA Specimen Repository for Remains Identification⁹ is the world's largest
16 DNA bank. As of September 1997, the DNA Repository has received approximately 2 million
17 DNA specimens. Specimens come into the DNA Repository at a rate of 10,000 per day, and the
18 tally is updated every seven seconds. It is estimated that by the year 2001 the DNA Repository
19 will contain approximately 3.5 million samples. All DNA specimens will be maintained for 50
20 years before being destroyed. However, donors may request that their specimens be destroyed
21 following the conclusion of their military service obligation or other applicable relationship to

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 DOD.

2
3 Since June 1992, DOD has required all military inductees, and all active duty and reserve
4 personnel to provide blood and saliva samples for its DNA Specimen Repository at the time of
5 enlistment, re-enlistment, annual physical, or preparation for operational deployment (McEwen,
6 1997). The DNA Repository also contains samples from civilians and foreign nationals who work
7 with the United States military in arenas of conflict. A total of three DNA specimens are
8 collected from each person: one bloodstain card is stored in a pouch in the service member's
9 medical record; another bloodstain card and a buccal swab are stored at the DNA Specimen
10 Repository. The blood is placed on special cards with the service member's Social Security
11 number, date of birth, and branch of service designated on the front side of the card, and a
12 fingerprint, a bar code, and signature attesting to the validity of the sample on the reverse side.
13 DNA will only be extracted from the specimens in the Repository when it is needed for the
14 purpose of remains identification.

15
16 The DNA Repository, along with the Armed Forces DNA Identification Laboratory
17 (AFDIL), comprises the DOD DNA Registry. The purpose of the DNA Registry is to identify the
18 remains of soldiers killed in combat or missing in action. The military's policy ensures that
19 specimens can only be used for remains identification and routine quality control except where
20 subpoenaed for the investigation or prosecution of a felony. The specimens cannot be used
21 without consent for any other purpose, such as paternity suits or genetic testing. In addition, the

⁹ Armed Forces DNA Identification Laboratory, <http://www.afip.mil/oafme/dna/afdil.html>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 specimens are considered confidential medical information, and military regulations and federal
2 law exist to cover any privacy concerns.

4 **National Institutes of Health**

6 The National Institutes of Health¹⁰ (NIH), founded in 1930, consists of 24 Institutes,
7 Centers, and Divisions. It is the principal health research agency of the federal government. NIH
8 is one of the highest funders of tissue and data resources for basic, applied and clinical research.
9 Some of the institutes at NIH that support tissue banks include the National Cancer Institute
10 (NCI), the National Institute of Allergy and Infectious Disease (NIAID), the National Heart,
11 Lung, and Blood Institute (NHLBI), the National Institute of Mental Health (NIMH), and the
12 National Institute on Aging (NIA). Examples of tissue banking supported by NIH are described
13 below.

15 NCI¹¹ is the largest of NIH's biomedical research institutes and centers. It supports
16 several human biological material and data resources for cancer research. For example, the
17 Cooperative Human Tissue Network (CHTN), in existence since 1987, provides biomedical
18 researchers with access to fresh surgical or biopsy specimens of normal, benign, pre-cancerous
19 and cancerous human tissues. CHTN is a tissue collection system and not a tissue bank. Only

¹⁰ National Institutes of Health (NIH), <http://www.nih.gov/index.html>

¹¹ National Cancer Institute (NCI), <http://www.nci.nih.gov>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 rare specimens that are difficult to obtain are stored to anticipate future requests. Except for a
2 collection of frozen tissue from rare pediatric tumors, banked specimens are generally not stored
3 for more than one year. Normally, the specimens are obtained prospectively to fill specific
4 researcher requests. Five member institutions coordinate the collection and distribution of tissues
5 across the United States and Canada. Tissues are provided by the CHTN only for research
6 purposes, and cannot be sold or used for commercial purposes.

7
8 During the first nine years of operation, the CHTN supplied over 100,000 specimens to
9 approximately 600 investigators. CHTN tissues have been used in many areas of cancer research
10 including molecular biology, immunology, and genetics. Researchers have used these tissues to
11 study mutations of proto-oncogenes in human tumors, the role of growth factors in cancer, and to
12 isolate new cancer genes. Over 2,000 publications have resulted from studies using CHTN
13 tissues.

14
15 CHTN obtains tissues from routine surgical resections and autopsies of adult and pediatric
16 patients, representing all organ systems, as well as blood and other body fluids. Specimens are
17 collected according to the individual investigator's protocol, and may be preserved as fresh, fixed
18 or frozen tissue, slides, or paraffin blocks. CHTN was designed for basic research studies not
19 requiring clinical follow-up information. Each specimen is given a unique identifier. A link is
20 kept by the parent institution for quality control purposes. Only minimal demographic data is
21 provided with the specimen. Other information routinely provided with the specimens includes

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 pathology reports and histological characterization.

2

3 The NCI-National Action Plan on Breast Cancer (NAPBC) Specimen and Data

4 Information System¹² contains information from 14 breast tissue banks. This database does not

5 represent an exhaustive national listing of all facilities holding breast cancer tissue. However, by

6 centralizing information on biological specimens, it provides access to breast tissue specimens and

7 facilitates collaboration among basic, clinical, and epidemiologic researchers. Cumulatively, the

8 14 breast tissue banks in the NCI-NAPBC database contain more than 130,000 cases of breast

9 cancer-related specimens and data, with banks ranging in size from 48 cases to approximately

10 101,000 cases. Three of the 14 banks are accruing as many as 200 new cases per year. A

11 specimen from a single case may generate several samples. For example, a specimen from a single

12 case may be split into 3 to 30 paraffin-embedded blocks, 10 slides, or matched frozen and

13 paraffin-embedded tissue blocks (i.e. one frozen and one paraffin-embedded sample from the same

14 case). A conservative estimate is there are approximately 240,000 samples in the database.

15 Samples available to the research and clinical communities include breast tissue, serum, urine,

16 cells, and DNA from patients diagnosed with breast cancer, those at high risk, and unaffected

17 individuals. Information on demographics (age, sex, race, ethnicity, family history of cancer),

18 clinical findings (pathologic diagnosis, stage, initial therapy), and outcome (subsequent breast

19 cancer, vital status) are also available from some institutions.

20

¹² NCI-NAPBC Breast Cancer Specimen and Data Information System,
<http://cancernet.nci.nih.gov/breastdata/contents.htm>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 The Transfusion Medicine Branch of NHLBI¹³ maintains a contractor-operated Blood
2 Specimen Repository available for use by the scientific community for research related to
3 transfusion-transmitted diseases, other blood disorders, or diseases of the cardiovascular system.
4 The repository, established in 1974, contains approximately 1.5 million well-characterized
5 specimens of serum, plasma, and cells from NHLBI-sponsored studies. Since 1991, the Blood
6 Specimen Repository has been storing an average of approximately 300,000 samples per year
7 (National Heart, Lung, and Blood Institute, 1996).

8

9 **Research Universities and Academic Medical Centers**

10

11 Research universities and academic medical centers maintain both formal human biological
12 material banks for distribution throughout the research community as well as core facilities to
13 support their own research. For example, the Harvard Brain Tissue Resource Center
14 (The Brain Bank) is a centralized repository for the collection and distribution of post-
15 mortem human brain specimens from both diseased and normal donors for use in research on the
16 brain and nervous system. Research on brain tissue has contributed to the understanding of
17 severe mental illness, the development of a genetic test for Huntington's disease, and a treatment
18 for Parkinson's disease. Since the majority of research requires a very small amount of tissue,
19 each donated brain provides a large number of samples for many researchers. Brain tissue
20 donations are accepted by the Brain Bank from individuals or the parents, siblings and offspring of

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 individuals with severe psychiatric or neurological disorders, as well as from unaffected
2 individuals for comparison.

3
4 Another example, the University of California-San Francisco (UCSF) AIDS Specimen
5 Bank, in existence since 1982, has banked over 76,000 specimens and sent out over 82,000
6 samples to researchers worldwide. Specimens include serum, tissue, saliva, cells, and
7 cerebrospinal fluid from HIV-infected individuals. Specimen data are archived on a computerized
8 database. The Bank provides investigators with specimens for basic, epidemiological, and clinical
9 research.

11 **Commercial Enterprises**

12
13 Some commercial enterprises maintain human biological material banks for their own
14 proprietary use, while others establish banks for storage and distribution purposes. OncorMed
15 and LifeSpan Biosciences, Inc. are examples of companies that maintain proprietary tissue banks,
16 while PathServe collects human tissues and organs for marketing to the research community.

17
18 OncorMed¹⁴ is a medical services company that provides genetic testing and information
19 services for the early detection and management of cancer. It offers cancer predisposition

¹³ National Heart, Lung, and Blood Institute (NHLBI), <http://www.nhlbi.nih.gov/nhlbi/nhlbi.htm>

¹⁴ OncorMed, <http://www.oncormed.com>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 counseling, genetic susceptibility testing, early diagnosis, and analysis of tumors. OncorMed=s
2 Hereditary Cancer Consulting Service, offered at sites around the country, determines a patient's
3 risk for developing cancer by analyzing family history information. OncorMed also offers genetic
4 testing for cancer susceptibility genes, including BRCA1 and BRCA2 for breast and ovarian
5 cancer, Hereditary Non-polyposis Colorectal Cancer (HNPCC), inherited melanoma, and
6 hereditary thyroid cancer. The company has an IRB for review and approval of protocols, and
7 has developed physician guidelines that closely parallel the American Society of Clinical Oncology
8 (ASCO) guidelines. In addition to genetic testing, OncorMed has established a proprietary
9 repository.

10
11 LifeSpan BioSciences, Inc.¹⁵, founded in 1995, is a genomics company focused on the
12 discovery and licensing of genes that play a role in the aging process and identifying disease-
13 associated genes for use as therapeutic or diagnostic targets. Because highly characterized
14 samples of normal and diseased tissues are critical in localizing disease-associated genes,
15 LifeSpan has an on-site tissue bank. LifeSpan's Tissue and Disease Bank contains 250,000
16 normal and diseased human samples. The tissue bank has over 175 different types of tissues from
17 virtually every organ in the body, covering all ages. The tissue bank also includes over 500
18 different pathologic disease categories such as autoimmune diseases, infectious diseases,
19 degenerative diseases, cancer and benign proliferative diseases, and genetic diseases.

¹⁵ LifeSpan BioSciences, Inc., <http://www.lsbio.com>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 PathServe Human Tissue Bank¹⁶, established in 1990 and commercial since 1996, is a
2 major supplier of human tissue to biotechnology and neuropathological research institutions.
3 PathServe also serves as a main training facility of autopsy technicians for private pathologists and
4 local hospitals. PathServe collects all types of organs and tissues including specimens from
5 placental and fetal origin. Tissues are obtained through post-mortem examinations, referrals from
6 transplant banks of nontransplantable organs, and donations by next of kin. PathServe collects
7 specimens from approximately 300 autopsies per year, and each autopsy yields approximately 100
8 specimens. PathServe has approximately 300 specimens stored at any one time, and distributed
9 approximately 30,000 specimens in 1996. Consent for donation is obtained from the family.
10 PathServe does not maintain a centralized storage facility. Instead, specimens are stored in the
11 morgues of different hospitals.

12

13 **Non-Profit, Non-Educational Organizations**

14

15 There are a variety of non-profit institutions that bank tissues for purposes of storage and
16 distribution. Non-profit institutions, such as the American Type Culture Collection (ATCC), the
17 Coriell Institute for Medical Research, the Research Foundation for Mental Hygiene, the Rocky
18 Mountain Multiple Sclerosis Center, the National Psoriasis Tissue Bank, the Kaiser Permanente
19 Center for Health Research, and the Hereditary Disease Foundation, receive millions of dollars in
20 federal funding to support their human biological material collections.

¹⁶ PathServe, <http://www.tissuebank.com/>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1

2

An example is the ATCC.¹⁷ Since its establishment in 1925, ATCC has served as an archive of living cultures and genetic materials for researchers in the biological sciences. The mission of the ATCC is to acquire, authenticate, and maintain reference cultures, related biological materials, and associated data, and to distribute these to qualified scientists in government, industry, and education. The ATCC maintains approximately 2,300 human cell lines as immortalized cultures. In addition, cloned human genes are stored and supplied to the research community by ATCC.

9

10

Another example is the Coriell Institute for Medical Research,¹⁸ a basic biomedical research institution that conducts research on the causes of genetic diseases, including cancer. The Coriell Institute's three missions are research, cell banking, and public education. The largest collection of human cells for research is maintained at the Corriell Institute, and these cells are available to the general scientific community. Seminal research on the genes associated with Huntington=s disease, cystic fibrosis, Alzheimer=s disease, ataxia telangiectasia and manic depression have used cells from the Coriell collection. The Coriell Cell Repositories also support the human genome project. Over 35,000 cell lines are currently stored representing approximately 1,000 of the 4,000 known genetic diseases, and more than 60,000 cell lines have been distributed to over 40 nations, resulting in over 8,000 research publications. Cultures are

11

12

13

14

15

16

17

18

19

¹⁷ American Type Culture Collection (ATCC), <http://www.atcc.org/>

¹⁸ Coriell Institute for Medical Research, <http://arginine.umdj.edu/info.html>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 established from both blood and skin, and the cells are stored frozen at the Institute. There are
2 three quarters of a million vials of cells in 37 tanks containing liquid nitrogen.

3 4 **PATHOLOGY SPECIMENS**

5
6 A large number of human biological materials are collected for diagnostic or therapeutic
7 reasons. These samples are usually sent to a clinical, diagnostic, or pathology laboratory for
8 examination. These laboratories may be located at GME teaching institutions, physicians' offices,
9 community hospitals, or independent laboratories. Most patients sign a general consent stating
10 that after completion of any diagnostic tests, some of the sample may be saved for research
11 purposes. Although the samples are made available for research, educational, and quality control
12 purposes, the vast majority is never used for these purposes.

13
14 To be accredited, laboratories are required to keep pathological specimens for a minimum
15 amount of time. The Clinical Laboratory Improvement Amendments of 1988 (CLIA) set forth the
16 conditions that laboratories must meet to be certified to perform testing on human specimens.
17 CLIA stipulates that laboratories must retain cytology slides for a minimum of 5 years,
18 histopathology slides for a minimum of 10 years, and paraffin blocks for a minimum of 2 years
19 (Clinical Laboratory Improvement Amendments, 1996). In addition, some states have regulations
20 that require retention of pathology specimens for longer periods of time. Once the regulated

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 length of time for storage is met, institutions continue to store pathology specimens based on the
2 room they have for storage or specific policies of the institution.

4 **Pathology Departments at Graduate Medical Education Teaching Institutions**

6 Graduate Medical Education (GME) teaching institutions include medical schools, Armed
7 Forces hospitals, Veterans Affairs medical centers, the Public Health Service, state, county and
8 city hospitals, non-profit institutions, and health maintenance organizations. In 1997, there were
9 1,687 accredited GME teaching institutions in the United States (American Medical Association,
10 1997). Collectively, pathology departments at GME teaching institutions constitute the largest
11 and oldest stores of human biological materials in the United States.

13 Most medical school pathology departments store samples indefinitely; some tissues have
14 been archived from 20 to over 100 years. Stored specimens are labeled with either a pathology
15 accession number that is linked to the patient's medical record, or directly with the patient's name
16 and medical record number. People who have access to the specimens include pathologists,
17 researchers, other physicians, and those who have a court order requesting access.

19 Cumulatively, the 1687 GME Teaching Institutions with residency programs in
20 cytopathology, hematology, and clinical and anatomic pathology accession more than 8 million
21 cases per year. In addition, pathology departments at GME Teaching Institutions without

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 pathology residency programs also accession pathology specimens, but most likely not at the
2 same rate as institutions with pathology residency programs. Since most GME Teaching
3 Institutions retain pathology specimens anywhere from 20 to 100 years, at a rate of 8 million cases
4 a year for a minimum of 20 years, a conservative estimate is that there are more than 160 million
5 cases stored at GME Teaching Institutions with pathology residency programs with several
6 million more stored at those without pathology residency programs.

8 **DNA Diagnostic Laboratories**

9
10 HELIX¹⁹ is a national directory of DNA diagnostic laboratories. It includes a
11 comprehensive listing of clinical service and research laboratories performing disease-specific
12 clinical molecular genetic testing for single-gene and contiguous-gene disorders. HELIX is
13 funded by the National Library of Medicine and administered through the National Network of
14 Libraries of Medicine. In January 1994, there were 148 laboratories listed in HELIX (McEwen
15 and Reilly, 1995).

16
17 In a 1994 survey of HELIX DNA diagnostic laboratories, 90 percent of the respondents
18 stated that they banked DNA. DNA banks ranged in size from having less than 100 to more than
19 1,000 samples in storage. Most laboratories banked DNA as a service to referring physicians or
20 for individuals and families at risk for a particular genetic disorder, for research purposes such as

¹⁹ HELIX, <http://healthlinks.washington.edu/helix>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 gene mapping, and as a service to clinical, forensic or research laboratories. Over 50 percent of
2 the respondents stated that their laboratories had released samples to researchers after stripping
3 them of identifiers (McEwen and Reilly, 1995).

4 5 **Clinical Service and Diagnostic Laboratories**

6
7 The majority of clinical service and diagnostic laboratories are not associated with GME
8 teaching institutions. These include laboratories within physicians' offices or community
9 hospitals, and independent laboratories. In 1991, there were approximately 640,000 clinical
10 laboratories and other facilities that perform laboratory tests on human specimens (Department of
11 Health and Human Services, 1991). The number of tissues stored at these laboratories varies
12 greatly, but the minimum storage time is determined by CLIA and state regulations.

13 14 **NEWBORN SCREENING LABORATORIES**

15
16 Archives of newborn screening cards for inborn errors of metabolism (Guthrie Cards)
17 represent an enormous source of banked DNA. Guthrie cards are used to test newborns for
18 several different diseases, including congenital hypothyroidism, phenylketonuria, galactosemia,
19 hemoglobinopathies (e.g. sickle cell anemia), biotinidase deficiency, homocystinuria, Maple Syrup
20 Urine disease, and cystic fibrosis. These newborn screening tests use bacterial inhibition assays
21 and automated enzymatic methods for disease diagnosis, although they are likely to become more

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 DNA-based over time. Interest in using Guthrie cards for population-wide genetic
2 epidemiological studies has grown, given the stability of DNA in dried blood, and the ability to
3 analyze the DNA in these samples (McEwen and Reilly, 1994). All states participate in some
4 form of newborn screening, but few have issued regulations that explicitly define the scope of
5 permissible use of Guthrie card samples (Andrews, 1995). By 1994, seven state departments of
6 public health had issued written regulations on third-party access to Guthrie cards, and 10 of the
7 laboratories had internal written policies on this matter (McEwen and Reilly, 1994).

8
9 A 1994 survey of all newborn-screening programs in all 50 states, the District of Columbia,
10 Puerto Rico, and the Virgin Islands revealed that the majority of laboratories have accumulated
11 less than 500,000 Guthrie Cards over the years. However, one laboratory reported a collection of
12 more than 6 million Guthrie cards. The number of cards collected over a 1-year period ranged
13 from less than 10,000 in 4 labs to more than 500,000 in 2 populous states (McEwen and Reilly,
14 1994).

15
16 The trend in most states is to save Guthrie cards for longer and longer periods of time. Forty of
17 the state newborn screening laboratories retain all the Guthrie cards that they receive through
18 their newborn-screening programs, including those cards that test negative, at least for a short
19 period of time (McEwen and Reilly, 1994). Twenty three laboratories indicated that they keep
20 their cards for a year or less, 10 plan to keep their cards for 1 to 5 years, 13 keep them for longer
21 than 5 years, three save all their cards for 20 to 25 years, and 4 plan to keep their cards

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 indefinitely (McEwen and Reilly, 1994). Thirteen other respondents discard their cards within
2 several weeks or months (McEwen and Reilly, 1994).

3
4 Guthrie cards contain identifying information, such as mother's name and address, hospital of
5 birth, baby's medical record number, baby's doctor's name and address. The conditions under
6 which Guthrie cards are stored vary from state to state. They might be stored in boxes at room
7 temperature, or in a freezer, refrigerator, or climate-controlled room. They might be kept in
8 boxes or folders in a basement or warehouse, or in a cabinet in folders or biohazard bags
9 (McEwen and Reilly, 1994).

10 11 **FORENSIC DNA BANKS**

12
13 In 1989, the Virginia Division of Forensic Science²⁰ was the first state laboratory to offer
14 DNA analyses to law enforcement agencies, and the first to create a DNA databank of previously
15 convicted sex offenders. By November 1997, 48 states had established forensic DNA data banks
16 from convicted criminals, especially violent sex offenders and other violent felons (Finn, 1997).
17 The two states without Forensic DNA banks, Vermont and Rhode Island, are planning legislation
18 to create them (Finn, 1997). In addition, the Federal Bureau of Investigation²¹ (FBI) is exploring
19 ways to create a Forensic DNA bank for the District of Columbia (Finn, 1997).

²⁰ Virginia Division of Forensic Science, <http://www.state.va.us/~dcjs/forensic/>

²¹ Federal Bureau of Investigations (FBI), <http://www.fbi.gov/>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20

The DNA Identification Act of 1994 (Pub. L. No. 103-322, 1994 HR 3355, 108 Stat. 1796, 210304), a federal law enacted in 1994 as part of the Omnibus Crime Control Law, created a national oversight committee to develop guidelines for DNA forensics and established a 5-year, \$40 million grant program to assist state and local crime laboratories in developing or improving forensic DNA testing capabilities. The DNA Identification Act also formally authorized the FBI to establish the Combined DNA Index System²² (CODIS) for law enforcement identification purposes (TWGDAM, 1989). CODIS is a national computer network containing DNA profiles of convicted offenders, unknown suspects, and population samples (which are used for statistical purposes only). Using CODIS, federal, state, and local law enforcement agencies are able to compare DNA profiles from crime scenes to DNA profiles of felons in the CODIS database.

In addition to collecting specimens from sex offenders and violent felons, a number of states also require samples from juvenile offenders, non-violent felons, such as drug or white collar offenders, and those convicted of misdemeanors (McEwen, 1997). South Dakota requires samples from people merely arrested (not convicted) of a sex offense (Finn, 1997), with several other states considering similar bills (McEwen, 1997). There is also a proposal to establish a federal DNA data bank that would include profiles from people convicted in federal or military courts of offenses similar to those covered by most state laws (McEwen, 1997).

²² Forensic Science Research and Training Center, <http://www.fbi.gov/lab/report/research.htm>

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 Convicted offenders are required to provide blood, or in some cases, saliva, either at
2 sentencing or before release from prison. Some states also require samples from people already
3 incarcerated before the law's effective dates. The DNA from these samples is analyzed for its
4 unique identification characteristics. Nationwide, samples from about 380,000 offenders have
5 been collected, mostly in Virginia and California, and about 116,000 samples (30 percent) have
6 been analyzed (McEwen, 1997). These DNA identification profiles are stored, along with the
7 samples themselves, to help identify suspects by matching biological evidence found at crime
8 scenes to state DNA databases.

9
10 DNA profiles prepared from these samples have already proven to be a valuable resource
11 for tracing biological material found at crime scenes to felons with prior convictions. By February
12 1997, forensic DNA databanks had achieved over 200 cold hits linking serial rape cases or
13 identifying suspects by matching DNA extracted from biological evidence found at a crime scene
14 to that of a known offender whose DNA profile was in the databank. The power of DNA testing
15 is to not only implicate an individual in a crime, but also to exonerate innocent individuals by
16 ruling them out as suspects.

17 18 **UMBILICAL CORD BLOOD BANKS**

19
20 Stem cells (progenitor cells that produce all other blood cells) are used to treat patients
21 with blood diseases, certain genetic disorders, and patients receiving chemotherapy and/or

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 radiation treatment for cancer. Until scientists discovered that umbilical cord blood contained
2 hematopoietic stem cells, the only known source of stem cells was from bone marrow. However,
3 retrieval of bone marrow is invasive, may be painful, requires general anesthesia, and is expensive
4 to harvest. In contrast, retrieval of umbilical cord blood is non-invasive, painless, and generally
5 only takes a few minutes to complete. After a baby is delivered and the umbilical cord is cut,
6 blood is withdrawn from the umbilical cord and placenta with a syringe and then cryogenically
7 stored. In addition, bone marrow is difficult to match between donor and recipient, while cord
8 blood is compatible with more people. Cord blood transplants also have a lower incidence of
9 graft versus host disease and are less likely to transmit infectious diseases. However, the Working
10 Group on Ethical Issues in Umbilical Cord Blood recently concluded that “until additional data
11 are obtained regarding safety and efficacy, umbilical cord blood banking and use ought to be
12 considered an investigational technology rather than a proven treatment” (Sugarman et al., 1997).

13

14 In 1988, the first successful human cord blood transplant was performed in a child with
15 Fanconi Anemia using cord blood from a sibling (Gluckman et al., 1989). Since then, over 500
16 autologous and allogeneic umbilical cord blood transplants have been performed worldwide, with
17 the majority done in the past two to three years (Perdahl-Wallace, 1997). Approximately two-
18 thirds of the cord blood transplants have been performed for malignant conditions including acute
19 lymphocytic leukemia, acute myelocytic leukemia, chronic myelogenous leukemia, and
20 neuroblastoma (Wagner et al., 1995). The other one-third have been for a variety of genetic
21 disorders including Hurler and Hunter syndromes, adrenoleukodystrophy, osteopetrosis, severe

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 aplastic anemia, severe combined immunodeficiency, and hemoglobinopathies such as beta
2 thalassemia and sickle cell anemia (Wagner et al., 1995; Wagner et al., 1996). The majority of
3 transplants have been in children, although a small number of adults have been transplanted as
4 well. Cord blood is now being stored at both public and private banks.

5
6 In the last few years, privately owned companies have begun offering umbilical cord blood
7 banking services to individuals and families. When dealing with private storage companies, users
8 pay a one-time fee for the collection, testing and freezing of the blood. In addition, an annual fee
9 is charged for storing the blood in liquid nitrogen. The stored cord blood may be withdrawn if
10 illness occurs later in life. In contrast, when parents choose to donate their child's cord blood to a
11 public bank, they generally pay no fees, but they give up all rights to the sample to help build the
12 public supply of cord blood for use in transplantation and research. In general, expectant mothers
13 who choose to donate their baby's cord blood are asked to consent to providing medical, ethnic
14 and related information, donating the cord blood to the cord blood bank for transplantation and/or
15 research, allowing blood to be drawn from the mother for tests including HIV testing, and
16 granting permission to track the newborn's medical history for up to one year. Collectively,
17 private and public cord blood banks store more than 18,000 units of cryopreserved umbilical cord
18 blood. The majority of this stored cord blood is used for transplants. However, both private and
19 public banks do supply some cord blood for research purposes.

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21

Organ and tissue banks recover, process, store and distribute human organs, bone and tissue for transplantation. Donations are from people who agree to donate upon their death and families who consent on behalf of the deceased. Some organ and tissue banks may also have tissue available for educational and research purposes. However, the demand for organs, bone and tissue usually exceeds the current supply. Therefore, usually only organs and tissues not suitable for transplantation are available for research.

BLOOD BANKS

The American Red Cross²³ collected approximately 5.8 million blood donations in 1996. The Red Cross represents about half of all United States blood donations, so annually, about 12 million units of blood are donated in the United States. The American Red Cross usually maintains about a 3-day supply of fresh blood as well as approximately 20,000 units of frozen blood at any one time. The American Red Cross also maintains the world's largest registry of frozen rare blood. Approximately 1000 units of rare blood a year are supplied to recipients around the globe.

The Food and Drug Administration (FDA) requires the tracking of blood from "arm to arm," however this information is confidential and coded. Donors who test positive for HIV are notified and counseled. The consent form signed by donors asks donors if excess or expired

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 blood may be used for research.

2
3 Fresh red blood cells have a shelf life of 21 to 42 days depending on the preservative used,
4 and platelets have a shelf life of 5 days. Plasma can be stored frozen for 1 to 5 years, and frozen
5 whole blood can be stored for at least 10 years. Platelets and red cells that expire are sold for
6 research purposes. Researchers are informed that the samples have been found negative for all
7 FDA required tests, and only by special request, may be provided with the donor' age and gender.
8 Plasma that can not be transfused is used for making blood derivatives such as Factor VIII for
9 hemophiliacs, or for making diagnostic reagents. Nothing goes to waste.

11 CONCLUSIONS

13 Collections of human biological materials vary considerably, ranging from formal
14 repositories to the informal storage of blood, tissue, or DNA in a researcher's laboratory. There
15 are a total of over 282 million specimens from more than 176 million cases of stored samples in
16 the United States, accumulating at a rate of over 20 million per year. The vast majority of
17 samples were originally collected for diagnostic or therapeutic reasons, although increasingly
18 samples are being collected with specific research protocols in mind. NBAC estimates that
19 approximately 2.3 million specimens exist in storage as a result of research collection.

²³ American Red Cross, [http:// www.redcross.blood](http://www.redcross.blood)

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 **REFERENCES**

2
3 American Medical Association. 1997. Graduate Medical Education Directory 1997-
4 1998. American Medical Association, Chicago.

5
6 Andrews LB. 1995. State laws and regulations governing newborn screening. American
7 Bar Foundation, Chicago.

8
9 Clinical Laboratory Improvement Amendments. 1996. Clinical Laboratory Improvement
10 Amendments of 1988 (CLIA). 42 CFR 493 (10-1-96 Edition); pp. 796-921.

11
12 Department of Health and Human Services. 1991. Clinical Laboratory Improvement
13 Amendments (CLIA). November 29, 1992. Press Release 1991.11.29.

14
15 Finn P. 1997. Revolution Underway in Use of DNA Profiles. Bid to Link U.S.
16 Databanks is Crime-Solving Edge. *The Washington Post*. Sunday, November 16, 1997; B4.

17
18 Gluckman E, Broxmeyer HE, Auerbach AD et al., 1989. Hematopoietic reconstitution in
19 a patient with Fanconi's anemia by means of umbilical cord blood from an HLA-identical sibling.
20 *New England Journal of Medicine* 321: 1174-1178.

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 McEwen JE and Reilly PR. 1994. Stored Guthrie Cards as DNA "Banks". *American*
2 *Journal of Human Genetics* 55: 196-200.

3

4 McEwen JE and Reilly PR. 1995. A survey of DNA diagnostic laboratories regarding
5 DNA banking. *American Journal of Human Genetics* 56(6): 1477-1486.

6

7 McEwen JE. 1997. DNA Data Banks. In Genetic Secrets: Protecting Privacy and
8 Confidentiality in the Genetic Era, MA Rothstein, ed., Chapter 11.

9

10 National Heart, Lung, and Blood Institute. 1996. Blood Specimen Repository: 1996
11 Catalog.

12

13 Perdahl-Wallace EB. 1997. Placental cord blood transplantation. *Transplant Forum*
14 4(2): 4-5.

15

16 Sugarman J, Kaalund V, Kodish E, Marshall MF, Reisner EG, Wilfond BS, and Wolpe
17 PR. 1997. Ethical issues in umbilical cord blood banking. *Journal of the American Medical*
18 *Association* 278(11): 938-943.

19

20 Technical Working Group on DNA Analysis Methods (TWGDAM). 1989. The
21 Combined DNA Index System (CODIS): A theoretical model. In DNA Fingerprinting: An

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 Introduction, LT Kirby, ed., New York: Stockton Press, pp. 279-317.

2

3 Wagner JE, Kernan NA, Steinbuch M, Broxmeyer HE, and Gluckman E. 1995.

4 Allogeneic sibling umbilical cord blood transplantation in children with malignant and non-
5 malignant disease. *Lancet* 346: 214-219.

6

7 Wagner JE, Rosenthal J, Sweetman R et al. 1996. Successful transplantation of HLA-
8 matched and HLA-mismatched umbilical cord blood from unrelated donors: Analysis of
9 engraftment and acute graft-versus host disease. *Blood* 88: 795-802.

May 8, 1998: This is a staff draft report developed for the National Bioethics Advisory Commission. It does not represent conclusions and should not be cited or referenced as such.

1 **Table 1. Stored Human Biological Materials in the United States**

2

Type of Repository	# of cases	# of specimens	Cases/Year
Large Tissue Banks, Repositories, and Core Facilities	>2.6 million	>96 million	364,825
Longitudinal Studies	>263,500	>263,500	
Pathology Specimens	>160 million	>160 million	>8 million
Newborn Screening Laboratories	>13.5 million	>13.5 million	<10,000 to >50,000
Forensic DNA Banks	380,000	380,000	
Umbilical Cord Blood Banks	18,300	18,300	
Organ Banks		>75,500	>75,500
Blood Banks		~12 million	~12 million
Grand Total	>>176.5 million	>>282 million	>20 million

3