The Ethical, Legal and Policy Implications of Using Human Biospecimens in Research: What You Need to Know

Lori Andrews, J.D.
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NATIONAL CANCER INSTITUTE

The Royal Caroline Medico-Surgical Institute at Hantverkargatan, Stockholm

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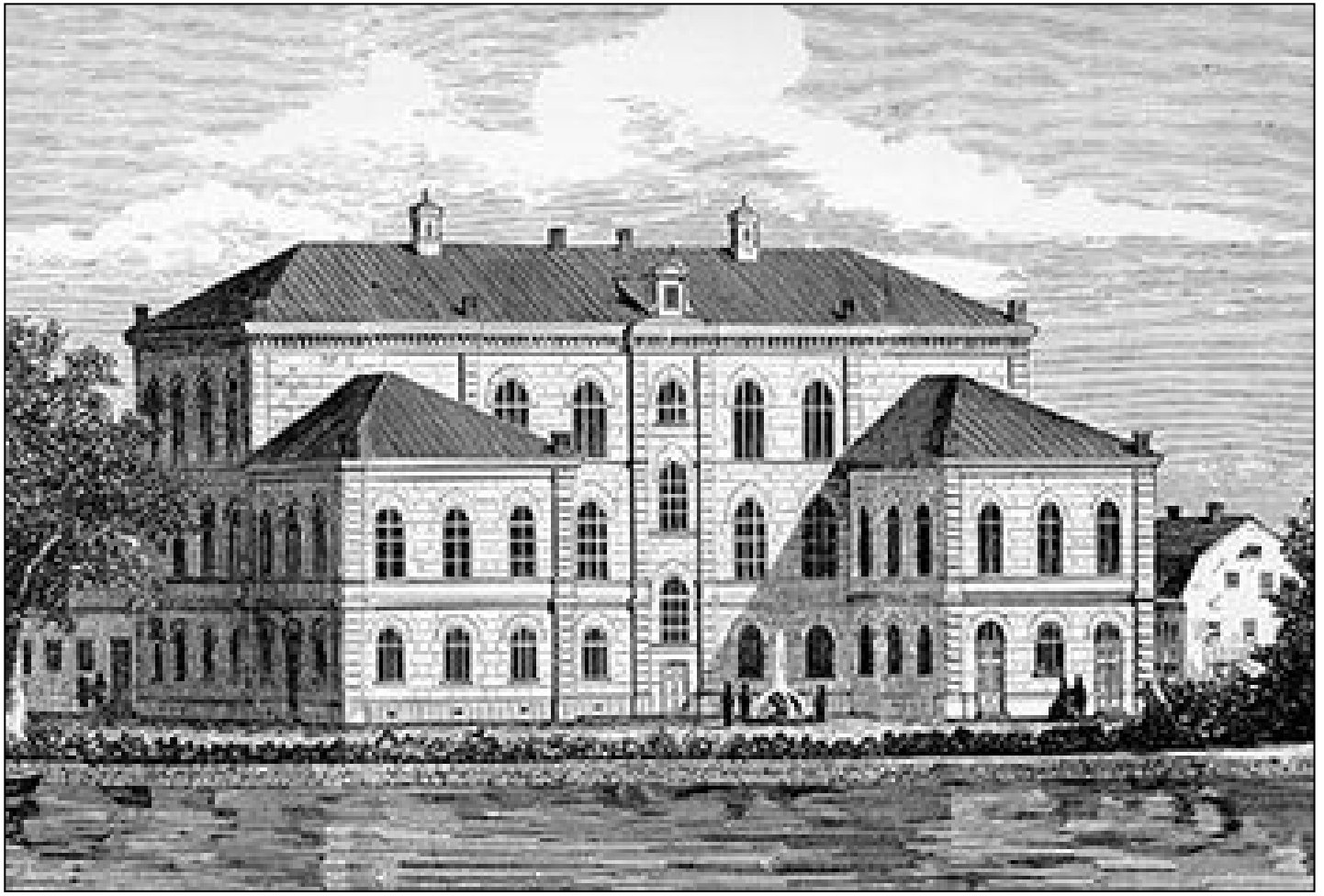

From http://nobelprize.org/alfred_nobel/biographical/articles/ringertz/index.html

The Toothdrawer

Steel engraving by D.J. Pound after painting by G. Honthorst ca 1840.

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From http://www.antiquemapsandprints.com/SCANSB/B-1441.jpg

Uniform Anatomical Gift Act

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"A donor may amend or revoke an anatomical gift…."

Revised Uniform Anatomical Gift Act § 6 (2006).

45 C.F.R. §46.116(a)(8)

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"[I]n seeking informed consent the following information shall be provided to each subject:

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled."

Best Practices ELSI Concerns

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- Informed Consent
- Privacy
- Custodianship
- Conflicts of Interest
- Intellectual Property

Florida Statute Annotated § 760.40 (2)(a)

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"…DNA analysis may be performed only with the informed consent of the person to be tested, and the results of such DNA analysis, whether held by a public or private entity, are the exclusive property of the person tested…"

Court's Dilemma

Does the tissue sources have a property right in his or her tissue?

Courts are divided, but the current trend is to say it is property.

Washington University v. Catalona

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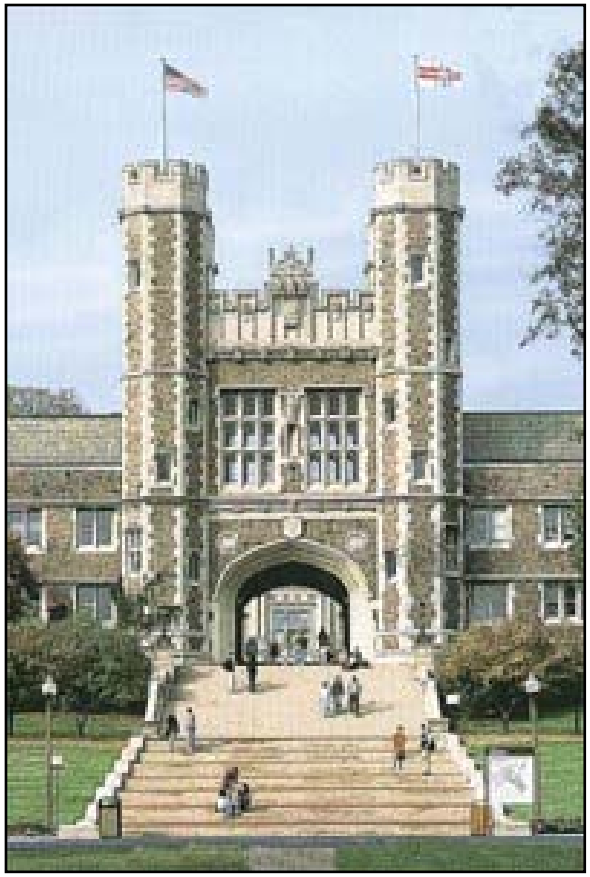

Washington University v. Catalona

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The *Catalona* case was not about the federal regulations, known as the “Common Rule,” but about state law. The court hearing only dealt with the question of whether patients had meant to make a gift of their tissue.

"[T]he existence of the informed consent forms is inconsequential."

Judge Stephen Limbaugh, Senior District Judge for the United States District Court, Eastern Division of Missouri.

Washington University v. Catalona

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A research institution might do something that doesn't matter for gift law purposes, but could cause it to lose NIH funding as a violation of the Common Rule.

Washington University v. Catalona

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A research institution could also still be sued for unjust enrichment.

The Greenberg Children

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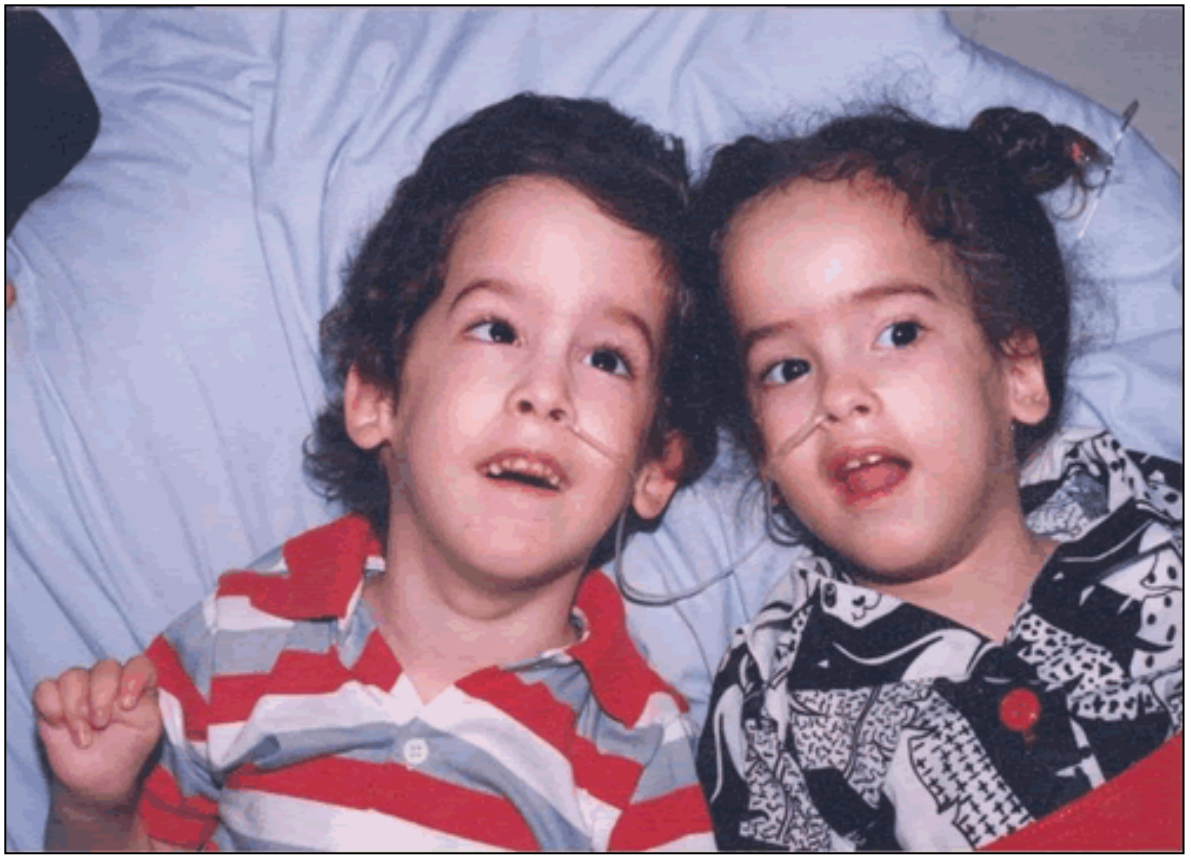

45 C.F.R. §46.116(a)(8)

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"[T]he subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled."

From Consent document drafted by WU

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"Your participation is voluntary and you may choose not to participate in this research study or withdraw your consent at any time. If you choose to participate in a study that uses code numbers to link participants to tissue and later change your mind, the tissue can be destroyed upon request. To withdraw your consent, call Dr. Catalona at 314-362-4241. Any research results already obtained cannot be destroyed or recalled."

OHRP Guidance

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Prohibited Language:

"By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research."

Allowed Language:

"By consenting to participate, you authorize the *use* of your bodily fluids and tissue samples for the research."

Office of Human Research Protections, Exculpatory Language in Informed consent, available at http://www.hhs.gov/ohrp/humansubjects/guidance/exculp.htm.

AMA Code of Ethics, E-2.08 6

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- “Informed consent must be obtained from patients for the use of organs or tissues in clinical research…
- Human tissue and its products may not be used for commercial purposes without the informed consent of the patient who provided the original cellular material…
- Profits from the commercial use of human tissue and its products may be shared with patients…”

Custodianship

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Custodianship plans should address how to handle specimens and associated data:

- When the grant ends
- When the initial study is completed
- In case of institution will no longer support the biobank

Privacy

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- Apply the highest possible ethical standards
- Analogize to the HIPPA rule
- Establish clear privacy protections that are appropriate to the type of biospecimen resource.

Tiered Options

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"If appropriate to the study design or the biospecimen resource's mission, human subjects may be allowed to specify the types of research for which the contributed biospecimens will be used via a tiered system of consent.

Examples:

- My tissue may be kept for use in research to learn about, prevent, or treat cancer.
- My tissue may be kept for research to learn about, prevent, or treat other health problems (e.g., diabetes, Alzheimer's disease, or heart disease)."

NCI Best Practices C.2.2.7.

The Havasupai

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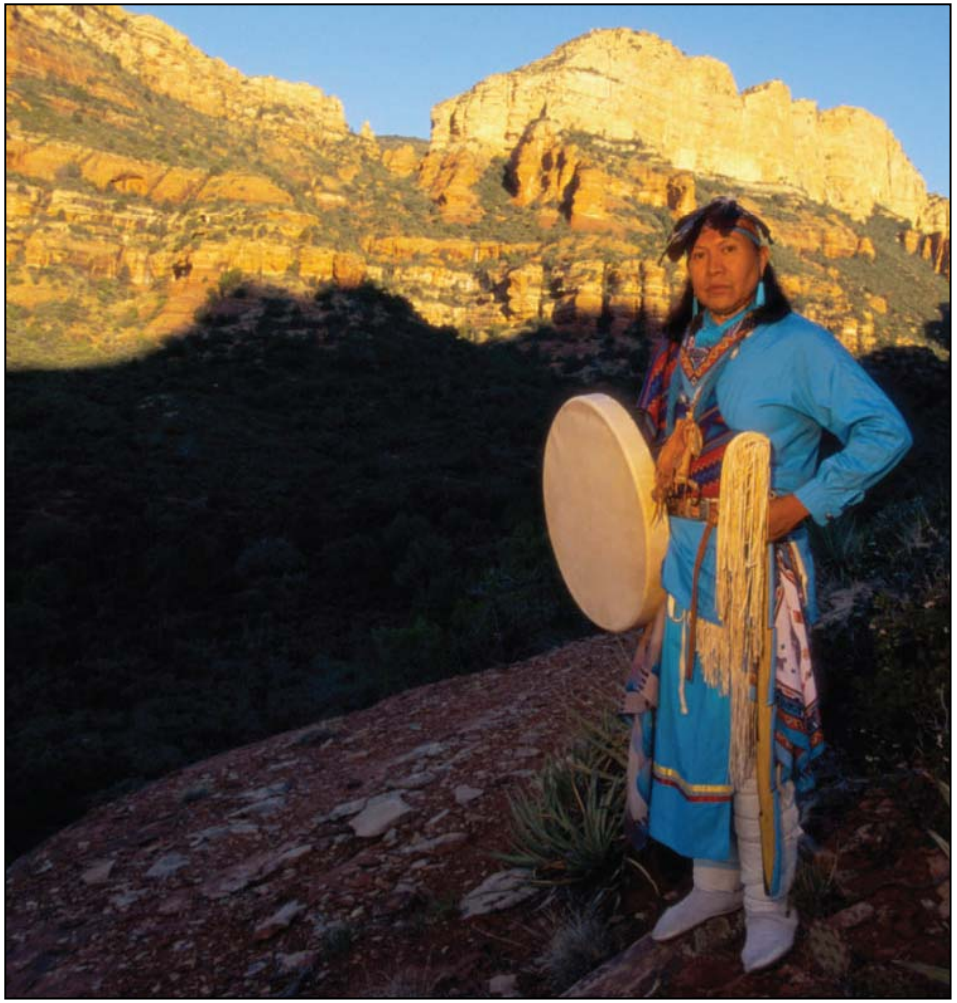

From “When Two Tribes Go To War,” Nature, July 29, 2004.

NCI Best Practices C.2.2.9

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“ Biospecimen resources should develop policies and procedures to track records for human subjects who discontinue participation. Informed consent documents should highlight the human subject’s ability to discontinue participation and describe what will take place should this occur.”

45 C.F.R. §46.101(b)(4)

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Except as provided [below], this policy applies to all [federally supported] research involving human subjects:

(4) Research, involving the collection or study of existing data, documents, records, *pathological specimens, or diagnostic specimens*, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

POLICYFORUM

GENETICS

No Longer De-Identified

Sequencing human DNA to discover genetic variation should be governed by existing regulations for human subjects.

Amy L. McGuire[1]* and Richard A. Gibbs[2]

As DNA sequencing becomes more affordable and less time-consuming, scientists are adding DNA banking and analysis to research protocols, resulting in new disease-specific DNA databases. A major ethical and policy question will be whether and how much information about a particular individual's DNA sequence ought to be publicly accessible.

Without privacy protection, public trust will be compromised, and the scientific and medical potential of the technology will not be realized. However, scientific utility grows with increased access to sequenced DNA. At present, ethical concerns about the privacy of subjects whose sequenced DNA is publicly released have largely been addressed by ensuring that the data are "de-identified" and that confidentiality is maintained (*1*–*2*). There is a large literature on the various data-management models and computer algorithms that can be used to provide access to genetic data while purportedly protecting privacy (*3*–*6*). We believe that minimizing risks to subjects through new developments in data and database structures is crucial and should continue to be explored, but that additional safeguards are required.

Scientists have been aware for years of the possibility that coded or "anonymized" sequenced DNA may be more readily linked to an

PHASE 1

Dr. A, from Excel University, is interested in studying whether there are genetic variances associated with Parkinson's disease. Dr. A obtains IRB approval for her study and recruits subjects from her clinic. She explains to potential subjects that she is conducting a genetic study of Parkinson's disease. Subjects are presented with a consent form, which explains that they will be asked to give a blood sample and to fill out a health survey. They are told the risks associated with the blood draw, warned that they may not benefit directly from participation in the study, and assured that confidentiality will be maintained within legal limits.

PHASE 2

Once the subject has consented and her sample collected, the sample is coded and given to Dr. B, a scientist who runs the sequencing center at Excel University. Dr. B does not know who the sample has come from and does not have access to any other patient information. Dr. B sequences the subject's DNA and publishes the sequenced data on a publicly accessible Web site. No additional IRB approval or informed consent is currently federally mandated for this research activity, because Dr. B provides no intervention for and has no interaction with human research subjects.

PHASE 3

Dr. C, at Datamine University, is interested in studying whether patients who have a particular genetic marker for Parkinson's disease also have genetic markers for Alzheimer's-type dementia. Dr. C accesses the public Web site and searches and analyzes the published DNA sequences, looking for associations.

James Ellis, *Catalona* Case Patient

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