Secrets Of A No Hassle MTA

Patricia A. Bass, J.D., M.P.H.,
Associate General Counsel
Boston Medical Center
April 13, 2016

Outline

- Description of Material Transfer Agreements
- Types of MTAs
- Effect of HIPAA and human subjects' regulations on MTA documentation
- Institutional nuts and bolts

Legal Basics

- Human and animal biological materials generated during research belong to the institution that received the funding to conduct the research
- Investigator-initiated research: belongs to the institution whose resources were used to generate the material
- MTAs are institutional agreements

Legal Basics - 2

- An MTA is a transfer of custody or possession, but not ownership – a “bailment”
  - —The owner (Provider) sets the terms of use of its property
- Typical MTA terms
  - —Establish that Provider remains the owner of the materials
  - —Limits uses of the materials
  - —Discusses ownership and IP rights to inventions that arise from Receiver’s research (might also claim Provider right to use invention in its own research)
  - —Avoidance of conflicts with other research of the investigator or at the institution

Time and Complexity Variables

- Status of Provider or Recipient as a tax exempt/non-profit institution or a for profit corporation

- Human material or non-human material
  - —HIPAA and human subjects' regulations
- Material as product of nature or invention

Provider Or Recipient Is Commercial Entity

- Negotiation brings up issues typically encountered in commercial clinical trial agreements
  - —Does proposed research further an exempt purpose?
    - BMC and BU are both tax-exempt public charities
    - Patient care, research, education
  - —Is the study scientific research?
    - Mere testing is not research
  - —Is the research in the public interest?
    - Right to publish
      - Timing
      - Non-interference
  - —Will IP (usually patents) arise from the use of tax exempt bond financed property?
    - Required to disclose private use on tax return
  - —Are IP rights being granted before they come into existence?

Non-Human Materials

- Except for biological materials which are inventions, non-human MTAs are fairly simple
  - —Uniform Biological Material Transfer Agreement (UBMTA) is commonly used
  - —Boston Medical Center and Trustees of Boston University are signatories to the Master UBMTA
  - —List of signatories is online at

    http://www.autm.net/resources-surveys/material-transfer-agreements/uniform-biological-material-transfer-agreement/master-ubmta-agreement-signatories/

Human Biospecimens

Human biological material encompassing the full range of specimens

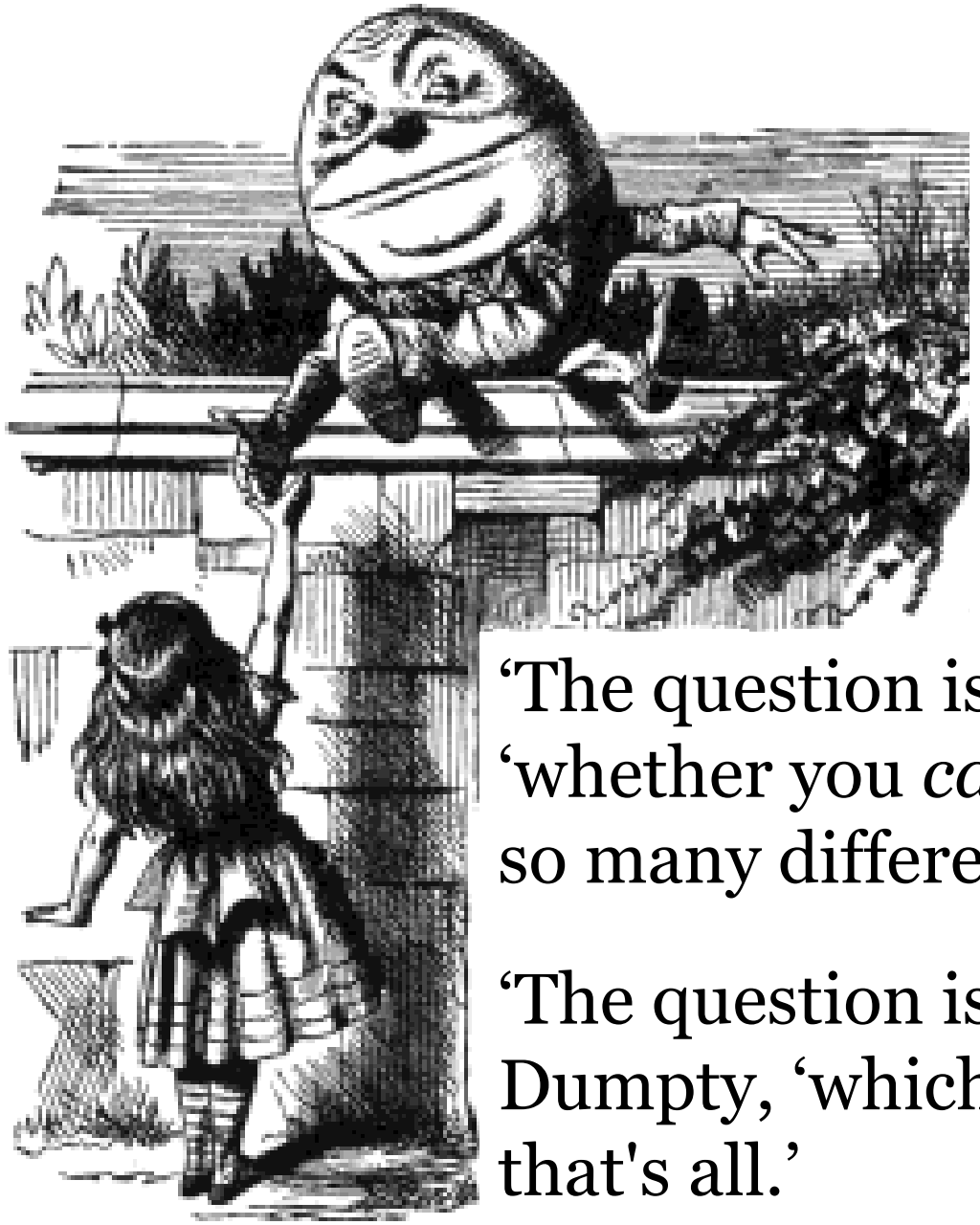
- Subcellular structures (DNA)
- Cells
- Tissues (blood, bone, muscle, connective tissue, skin, etc.)
- Organs (e.g., liver, bladder, heart, kidney, placenta, etc.)
- Gametes (sperm and ova)
- Embryos
- Fetal tissues
- Waste (hair, nail clippings, urine, feces, and sweat, which often contains shed skin cells)

Complexities of Human Biospecimens

- In addition to the usual MTA standards, the transfer of human materials includes compliance with both HIPAA and the federal human subjects' regulations
  - Human materials associated with a certain amount of health information
  - How materials acquired matters
- Derivatives of biospecimens may be patentable; e.g., cDNA and certain cell lines
- Natural DNA is not patentable [Association for Molecular Pathology v. Myriad Genetics, Inc., 133 S.Ct. 2107 (2013)]

Repository Rules

- For legal analysis purposes, any data or human tissue saved and set aside for research purposes is a "repository"
- Other names: tissue bank, biospecimen bank, registry
- A repository can be formal or informal; large or small
- OHRP

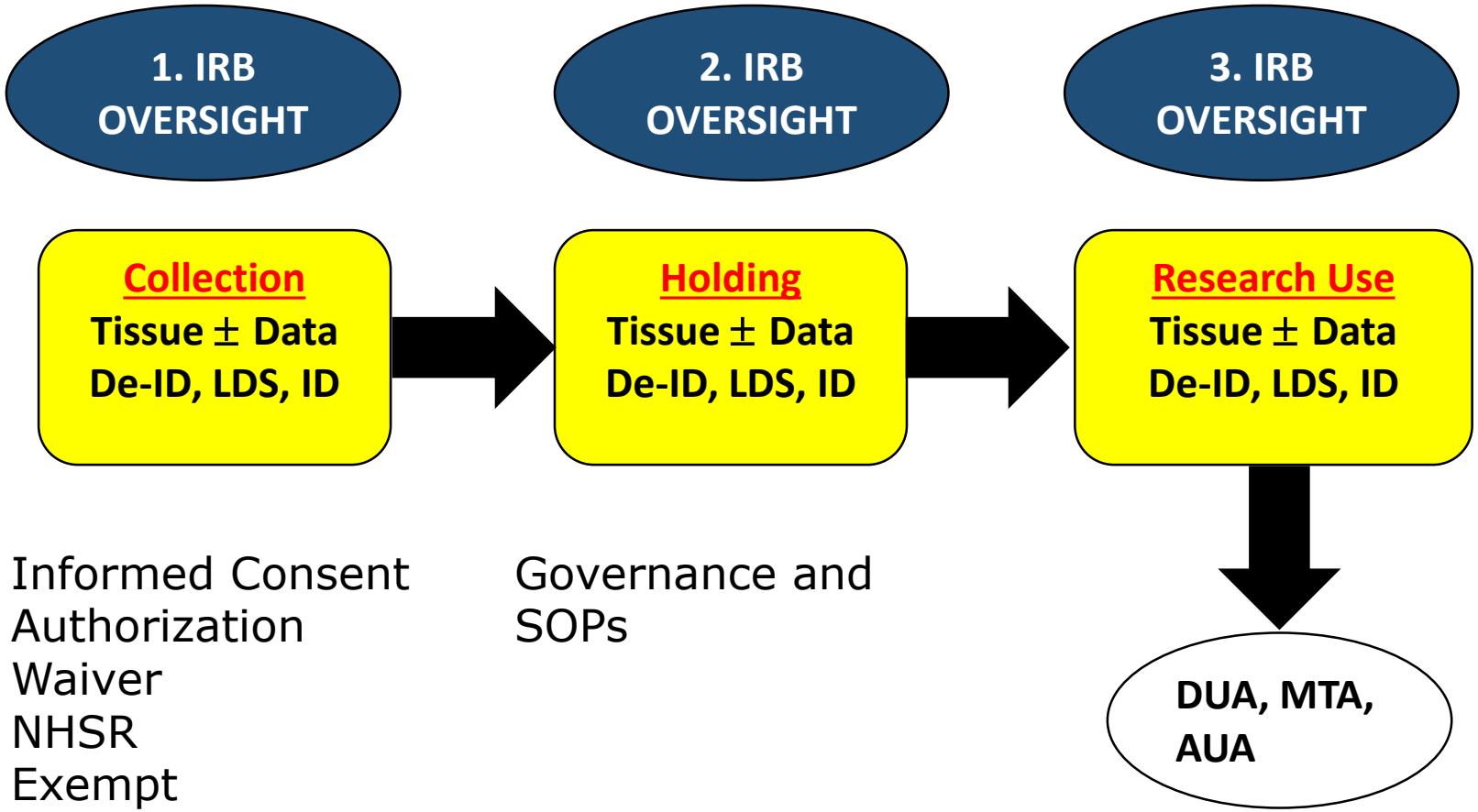


‘When I use a word,’ Humpty Dumpty said, in rather a scornful tone, ‘it means just what I choose it to mean -- neither more nor less’

‘The question is,’ said Alice, ‘whether you *can* make words mean so many different things.’

‘The question is,’ said Humpty Dumpty, ‘which is to be master -- that's all.’

The 3-Part Repository Model



Informed Consent
Authorization
Waiver
NHSR
Exempt

Governance and SOPs

Basic HIPAA For Data Associated With Human Biospecimens

- Both Use and Disclosure of individually identifiable health information for research require either
  - —AUTHORIZATION
  - —WAIVER of AUTHORIZATION, or
  - —Exception to AUTHORIZATION

Collection with Authorization and Informed Consent

- Consent form must describe research activity including banking or registry activities
- Maintenance and secondary uses should be described
- You are held to what you “promise”

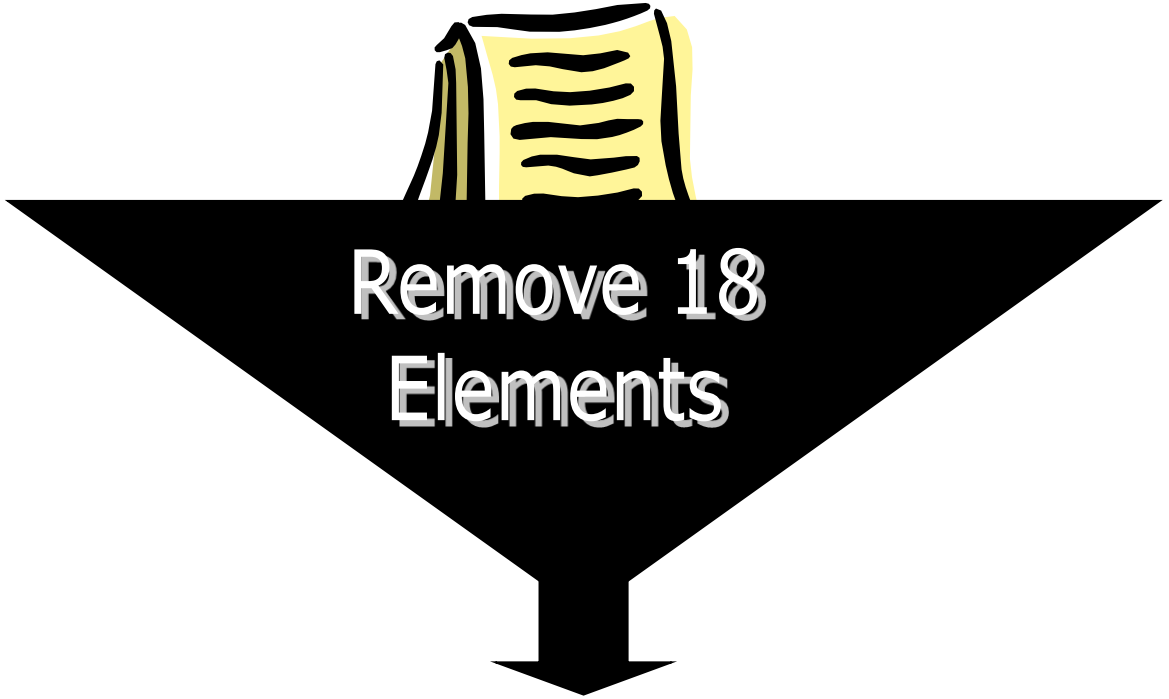
Waiver of Consent and Authorization

HIPAA Waiver of Use and Disclosure Authorization

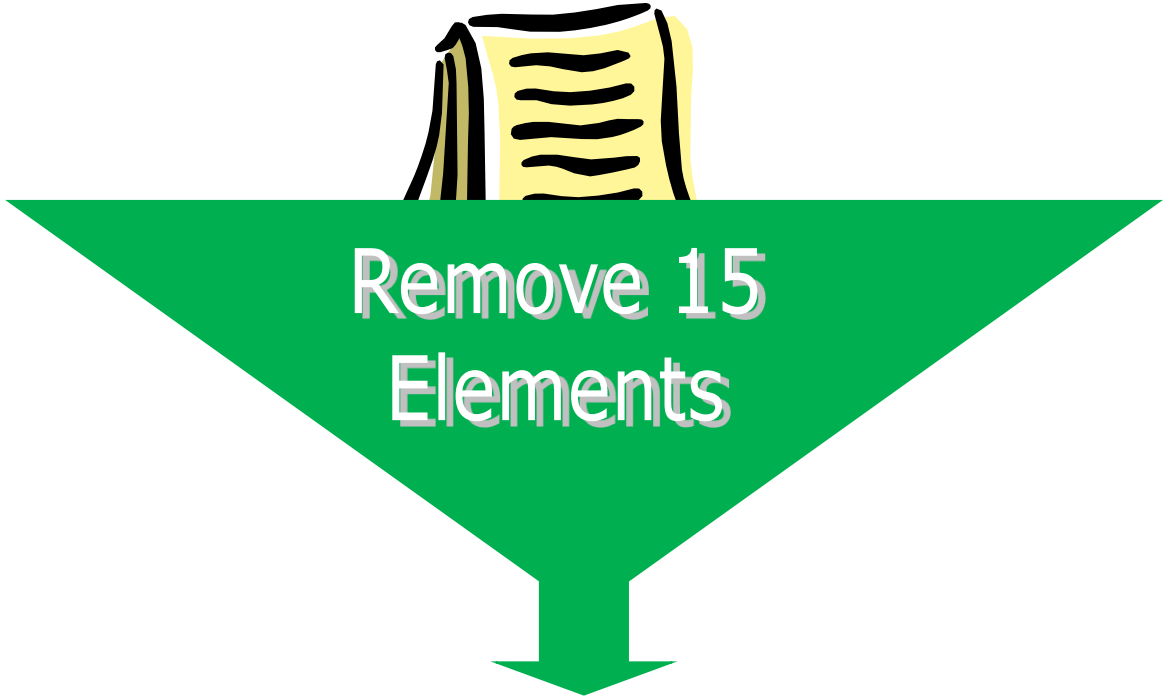
- Privacy Risk ≤ Minimal
  - Protection plan
  - Destruction at earliest possible
  - Assurance of no re-disclosure or reuse
- Research impracticable without waiver
- Research impracticable without access to and use/disclosure of PHI

Common Rule Consent Waiver

- research ≤ minimal risk
- waiver will not adversely affect the subjects' rights and welfare
- research could not practicably be carried out without the waiver or alteration; and
- whenever appropriate, the subjects will be provided with additional pertinent information



De-Identified Data Set



Limited Data Set

Do Not Confuse These Two Ideas

Safe Harbor De-Identification: 18 Elements To Remove

- Name
- Medical Record #
- Telephone/Fax #
- License #
- E-mail address
- Social Security #
- Health Plan Beneficiary #
- Geo-division < state
- Date elements
- Web URL
- Health Plan ID #
- Account #
- Certificate/License #
- Vehicle identifier
- Device identifier
- Internet Protocol Address
- Biometric identifiers
- Photographic Images
- Any other unique identifying number, characteristic, or code

Limited Data Set: Remove These Elements

- Names
- Postal address information, other than town or city, State, and zip code
- Telephone numbers
- Fax numbers
- Electronic mail addresses
- Social security numbers
- Medical record numbers
- Health plan beneficiary numbers
- Account numbers
- IP address numbers
- Certificate/license numbers
- Vehicle identifiers and serial numbers, including license plate numbers
- Device identifiers and serial numbers
- Web URLs
- Biometric identifiers, including finger and voice prints; and
- Full face photographic images and any comparable images

DDS & LDS: What's Different

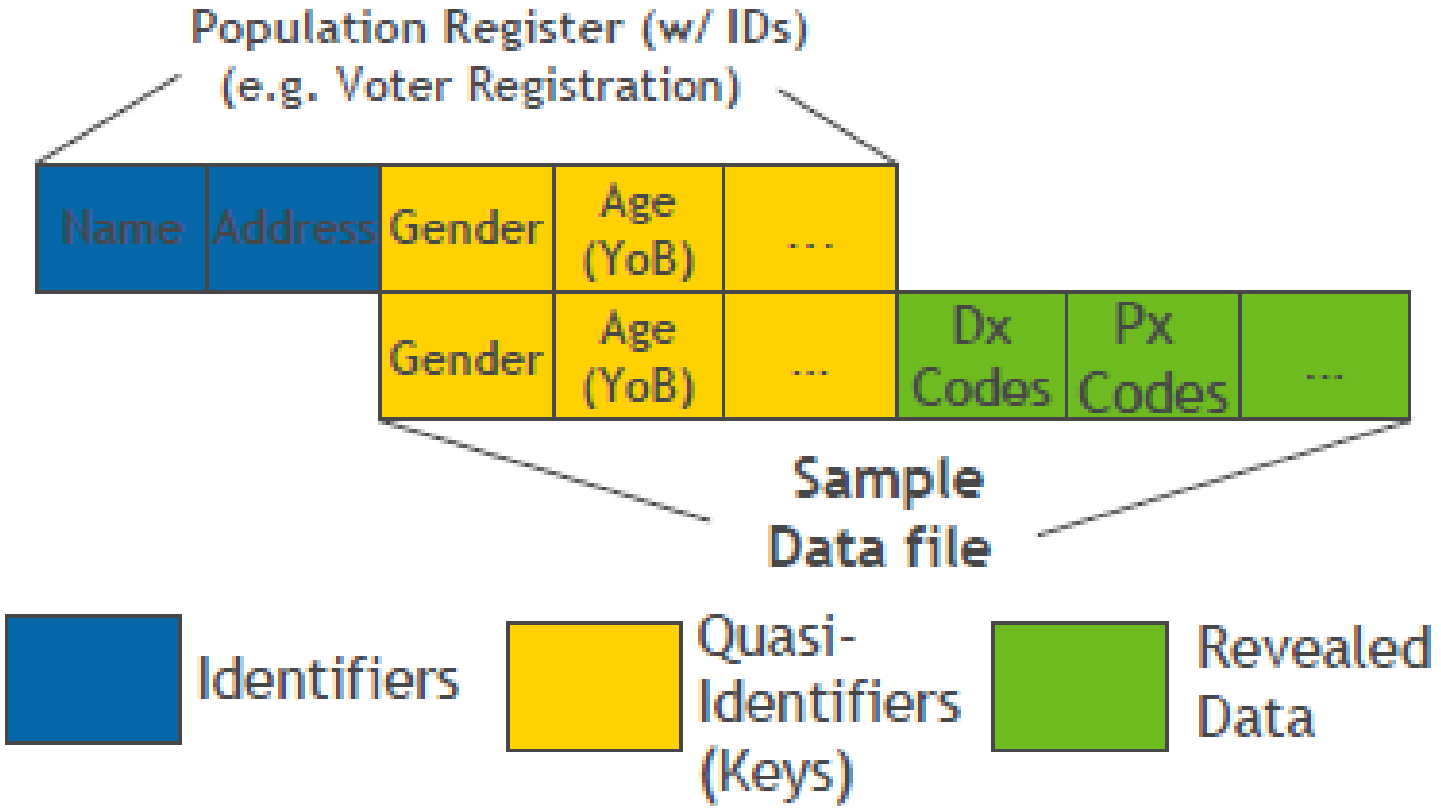
De-identified Data Set Must Exclude All of the Following Elements	Limited Data Set Must Exclude All of the Following Elements
All **geographic subdivisions smaller than a State**, including street address, city, county, precinct, **zip code**, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census: (a) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (b) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000	Postal address information, other than town or city, State, and zip code **Less Stringent**
All elements of dates (except year) for dates directly related to an individual, including birth date, **admission** date, **discharge date**, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older	**Can Be Retained**
Any other unique identifying number, characteristic, or code;	**Can be Retained**

Limited Data Set ≡ Identifiable Data

- Legally a Limited Data Set is still considered identifiable information under HIPAA
- Limited Data Set transfer with biospecimens requires a Data Use Agreement addendum to MTA

The Scary Truth

Record Linkage is achieved by matching records in separate data sets that have a common "Key" or set of data fields.



"*Understanding De-identification, Limited Data Sets, Encryption and Data Masking under HIPAA/HITECH: Implementing Solutions and Tackling Challenges*," Barth-Jones, Daniel C

Not Human Subjects Research

- Common Rule regulatory analysis is done in tandem with HIPAA analysis
- OHRP has issued guidance on circumstances when research is not NHSR

NHSR Conditions

- OHRP does not consider research involving **only** coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) if the following conditions are both met:
  - —the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and

NHSR - 2

- the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
  a) the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);
  b) there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
  c) there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

Is the Research Exempt?

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.

Common Rule Coded ≠ HIPAA Deidentified or Limited Data Set

Common Rule

Coded means

- identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and
- a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

HIPAA

- DDS - 18 Safe Harbor identifiers removed or statistician certified
- LDS - 15 specified direct identifiers removed
- Code
  - Not derived from subject related information
  - Cannot be translated
  - Non-disclosure of code or mechanism

Regulatory Summary

- How human subjects' information was collected, held, and to be given out are examined by MTA drafters
- Clarity about the type of IRB review or approval help speed the process
- Sometimes it becomes necessary to amend an IRB protocol—if possible—to accommodate a proposed MTA

What Does this Mean for MTAs?

- Proposed MTA and representations in the IRB protocol, such as repository maintenance rules, users, research purposes, authorization/consent waiver, informed consent should be consistent; e.g.,
  - Provider collected Materials collected in accordance with informed consent procedures approved by its Institutional Review Board ("IRB") or with an exemption or waiver determination by the IRB. The Original Human Material provided to Recipient will not be accompanied by Protected Health Information ("PHI") as defined by 45 C.F.R. §164.501 of the Health Insurance Portability and Accountability Act ("HIPAA") regulations. The parties acknowledge that laws relating to data security and `privacy are evolving and that amendment of this Agreement may be required to provide for procedures to ensure compliance with such developments.

What Does this Mean for MTAs - 2

- Users per se are generally not co-investigators on the BU/BMC protocol
- BU/BMC investigator is generally not a co-investigator on a user protocol
- MTA must be consistent with sponsor or funder requirements and other institutional contractual obligations including IP and licensing

What Does this Mean for MTAs? - 3

- International Committee of Journal Medical Editors Standards
  - Authorship credit should be based on 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.
  - Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship.

MTA Direction and Institutional Procedures

- MTAs which transfer material away from BMC or BU are called Outgoing MTAs
  - —For non-human materials these are generally handled by the BU Office of Technology Development (OTD)
  - —Many outgoing MTAs which have HIPAA and human subjects' implication are handled by BMC
- MTAs which bring material to BMC or BU are called Incoming MTAs
  - —Incoming MTAs: the outside Provider Institution generally provides the template for the agreement

Incoming MTAs

- Boston Medical Center
  - Material Transfer Agreement Policy (Incoming MTAs) BMC Policy 39.03.33
  - Agreements negotiated in Clinical Trials Office of Office of the General Counsel for material belonging to BMC
- Boston University Office of Sponsored Programs negotiates for materials belonging to BU

HIPAA Omnibus Rule

- January 25, 2013 DHHS issued final regulations for the Health Information Technology for Economic and Clinical Health (HITECH) Act
- Effective March 26, 2013, research consent forms may combine conditioned (for the research treatment) and unconditioned Authorizations (for the repository)

Future Research

- DHHS no longer interprets the “purpose” requirement of research authorizations to be study specific
- Future research authorizations that “adequately” describe purpose such that it could be reasonable for individual to expect his/her PHI could be used or disclosed for such purposes
- “Adequate” is a circumstance that will be left to the IRB’s judgment

The Common Rule NPRM

- On September 8, 2015, the federal Common Rule agencies published a Notice of Proposed Rulemaking that would significantly change the regulations for the protection of human subjects
- Among the biggest changes is that all biospecimen research would require consent
- Long phase-in period: 3 years for biospecimen provisions

Questions

DON’T SHOOT THE MESSENGER!