*R4 G/BMaP Workshop
16 February 2013

*Ethics of biospecimen research
* Three Case Vignettes
* Regulations
* Case Definition
* Ethical Issues
* Ethical Obligations
* Understanding and Assessing Risks and Harms
* Responsibilities
* Resources

* Presentation Overview
Understanding and Assessing Risks

Participant issues or questions

Study design issues or questions

Privacy/Confidentiality issues or questions
* Understanding and Assessing Risks

- Custodianship and Ownership Issues
- Future and Secondary Uses of Biospecimens
- Cultural Issues
* A community-based project is approved to study genetics of rheumatoid arthritis.
* Blood samples are collected and cell lines are established.
* Study is concluded.
* Years later, doctoral student uses samples to study origins of the population.

*Vignette #1*
* A hospital process allows for use of leftover specimens for research by institution-based researchers.
* A researcher studying infertility leaves the institution.
* And takes all specimens in their lab with them.
* A national specimen repository accepts and disseminates samples from and to researchers.

* Individuals learn DNA from a study they participated in is in the repository and demand their samples be returned.

* Researchers who accessed these samples are requested to return samples and refuse.
*Unprecedented advances, both as a tool and as a science, in medical and in scientific inquiries*

*Ethical, Social and Legal Implications lag behind*

*Regulations*
Institutional Review Boards

IRB
- Protect the rights and welfare of research subjects
- Risks reasonable in relationship to benefit

AND
- Additional safeguards for children, prisoners, pregnant women
- Students, economically, educationally disadvantaged

PI
- Comprehensive description of procedures, methodology
- Sound design, no unnecessary exposure to risk
45 Code of Federal Regulations 46 Subpart A
Permits consent of participants to future unspecified research
• Health Insurance Portability and Accountability Act Privacy Rule

  • Requires that each authorization by the patient for release of protected health information includes a specific research purpose

* Federal Regulations
• 21 CFR Parts 812, 50, 56

• FDA regulations need to be considered when human specimens are used for *in vitro* diagnostic device studies that utilize “leftover” biospecimens
NCI Best Practices for Biospecimen Resources

Office of Biorepositories and Biospecimen Research
National Cancer Institute
National Institutes of Health
U.S. Department of Health and Human Services
November 2009, the Presidential Commission for the Study of Bioethical Issues was established by President Obama. The Commission is an advisory panel of the nation’s leaders in medicine, science, ethics, religion, law, and engineering.

The Commission advises the President on bioethical issues arising from advances in biomedicine and related areas of science and technology.

The Commission seeks to identify and promote policies and practices that ensure scientific research, health care delivery, and technological innovation are conducted in a socially and ethically responsible manner.

* Oct 2, 2012 — Privacy and Progress in Whole Genome Sequencing
* Dec 15, 2011 — Moral Science: Protecting Participants in Human Subjects Research
* Sep 13, 2011 — "Ethically Impossible" STD Research in Guatemala from 1946 to 1948
* Dec 16, 2010 — New Directions: The Ethics of Synthetic Biology and Emerging Technologies

State Regulations

- State genetic privacy statutes

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<th>State and Statute</th>
<th>Personal Access to Genetic Information Required</th>
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etc...

* Scientific Advisory Committee
* Biosafety & Biosecurity Committee
* Tissue Repository Committee
* Radiation, Chemical & Biological Safety Committee
* Export Control
* Conflict of Interest

* University Regulations
* Informed consent - each biospecimen resource should have documentation of informed consent
* Equipment monitoring, calibration, maintenance and repair
* Control of biospecimen collection supplies (reagents)
* Biospecimen identification and labeling conventions
* Biospecimen collection and processing methods
* Training and security (physical and informatics)
* Storage and retrieval
* Shipping and receiving
* Biospecimen quality control
* Biosafety

* Laboratory SOPs
Dealing with what is good and bad and with moral duty and obligation

* Ethics

Merriam-Webster Dictionary
• Her name was Henrietta Lacks, but scientists know her as HeLa.
• She was a poor black tobacco farmer whose cells were taken without her knowledge in 1951.
• HeLa cells were used for developing the polio vaccine, cloning, gene mapping and in vitro fertilization.
• Henrietta’s cells have been bought and sold by the billions.
• She remains virtually unknown, and her family can’t afford health insurance.

*Ethical Issues*

• Between 1982 and 1985, 883 vials of blood were taken to study rheumatic disease
• A component of the study was to study whether there was a genetically inherited aspect to the disease
• These Nuu-chah-nulth blood samples were used to produce over 200 papers as diverse as HIV/AIDS and population genetics

*Ethical Issues*

• July 9, 1990, John Moore underwent treatment for hairy cell leukemia at the UCLA Medical Center under the supervision of Dr. David W. Golde.

• Moore's cancer was later developed into a cell line that was commercialized.

• The California Supreme Court ruled that Moore had no right to any share of the profits realized from the commercialization of anything developed from his discarded body parts.

*Ethical Issues*

* Unprecedented advances, both as a tool and as a science, in medical and scientific inquiries
* Ethical, Social and Legal Implications lag behind
Researchers’ do retain ethical obligations to subjects beyond the time they donate their biospecimens.
• Religion does not separate between physical, spiritual, psychological - seen as whole

• Continuum from present life to after life and the need to keep physical being intact

• World view has established origin stories, intra- and inter-tribal relationships, family relationships understandings

* Custodianship and Ownership Issues
• Established disease/illness explanations

• Culture/Tradition where community and family decisions trump individual autonomy and decision

• Relevance of the research within the context of competing health research needs and responsibilities

* Custodianship and Ownership Issues
AI/AN tend to have fewer high school graduates, higher unemployment, lower annual median household income, higher birth rate, more high birthweights, higher uninsured, higher prevalence rates of chronic disease risk factors such as obesity, hypertension, high blood cholesterol, higher infant and maternal mortality c/c US all race rates

- Tuberculosis—750 percent greater;
- Alcoholism—524 percent greater;
- Motor Vehicle Crashes—234.6 percent greater;
- Diabetes mellitus—193 percent greater;
- Unintentional injuries—153 percent greater;
- Homicide—103.3 percent greater;
- Suicide—66 percent greater

*American Indians & Alaska Natives*

Trends in Indian Health 2002-2003 edition
Distribution of Incident Cancer Cases for American Indians, Arizona, 2001-2004

Arizona Indian Yearly Average Incidence = 363
(N = 1,454)

- Lung and Bronchus: 5.6%
- Prostate: 9.2%
- Liver: 3.9%
- Leukemia: 3.8%
- Pancreas: 3.3%
- Kidney/Renal Pelvis: 9.5%
- Breast: 12.2%
- Colon/Rectal: 7.2%
- Stomach: 3.9%
- Other (specified sites): 18.8%
- Non-Hodgk. Lympho: 3.9%
- Hodgk. Lymph: 0.3%
- Urinary Bladder: 0.9%
- Corpus Uteri and Uterus, NOS: 5%
- Other sites combined: 20.2%

Source: Arizona Cancer Registry, IBIS. April 24, 2008
• Respect and work within boundaries of individual and community world views

• Respect use of remains, concepts of respect for ancestors, reburial, immortal cell lines, storage, identification, etc.

* Custodianship and Ownership Issues
• Insurability
• Job discrimination [via insurance]
• Misattributed paternity
• Misattributed non-relationship
  - adoption with later marriage of people who turn out to be close kin
• False positive--or false negative--diagnosis of a individual or family member or results

*Potential Harms - Individual*
• Altered family dynamics
  * distancing carrier sibs/members

• When the family recruits participants, altered family dynamics
  * intra-family coercion
  * intra-family discord
  * raise expectations that are not met--mobilize the family to get more benefit from the research than the research and researcher can give or therapeutic misconception (clinical trials)

* Potential Harms - Familial
• Altered feelings of self
  * "survivor guilt" if test negative
  * "fear-of-future" if test positive

• Adherence to rules of disguising data, small sample size, aggregation of data, anonymity of individuals, families, and communities - especially in reports and publications

* Potential Harms - Familial
LEGEND

- Female
- Male
• Genetic (biologic) determinism, e.g., in/by public policy
  * determining group membership by genes [tribal removed from its membership rolls people lacking the "Indian markers"]

• Results alter community, e.g., a community's religious understanding of “Who we are.”

• Decreased political or social status in dominant society
  * "Indians are immigrants just like us"

* Potential Harms - Community
• “Dignitary harms” -- insult to a community's respect and control

* taking specimen and putting it in a repository, especially without explicit approval

* recruiting urban-residing members of a Tribe to obtain specimens from that Tribe without Tribal permission (violating or disregarding a community's decision)

* Potential Harms - Community
♦ Ensure understanding and good communication, transparency
♦ Respect culture and traditions
♦ Respect concerns and opinions of families and community
♦ Respect local research priorities and needs
♦ Respect individuals, families, and communities
♦ Respect rights and dignity

*Responsibilities*
Demystify research
Be accessible
Provide feedback and findings in a timely manner
Respect the autonomy and decisions of involved parties
Maximize benefits and minimize risks
Protect participants’ data
Share results of the research with patients, subjects, communities
Build capacity

*Responsibilities*
*In conclusion, the balance of health and disease ...*

- *Is promoted by:*
  - *basic science, and*
  - *the individual, and*
  - *the physical environment, and*
  - *the family “environment”, and*
  - *the community “environment”,*
  - *the larger society*
  
  -- and --

- *Is promoted by the interactions among the 6 factors*
• Science is a powerful tool for progress against disease

• Individuals and populations can promote good science to improve health

• Protections include ethical behavioral norms for those with access to data
Back row: COL Nelson Michael, M.D., Ph.D., Yolanda Ali, MBA, Stephen L. Hauser, M.D., Alexander G. Garza, M.D., John D. Arras, Ph.D., Daniel Sulmasy, M.D., Ph.D., Christine Grady, R.N., Ph.D., Barbara F. Atkinson, M.D.

Front row: Raju Kucherlapati, Ph.D., Nita A. Farahany, J.D., Ph.D., Amy Gutmann, Ph.D., James W. Wagner, Ph.D., Anita L. Allen, J.D., Ph.D.

*Be the investigative team that sets the bar for integrity and respect*

• 2007 Institute of Aboriginal People’s Health
  • DNA on loan
• 2012 American Indian & Alaska Native Genetics Resource Center
  • Tools and information to make informed decisions about genetic research
Ethical Principles for Whole Genome Sequencing

- **Respect for Persons**: Individuals’ privacy values should be respected
- **Public Beneficence**: The benefits should be widely shared
- **Intellectual Freedom and Responsibility**: Benefits should be pursued in an ethically responsible way
- **Responsible Stewardship**: Concern for those who cannot represent themselves (e.g., biological relatives of those who share data)
- **Justice and Fairness**: Burdens should not fall on any one group; benefits should be broadly shared
- **Democratic Deliberation**: Seeking continued input from the public, including those who call for more participatory research and from researchers who fear additional administrative burden
• **Recommendation 1.1:** Maintain or establish clear policies defining acceptable access to and permissible uses of genomic data; policies should promote opportunities for models of data sharing by individuals.

• **Recommendation 1.2:** Ensure a consistent floor of federal and state privacy protections covering genomic data regardless of how they were obtained; policies should prohibit unauthorized whole genome sequencing without the consent of the individual from whom the sample came.
• **Recommendation 2.1:** All persons who work with genomic data must be (1) guided by professional ethical standards related to the privacy and confidentiality of data and not intentionally, recklessly, or negligently access or misuse that data, and (2) held accountable to laws and regulations that require remedial or penal measures in the case of lapses in data security.

• **Recommendation 2.2:** Outline to donors acceptable access to and permissible use of genomic data; data should be stripped of traditional identifiers whenever possible; only in exceptional circumstances should entities such as law enforcement, defense, or security have access to biospecimens or genomic data for non-health-related purposes without consent.

• **Recommendation 2.3:** Ensure data complies with relevant regulatory norms and share data security best practices across the industry in both the public and private sector.
Informed Consent

- **Recommendation 3.1:** Evaluate and adopt robust and workable consent processes that allow research participants, patients, and others to understand who has access to their genomic data and know how these data might be used in the future; consent processes should ascertain participant or patient preferences when samples are obtained.
- **Recommendation 3.2:** Establish clear and consistent guidelines for informed consent forms for genomic research.
- **Recommendation 3.3:** Inform individuals that incidental findings are likely to be discovered in the course of whole genome sequencing.
- **Recommendation 3.4:** Support studies to evaluate proposed frameworks for returning incidental findings and other results and investigate the preferences and expectations of the individuals.
Facilitating Progress

• **Recommendation 4.1:** Facilitate explicit exchange of information between researchers and clinicians, while maintaining robust data protection safeguards to advance genomic medicine.

• **Recommendation 4.2:** Promote opportunities for the public to benefit from genomic research. Promote opportunities for the exploration of alternative models of the researcher – participant relationship, including participatory and collaborative relationships.
* National Congress of the American Indian
  http://genetics.ncai.org/
* Jimmie B. Vaught, Nicole Lockhart, Karen S. Thiel and Julie A. Schneider. Ethical, Legal, and Policy Issues: Dominating the Biospecimen Discussion Cancer Epidemiol Biomarkers Prev December 2007 16; 2521
* CIHR GUIDELINES FOR HEALTH RESEARCH INVOLVING ABORIGINAL PEOPLE, May 2007
* Skloot, R. The Immortal Life of Henrietta Lacks, Random House

*Resources*
* 45 CRF 46 Subpart A, Office for Human Research Protections: http://www.hhs.gov/oahrp/


* HITECH Act Enforcement Interim Final Rule: http://www.hhs.gov/ocr/privacy/hipaa/administrative/enforcementrule/hitechenforcementifr.html

* Additional Resources
* **NCI Best Practices for Biospecimen Resources:**

* **National Conference of State Legislatures, Genetic Privacy Laws:**

* **Presidential Commission for the Study of Bioethical Issues,**
http://bioethics.gov/cms/about

* **Additional Resources**
* Office for the Responsible Conduct of Research, http://orcr.arizona.edu/hcpp
  * Conflict of Interest  *Protected Health Information
  * Export Control  *HIPAA
  * Human Subjects Protection Program
  * Research Integrity Office  *Responsible Conduct of Research
  * Institutional Animal Care & Use Committee

* Office of Radiation, Chemical & Biological Safety, http://orcbs.arizona.edu/biosafety/
  * Agency Guidelines  *Laboratory Close-out, Forms, Training
  * Autoclaving  *Recombinant Material
  * Biosafety Cabinet  *Safety Committees
  * Biosafety Levels
  * SOPs, Biosafety Manual

*U of A Resources
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