The Tao of Repositories

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Agenda

- Federal Human Subjects and HIPAA Regulations
- Implications for material transfer agreements and data use agreements
- HIPAA HITECH Omnibus Rule changes that will affect repositories starting March 26, 2013

What's in a Name?

- For legal analysis purposes, any data or human tissue that you have 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

Dimension	Variation

Primary purpose of specimen collection	• clinical care
	• clinical care with subsequent research use
	• research
	  ➢ placement in a bank was the primary research goal
	  ➢ placement in a bank was anticipated at the time of subject enrollment
	  ➢ placement in a bank was not anticipated at the time of subject enrollment

Who can provide human specimens to the bank?	• any investigator or clinician • approved investigators or clinicians • only investigators or clinicians within the 'home' institution • only investigators or clinicians outside the 'home' institution • authorized depositors • any depositor

Dimension	Variation

Who can access specimens from the bank?	• investigators from the repository's institution
	  ➢ any investigator
	  ➢ approved investigators
	• investigators external to the repository's institution
	  ➢ any investigator
	  ➢ investigators from not-for profit institutions
	  ➢ investigators from commercial institutions
	  ➢ investigators meeting specific criteria

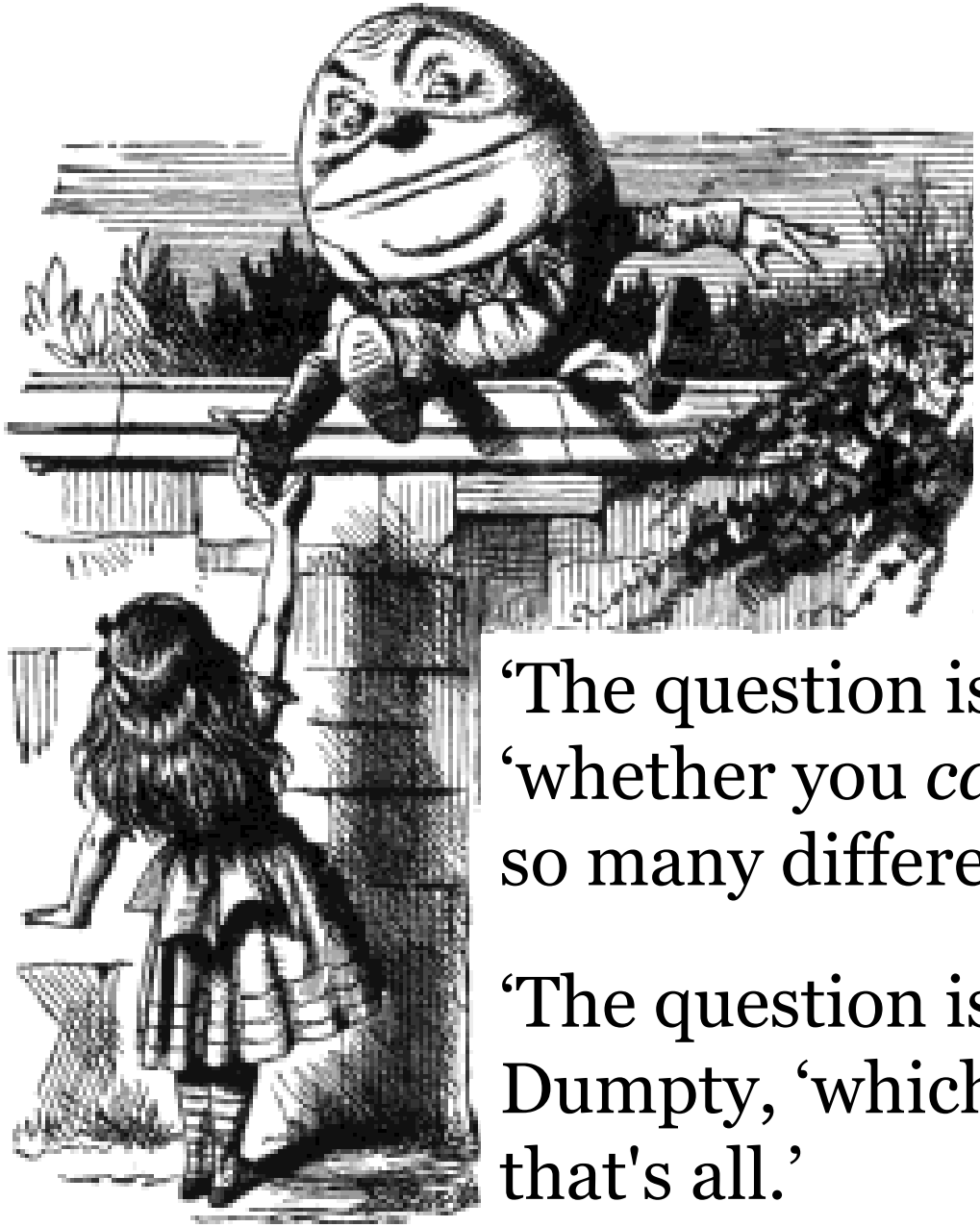
Scope of banked material	• type of human specimens:
	  ➢ single disease/condition/type of specimen
	  ➢ multiple specified diseases/conditions/ types of specimens
	  ➢ global – no limitations
	• types of associated data
	  ➢ demographics and pathology diagnosis
	  ➢ clinical information
	  ➢ research data

Dimension	Variation

Custodianship	• academic medical center
	  ➢ individual investigator
	  ➢ individual department/division
	  ➢ institutional
	• academic consortium
	• federal agency (e.g., NIH)
	• industry
	• private
	  ➢ specific advocacy group
	  ➢ not-for profit multi-use bank

HIPAA Privacy Rule status of bank	• covered entity • not a covered entity

Excerpted from "Report of the Public Responsibility in Medicine and Research (PRIM&R) Human Tissue/Specimen Banking Working Group "(March 2007)



‘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.’

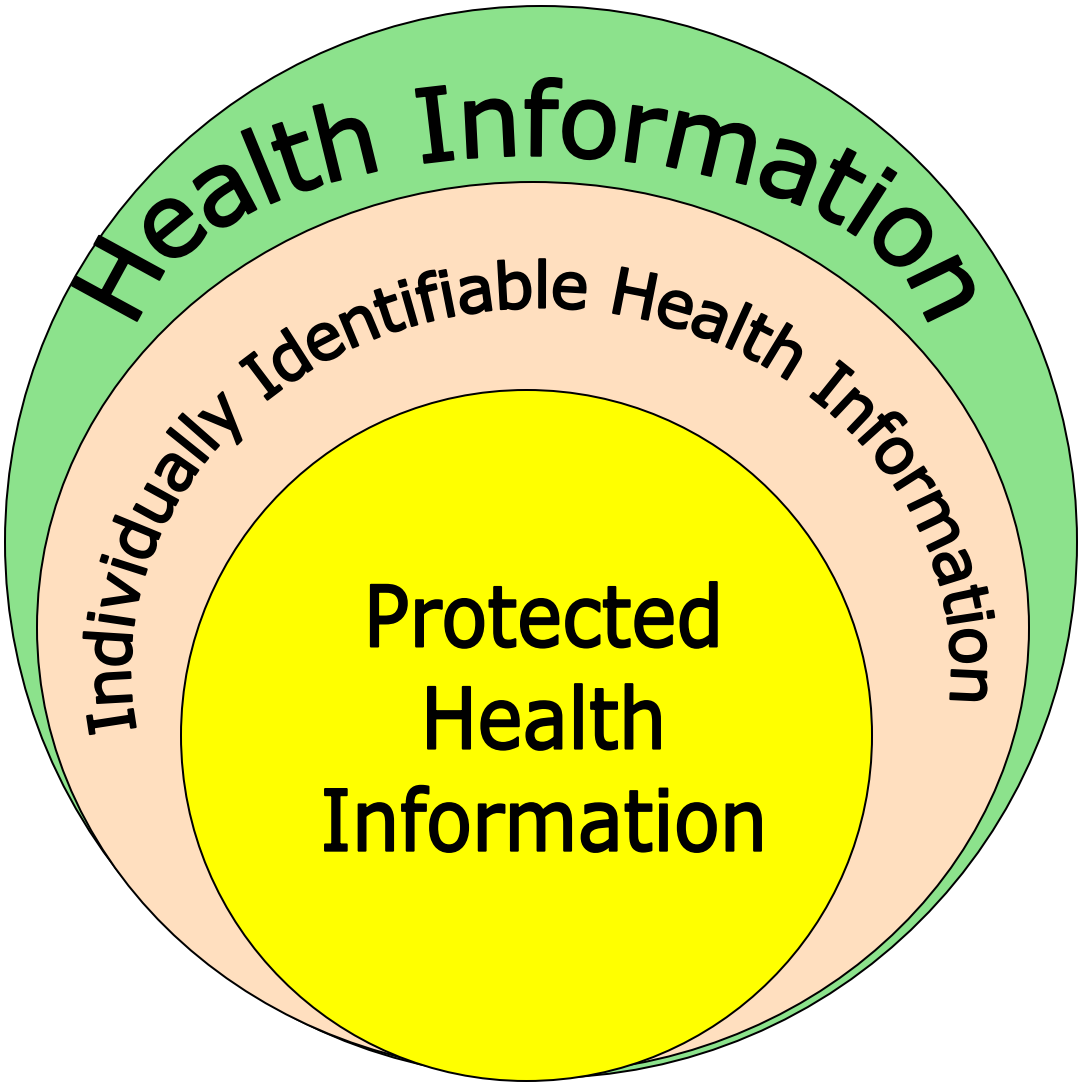
‘The question is,’ said Humpty Dumpty, ‘which is to be master -- that's all.’

Quick HIPAA Mind 101

- These are the basic concepts that apply to health information in repositories that are registries, the extraction of data from medical records, the collecting of information directly from a patient-subject, and data elements associated with tissue samples

HIPAA's Basic Concept

- The primary release from the patient of his/her health information is treatment and its relatives: payment and health care operations
- Research, fundraising, and marketing are on a short tether
- Both Use and Disclosure for research require either authorization, authorization waiver, or research specific exceptions to HIPAA


Health Information
Individually Identifiable Health Information
Protected Health Information

Health Information

- Information in any form--oral or recorded in any medium
  - created or received by health care provider, health plan, employer, university AND
  - relates to past, present, or future
    - physical or mental health or condition
    - provision of HEALTH CARE
    - payment for provision of HEALTH CARE

Health Care

- Care, services, or supplies related to an individual's health; includes:
  - Preventive, palliative, diagnostic, therapeutic, rehabilitative care and assessment of physical or mental condition or functional status
  - Sale/dispensing of drug, device, or equipment by prescription

Individually Identifiable Health Information (IIHI)

- Subset of HEALTH INFORMATION
  - that identifies an individual, or
  - with respect to which there is a reasonable basis to believe the information can be used to identify an individual

Protected Health Information (PHI)

- Subset of IIHI that is
  - Transmitted by electronic media
  - Maintained in electronic media
  - Transmitted or maintained in any other form
- Excludes
  - Employer records and student records

The Common Rule

- 45 C.F.R. Part 46
- The primary Belmont principle of respect for persons is grounded in the concept of autonomy and is realized through informed consent
- Waiver of consent must meet the regulatory criteria

Utility versus Autonomy

- Let us stipulate: research is useful and beneficial to society
- The gold standard is that people should get to decide to be in research

Rational Medicine

I am of opinion that the Art of Medicine ought to be rational, . . . to draw instruction from evident causes . . . but to lay open the bodies of men while still alive is as cruel as it is needless. . . [A]ctual practice will demonstrate . . . in the course of treating the wounded in a somewhat slower yet much milder way.

Aulus Cornelius Celsus, De Medicina c. 30 A.D.

The Conflict of Biomedical Research

[Patients have] a right to immunity from experiments merely as such, and outside of therapeutic application. This right is one that is especially liable to violation by enthusiastic investigators

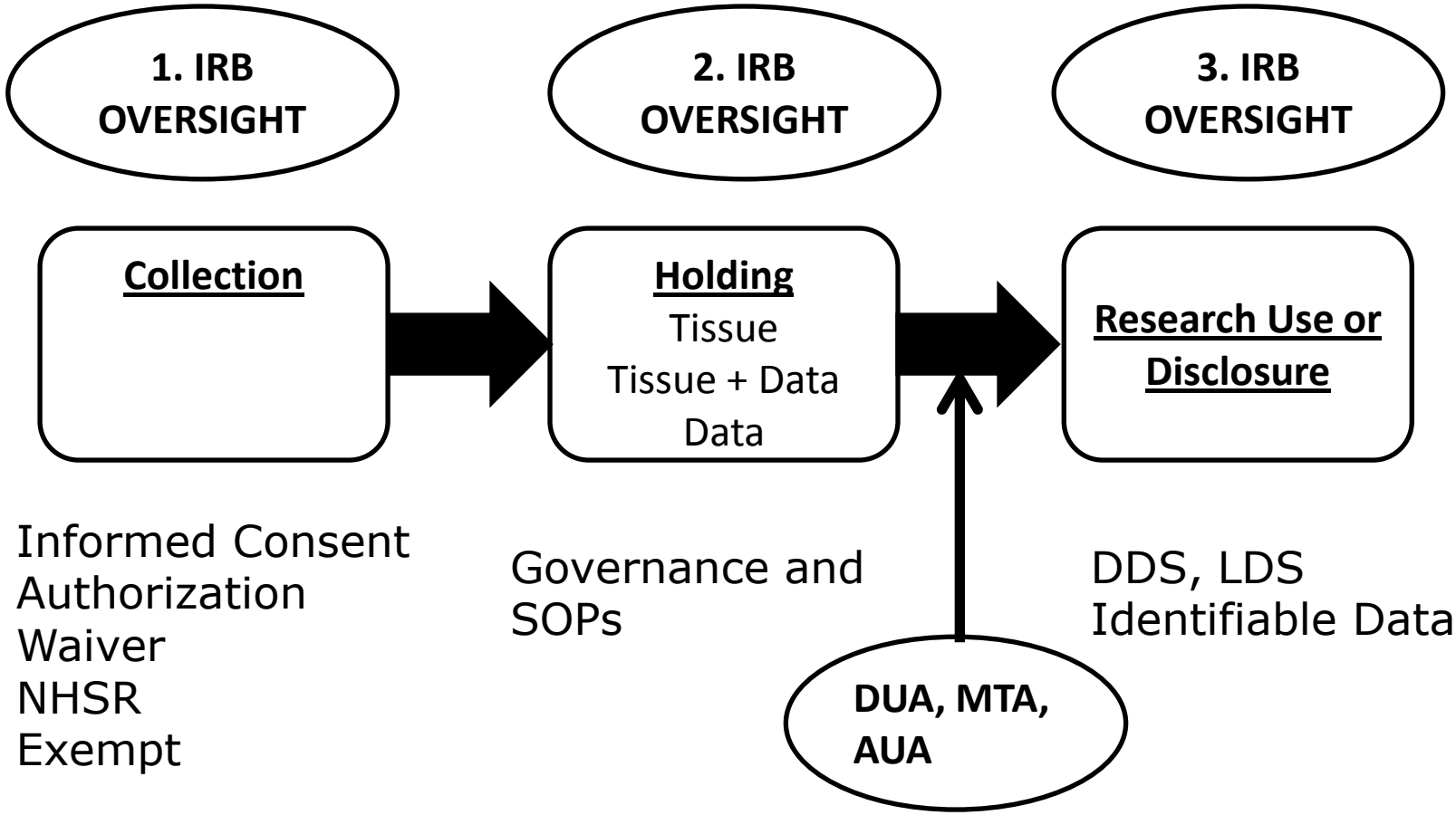
"The Possible Conflict between the Interests of Medical Science and Those of the Individual Patient, and the Latter's Indefeasible Rights," Withington, The Relation of Hospitals to Medical Education (1886)

The Conflict of Biomedical Research - 2

Just because an operation is a minor one and is very likely to be harmless, there is danger in assuming that the new knowledge . . . justifies the test. . . There is no more primitive and fundamental right which any individual possesses than that of controlling the uses to which his own body is put.

"The Right and Wrong of Making Experiments on Human Beings," JAMA, November 4, 1916

The 3-Part Repository Model



1. IRB Role – Data In

- Oversight of Informed Consent
  - Included among the basic elements of informed consent should be a clear description of (i) the operation of the cell repository; (ii) the specific types of research to be conducted; (iii) conditions under which data and specimens will be released to recipient-investigators; and (iv) procedures for protecting the privacy of subjects and maintaining the confidentiality of data. Informed consent information describing the nature and purposes of the research should be as specific as possible. Where human genetic research is anticipated, informed consent information should include information about the consequences of DNA typing (e.g., regarding possible paternity determinations). Informed consent documents may not include any exculpatory language through which subjects are made to waive or appear to waive any legal rights.

2. IRB Role - Oversight

The IRB should review and approve a protocol specifying the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. The IRB should also review and approve a sample collection protocol and informed consent document for distribution to tissue collectors and their local IRBs. A Certificate of Confidentiality should be obtained to protect confidentiality of repository specimens and data.

3. IRB Role - Users

Acceptable Use Clause of MTA or AUA

Recipient acknowledges that the conditions for use of this research material are governed by the cell repository Institutional Review Board (IRB) in accordance with Department of Health and Human Services regulations at 45 CFR 46. Recipient agrees to comply fully with all such conditions and to report promptly to the cell repository any proposed changes in the research project and any unanticipated problems involving risks to subjects or others. Recipient remains subject to applicable State or local laws or regulations and institutional policies which provide additional protections for human subjects. This research material may only be utilized in accordance with the conditions stipulated by the cell repository IRB. Any additional use of this material requires prior review and approval by the cell repository IRB and, where appropriate, by an IRB at the recipient site, which must be convened under an applicable OPRR-approved Assurance

Collection with Authorization and Informed Consent

- Consent form must describe research activity including banking or registry activities
- Maintenance and secondary uses should be described

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

IRB Oversight of Exempt and NHSR

- Question 1 – Is research involved?
- Question 2 – Are Human Subjects Involved
- Question 3 – Even if human subjects research, is it exempt?

Is It Research?

- Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Is It Human Subjects Research?

- Direct interaction with individuals or their data to either record coded data or record non-identifiable data is research

OHRP NHSR

- 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:

  1. the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and

OHRP NHSR -2

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 - 16 specified direct identifiers removed
- Code
  - Not derived from subject related information
  - Cannot be translated
  - Non-disclosure of code or mechanism

Practical Effect

- You must satisfy both HIPAA and Common Rule Requirements
- Data that contain linkers (codes) are not anonymous

What Does this Mean for MTAs and DUAs?

- The MTA should meet all the criteria that flow backward
- Proposed MTA and representations in the IRB protocol, such as repository maintenance rules, users, research purposes, authorization/consent waiver, informed consent should be consistent
- Clarity about data elements

What Does this Mean for MTAs and DUAs? - 2

- MTA must be consistent with sponsor or funder requirements and other institutional contractual obligations including IP and licensing
- 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

What Does this Mean for MTAs and DUAs? - 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.

Instructions:	Please provide your registry data in the proper columns below. Refer to the Common Data Element documentation located on the www.grdr.info website for detailed descriptions of each data element.
	For those GRDR data elements that allow multiple values to be provided, list all values in a single cell with a pipe '|' delimiter. For example: For GRDR ID# GRDR0030 Family members, record multiple values as: Mother|Brother|Neice if multiple values are being provided.
	Do not change the column headings below, the GRDR ID is used in the load process to determine the proper validations.
	You need provide only those columns of data your are submitting to the GRDR, you may either delete unused columns, or leave them blank.

GRDR001	GRDR002	GRDR003	GRDR004	GRDR005	GRDR006	GRDR007	GRDR008	GRDR009	GRDR010	GRDR011	GRDR012	GRDR013
Registry Unique Participant ID	Participant Identifier Source	Source Registry	Registry Record Date	State of Participants Residence	Zip/Postal Code of Participants Residence	Country of Participants Residence	Record of Self Completion	Proxy Relationship to Participant	Participant Year of Birth	Vital Status	Year of Death	Sex of Participant

GRDR029	GRDR030	GRDR031	GRDR032	GRDR033	GRDR034	GRDR035	GRDR036	GRDR037	GRDR038	GRDR039	GRDR040	GRDR041
Rare Disease Diagnostic Testing	Rare Disease Family History	Birth Weight	Participant Term Delivery	Participant Premature Gestational Age at Birth	Participant Weight	Participant Age for Weight	Participant Height	Participant Age for Height	Current Medications	Medical Foods/Special Diet	Previous Surgeries	Participant Hospitalization Count

GRDR043	GRDR044	GRDR045	GRDR046	GRDR047	GRDR048	GRDR049
Participant Previous Trial Participation	Participant Current Trial Participation	Participant Future Trial Participation	Participant Future Biospecimen Donation	Participant Existing Biospecimen	Participant Existing Biospecimen Type	GRDR ID

Spreadsheet Method of Data Specification

Consent Form Extracts

A patient registry is a place where medical information, family history and other related information from patients is collected and stored for medical research. The purpose of the xxx registry is to collect and store medical information and other information from individuals with the same disease). Sometimes the registry may also be linked to a biobank which is a place that stores tissue, blood or other samples from the patients. If there is a biobank for people with your disease, you may be asked to donate your samples to the biobank. If you decide to donate your samples, you will need to provide separate consent for the biobank.

Consent Form Extract -2

If you join the registry, you will be asked to provide medical information on your disease and diagnosis. The goal of the registry is to share detailed medical and other information with scientists and other researchers, while still protecting your privacy. This is done by hiding the name, address and other "identifying" information from the researchers. We call this information "de-identified" because it has been removed of all personal identifiers. Your personal information such as, your name, address, or other information that identifies you or your family will be labeled with a code number and stored in a secure place and protected with a password. Only authorized people who work in the registry will know the code and be able to identify you if needed. All measures will be taken to protect your privacy. However, because your disease is rare, there is a small risk you may be identified.

Rare Diseases have no borders! They don't affect individuals, they affect entire families

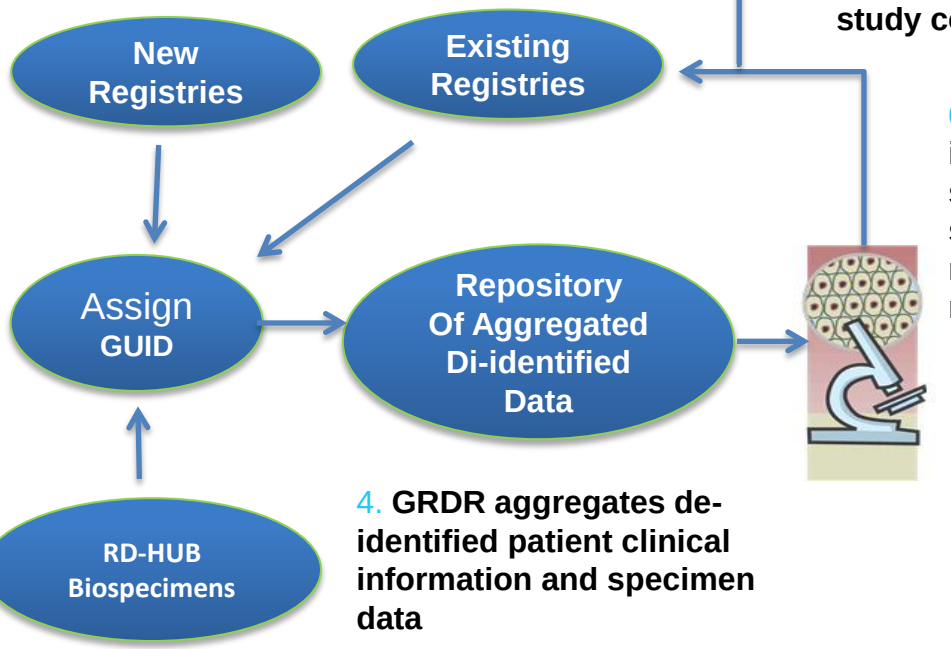
GRDR

Patient Registries

1. Patients Provide health information and test results

2. A Global Unique Patient ID (GUID) is assigned and patient data is mapped to common data elements (CDE's)

3. Patient data linked to biospecimens via the GUID interfacing with RD-HUB



4. GRDR aggregates de-identified patient clinical information and specimen data

5. De-identified registry data is available to researchers for studies and clinical trials

6. Researchers can identify potential study participants and submit a contact request to the original registry owner

7. Registry owners notify identified participants. Interested patients are directed to the study contact

Office of Rare Diseases Research
National Center for Advancing Translational Sciences – NIH

The Children's Hospital of Philadelphia
Hope lives here.

PATIENTCROSSROADS

WebMD
Better information. Better health.

Omnibus Rule

- January 25, 2013 DHHS issued final regulations for the Health Information Technology for Economic and Clinical Health (HITECH) Act, that was part of the American Recovery and Reinvestment Act of 2009

Changes to the Non-Combining Rule

- In addition to the basic elements and statements of Authorization, HIPAA former prohibited the combining of conditioned and non-conditioned Authorizations
  - Treatment, except research treatment, could not be conditioned on Authorization
  - Repository participation is usually optional and under a non-conditioned Authorization

Research Exception

- Effective March 26, 2013, research consent forms may combine conditioned (for the research treatment) and unconditioned Authorizations (for the repository)
- Combining Methods
  - Check box, 1 signature
  - 1 form with 2 signatures

New Combining Method

- Check box for banking with 1 signature incorporating by reference a separate brochure that describes the banking activity
  - Brochure must be present before ICF signed and kept on file
- Banking is opt in only

Future Research

- DHHS no longer interprets the "purpose" requirement of research authorization to be study specific
- Future research authorization that "adequately" describes purpose such that it could be reasonable for individual to expect his/her PHI could be used or disclosed for such purposes

Future Research - 2

- “Adequate” is a circumstance that will be left to the IRB’s judgment

Limited Data Sets and Breach

- A Covered Entity must analyze the impermissible use or disclosure of a Limited Data as a possible reportable data breach
  - This is a change from the proposal to except LDS impermissible use/disclosure from breach reporting

問題

Questions