The Tissue Issue

Perspectives on Protection and Privacy Issues in Data/Tissue Repositories

INDIANA UNIVERSITY

HCCA Research Compliance Conference, 2018

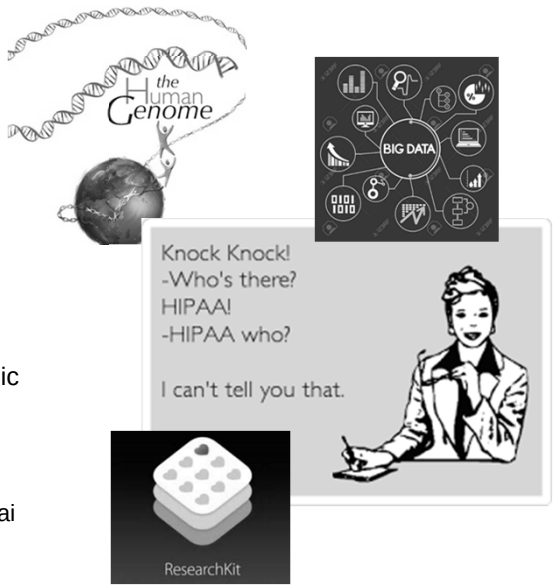
Recent Regulatory Changes impacting Tissue Research

Tissue Research under Current Regulations

- Common Rule – almost no mention of specimens
  - Biospecimens can be included under expedited category 5 and exempt category 4
- FDA human subjects regulations – minimal provisions regarding specimens
  - Device regulations specify that “subject” includes specimens (even if fully de-identified)
- No specific protections or provisions related to genetic research, tissue, or biospecimens

Since Common Rule…

- **New technologies**: digital records, EMR, human genome project, mobile tech, big data
- **New initiatives**: repositories, precision medicine, translational research, comparative effectiveness
- **New environment**: privacy, focus on research, public engagement
  - The Immortal Life of Henrietta Lacks
  - Secondary use of specimens donated by Havasupai for genetic research
  - Use of newborn blood spots for research



Proposed Common Rule Revisions – Focus on Biospecimens

- 2011 ANPRM (Advanced Notice of Proposed Rulemaking):
  - Consent required for research use of biospecimens, even if de-identified and originally collected for clinical purposes
  - Option to use a brief/broad consent at time of clinical collection of sample
  - Comments contemplate opt-in/opt-out for special categories of research, such as creation of cell lines
  - Special privacy protections required for storage of all biospecimens, regardless of identifiability

Proposed Common Rule Revisions – Focus on Biospecimens

- 2015 NPRM (Notice of Proposed Rulemaking):
  - Retains special rules for biospecimens as described in ANPRM
  - Adds new criteria for waiver of informed consent for research involving biospecimens to make it very difficult for IRBs to grant waivers
- A new approach
  - Citing advances in genomic technology among other factors
  - Intent: researchers can no longer avoid human subjects protection requirements by de-identifying biospecimens

Final Rule – HHS Reconsiders

- In response to comments, restrictive provisions regarding biospecimens were removed from Final Rule
  - For now, genetic information still not considered an identifier
- Requirement that definition of identifiable be reexamined at least every four years
  - Changes to definition can be made via future guidance rather than revisions to Common Rule
  - Whole genome sequencing will be first technology to be examined
- Tissue treated the same as data for most purposes
- Secondary use of de-identified, leftover tissue collected for clinical purposes remains non-human subjects research
  - IRB review not required

Biospecimens in Final Rule

- Emphasis placed on research data being recorded in de-identified fashion
  - New criteria for waiver of informed consent
  - IRB must find that research cannot practicably be carried out without using data or specimens in identifiable format
- New Informed Consent elements:
  - Statement that either identifiers may be removed and data or specimens shared with other researchers OR data and specimens will not be used for future research purposes even if de-identified
  - Statement that biospecimens may be used for commercial profit and whether subject will share in this profit
  - Whether research will or might include whole genome sequencing

Biospecimens in Final Rule

- Broad consent is still an option but only when **identifiable** biospecimens are to be stored or used for secondary research purposes
- Why the change?
  - Almost half of public comments to NPRM related to biospecimens provisions
  - Administrative burden for health systems, researchers, and IRBs
  - Increased risk of breach of confidentiality if incentive for de-identification is removed
  - Possibility of stifling scientific discoveries due to fewer biospecimens being available for research

Broad Consent: Is it Worth It?

What is Broad Consent?

- Intended to be used in place of a standard research consent form/process
- Allows researcher to obtain general (broad) consent to the use of biospecimens for future unspecified research
- Broad consent does not cover research **collection** of biospecimens – only storage, maintenance, and use
    - If specimens are collected specifically for research (are not leftover clinical specimens), standard informed consent is still needed for collection

Why Use Broad Consent?

- Relatively easy to develop a broad consent template to be provided to all patients to request permission to use identifiable specimens and data for future unspecified research
- Allows for storage, maintenance, and **future use** to be exempt under the new Common Rule
    - At most institutions, exempt research is reviewed by IRB office, but process often requires less information and approval is faster than expedited or full board review

But There's a Catch:

- If an individual is asked to provide broad consent for storage, maintenance, and secondary use of identifiable information or biospecimens and refuses to consent, an IRB cannot waive consent for secondary research use of identifiable information or biospecimens
- Would require careful tracking of all refusals and a method for "flagging" patients whose data and specimens cannot be used for future research without their consent
- Loopholes:
  - Data/specimens could still be de-identified and used for research as this would not require IRB review
  - Identifiable data/specimens could still be used for other non-research purposes, such as quality improvement and program evaluation

What is Refusal to Provide Broad Consent?

- Clear refusal to broad consent would need to be tracked
- What about refusal to participate in a specific biobanking effort? Does this need to be treated as refusal to broad consent?
- What about non-response? If consent process is presented electronically or as part of a registration process and the patient skips over that form, is that construed as a refusal?

IRB Difficulties

- Restriction on granting future waivers is directed toward IRBs
- What if subject refused broad consent at one institution but also receives care at another facility that does not have a broad consent process? Ethically waiver should not be granted, but logistically, there is no way to track this.
- No guidance on how this can be operationalized in a single IRB world
  - Will IRBs need to assume that all institutions may have a broad consent process and address this when granted waivers of consent?
  - How should IRBs document granting of waivers for all subjects but those who have refused broad consent?
  - Does the IRB have a responsibility to review the institutions processes for tracking broad consent and refusals before granting any waiver of consent?

Additional Complications

- Final Rule only allows exempt review of secondary research use of specimens/data collected under broad consent if individual research results are not returned to subjects – what about unexpected clinically relevant findings?
- Can a patient who has declined or not responded to request for broad consent be approached again? How often? What about being approached by a different investigator?
- Will patients understand the difference between refusal of broad consent and being approached for subsequent specific research studies?

Best Practices for Protection of Data and Confidentiality while Encouraging Sharing

Emphasis on Data Sharing

- Data sharing is no longer an option – it has become an expectation
- In 2014 NIH published Genomic Data Sharing Policy
  - Ensure the broad and responsible sharing of genomic research data
  - "Sharing research data … is essential to facilitate the translation of research results into knowledge, products, and procedures that improve human health."
- Increased requirements for and enforcement of clinicaltrials.gov registration and results reporting

Facilitating Sharing

- Default: data shared outside the research team is de-identified
- Ensure unnecessary regulatory burdens are eliminated
  - Repository protocols and consents should not state that IRB approval will be required for all data sharing
  - Encourage researchers to broadly describe possible future uses – generally not necessary to limit future use unless subjects are unlikely to consent to future unspecified research
- Proactively consider what happens to specimens/data if researcher leaves your institution
  - Include appropriate language in initial consent and Authorization

Importance of Confidentiality and Security

- ANPRM and NPRM focused heavily on data protections
- Due to lack of details regarding requirements, most data security provisions were left out of Final Rule
- Researchers, IRBs, and compliance offices are left with little guidance regarding data security requirements and best practices
- But importance was recognized in Final Rule with new requirements for limited IRB review for certain categories of exempt research

Intersection of Common Rule and HIPAA

- Preamble discusses comments that urged adoption of HIPAA definition of personally identifiable information for purposes of defining "identifiable" under Common Rule
  - HIPAA definition was **not** adopted
- New exempt category 4 allows for collection and analysis of identifiable data when the use is subject to HIPAA protections
  - Recognition that HIPAA provides adequate privacy protections and IRB review is not needed as additional safeguard to protect subjects' rights and welfare

Start with HIPAA Protections

- Most data and bio-repositories will be subject to HIPAA, but even if not, HIPAA protections should be applied
  - HIPAA Privacy and Security Officer can provide guidance to IRB and researchers regarding adequate protections
  - Data security plan should address both electronic storage of information and physical access to and labelling of specimens
- Don't rely on non-technical staff or IRB members who are not data security experts for review and approval of security plans

Provide Resources for Researchers

- Collaborate on guidance for researchers regarding acceptable systems for collecting, storing, transmitting, computing, and archiving research data
- Provide strong incentives to use approved/vetted systems and processes for storage of research data
- Define process for review of research proposing to use systems not yet vetted by appropriate data security staff

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