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Institutional, Ethical, and Regulatory Considerations for Using Biospecimens in Research

Objectives

- Review history of and institutional requirements for use and transfer of biospecimens in research
- Discuss ethical and regulatory considerations to be aware of when engaging in research with biospecimens
- Outline helpful tips to streamline the IRB/Biospecimen Transfer Committee (BTC) review processes

Henrietta Lacks & HeLa Cells: Impact on Medicine & Research

Henrietta Lacks
(August 1, 1920 – October 4, 1951)

- January 1951 went to Johns Hopkins Hospital for treatment of a pain in her “womb”
- was diagnosed with “epidermoid carcinoma of the cervix, Stage I”
- treated with biopsy, radium implants and radiation

Key players in the discovery of HeLa cells

Richard W. TeLinde (1894 - 1989)

•interested in studying the progression of cervical cancer (carcinoma *in situ* vs. invasive carcinoma)

George Gey (1899 - 1970)

•spent decades trying to culture human cells

Consent Process in US Hospitals in the 1950s

I hereby give consent to the staff of The Johns Hopkins Hospital to perform any operative procedures and under any anaesthetic either local or general that they may deem necessary in the proper surgical care and treatment of

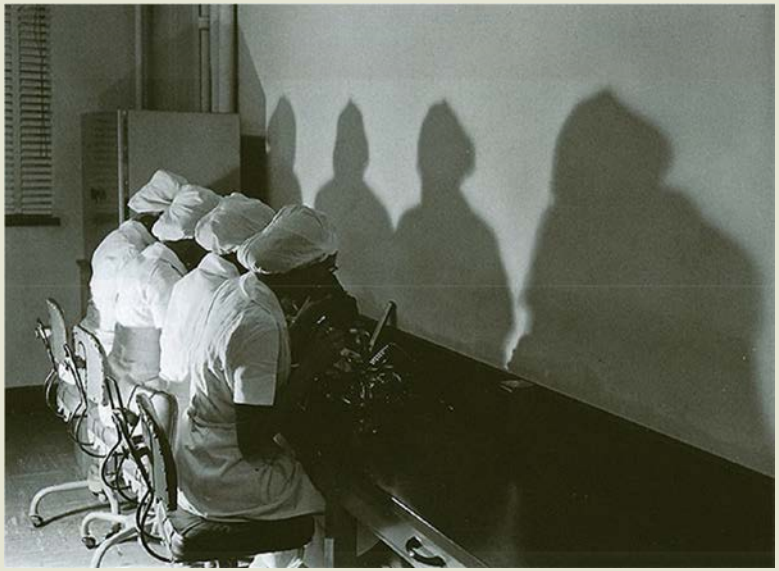
_____

- consent form signed by Henrietta Lacks

By 1952, HeLa cells were travelling by planes, trains, and automobiles (and pack mule) all over the world

- HeLa cells eventually even went into space
- HeLa cells given freely to other researchers

Technicians inspecting HeLa cells for shipment from the Tuskegee Institute



Within a few years companies began selling HeLa cells and the media required to grow them

- led to standardization and optimization of cell culture
- allowed scientists quick and cheap access to HeLa cells
- launched the cell culture industry (today a multibillion dollar business)

What have we learned from the Henrietta Lacks story?

Biospecimens can last for years so ethical oversight is essential

Many individuals have deep connections to living cells

- Need to balance support for fast path to cures with fairness and equity

Whenever commercial interests are included, additional thought must be given to fair and just use of the biospecimens

It takes a multidisciplinary team to make decisions on use of biospecimens

Background & Rationale for Biospecimen Transfer Policy

- Honoring the Legacy of Henrietta Lacks
- Commitment to the ongoing efforts to honor the contributions of precious resources such as biospecimens
- Commitment to thoughtful and responsible stewardship of all biospecimens collected through clinical or research procedures at Johns Hopkins Medicine

Policy & Related Guidance

- Johns Hopkins Medicine Policy: Transferring Human Biospecimens to Outside Organizations
- Office of Human Research Subjects' Guidance: Guidelines on Transferring Human Biospecimens to Outside Organizations

Definition of Human Biospecimen

- **Human Biospecimen**:
  - Tissue, blood product, serum, urine, saliva, DNA, and other biological materials or specimens. This includes cell lines, organoids, and PDX models derived from JHM human specimens.
  - Obtained as part of regular clinical care, or via clinical research where individuals have agreed to donate their specimens for a specific research purpose.

Human biospecimens obtained through clinical or research procedures at any JHM facility or by JHM researchers are the property of JHM and fall under the JHM Biospecimen Transfer policy.

Key Requirements of the Policy

- Research collaboration with the entity wishing to access JHM biospecimens.
- Biospecimen Transfer Committee must meet at least quarterly.
- JHM researcher must detail the role of JHM in the design, research, analysis, and proposed publication plans.
- Once a BTC request is approved, the agreement must be documented by designated JH office.

Exceptions to Policy

- Biospecimens contained in or transferred to NIH funded tissue bank;
- Biospecimens collected and transferred as part of CTA or prospective sponsored research agreement;
- Biospecimens are collected/transferred to service provider to perform requested services – data nor specimens retained by service provider.

The Role of the Biospecimen Transfer Committee

- Role
  - To review all new transfer requests when outside entities wish to access JHM Biospecimens (via convened or expedited review process)
- Factors Considered:
  - Utilized under highest and best use;
  - Managed in compliance with regulatory, ethical, privacy standards;
  - Conflicts of Interest are considered

BTC Process in a Nutshell

- **Common pathways through which PIs learn of BTC requirement**
  - Reaches out to BTC staff for instructions on how to get process started; or
  - Submits MTA request and is notified to complete BTC process as a component of MTA process.
  - Triggers in eIRB, Section 23
- **PIs must submit a new application (if one does not exist) or Change in Research (CIR) to request biospecimen transfer.**
  - IRB application required to facilitate biospecimen transfer review even if the activity qualifies as “not human subjects research”

BTC Process in a Nutshell

- When Biospecimen section (23.4) is updated to indicate “Other,” BTC review is triggered.
- BTC staff screen for all required elements
  - Biospecimen Transfer Information form/sheet
  - Documentation related to MTA and DUA
  - Consent form with applicable language highlighted

IRB Considerations Related to Biospecimen Transfer

- BTC is just one component of the Human Research Protections Program (HRPP)
- IRB reviews the plan for biospecimen transfer as part of a new application or a change in research in accordance with federal regulations, institutional policies and required ancillary reviews (including BTC review)

IRB Considerations

- Ethical Principles
- Regulatory Requirements for Informed Consent
- Participant/Patient/Community Expectations
- Risk
- Transparency and Trust in Research

The Belmont Report - Three Ethical Principles

- **Respect for Persons**
  - Recognize & Respect Individual Autonomy
  - Protect those with diminished Autonomy

    [Informed Consent Process, Special Protections for Vulnerable Populations]
- **Beneficence**
  - Do No Harm
  - Maximize potential Benefits/Minimize Potential Harms

    [Study design, Risk/Benefit Ratio]
- **Justice**
  - Fairness in selection of subjects
  - Be sure access to research is not denied from certain subjects
  - Be sure research burden is not imposed on certain populations

Federal Regulations: Criteria for IRB Approval

- Risks are minimized
- Risks are reasonable in relationship to the potential benefits
- Subject selection is equitable
- Informed Consent is obtained and documented
- Plans for monitoring are appropriate to ensure safety
- Protections for privacy & confidentiality are adequate

Informed Consent

- Ensures that participants have adequate information to make a decision about study participation, including:
  - Information about the research procedure
  - Purpose of the research
  - Must describe procedures for protecting subject confidentiality
  - Explanation of anticipated risks/benefits
  - Must identify research participation as voluntary
  - Must provide person to contact for questions about the research
  - Must provide key information first
- Information must be provided at an 8th grade reading level in the primary language spoken by the participant
- Information must be free of coercive elements or undue influence

Optional Elements for Informed Consent

- A statement that there may be unforeseeable risks
- The circumstances when subject participation may be terminated by the investigator
- Any additional costs to the subject
- The consequences of a subject's decision to withdraw/explanation of how to withdraw
- A statement that significant new findings which may affect willingness to continue participation will be provided to the subject
- The approximate number of subjects involved in the study.

New Required Consent Elements under the Revised Common Rule : Research with Identifiable Data or Biospecimens

(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility;

OR

(ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

New Consent Elements under the Revised Common Rule

- A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)

Special Considerations: Consent

- Longitudinal studies involving collection of biospecimens – more than one version of consent is likely
  - Variations of consent may include conflicting language based on historical evolution of consent forms
- Re-consent may be required in order to share
- Clinical biospecimens where consent was never obtained makes it difficult to transfer those specimens for research

Special Considerations: Contractual Limitations on Use

- MTA
  - To send human biospecimens maintained or collected at JHM, an MTA or research agreement is required.
- DUA*
  - Required to send JHU data outside the University/JHM.

*In some circumstances, DUA language may be built into the MTA for the same project/transfer

In certain cases the original specimen source is external to Hopkins but the specimens have been manipulated in a way that makes them "ours". In these cases the original MTA must still be reviewed for any limitations of specimen use/sharing

Case Study #1

A longitudinal research study has been open for 10 years. Over the course of the study's history, the consent form has been revised multiple times. As part of a new research effort, the PI submits a change in research to the IRB to transfer blood samples from 100 participants to a colleague at an external academic institution whose lab has special equipment to perform analyses on the samples. Limited clinical data with samples. The external collaborator plans to retain data and residual specimens for additional future use.

- **Does this transfer require BTC review?**
- **What considerations might the BTC/IRB have?**

Case Study #2

A clinician submits a request for a material transfer agreement to transfer 20 de-identified clinical samples from patients with a rare genetic disorder to a commercial 3rd party for testing and development of a new lab assay. The samples were originally collected from patients in the clinical setting without any research consent. The company has reached out to the clinician as JHU has a robust clinical program for patients with this rare disorder.

Does this transfer require BTC review?

What considerations might the BTC/IRB have?

Streamlining the BTC Process

- Reach out to jh-biospecimens@jh.edu for assistance
- Contact us by Requesting a Consult: https://www.hopkinsmedicine.org/institutional-review-board/about/contact
- Visit our site for guidance: https://www.hopkinsmedicine.org/institutional-review-board/guidelines-policies/guidelines/transferring-human-biospecimens-to-outside-organizations

Questions?