

Ethical and legal issues/government regulations

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Presumed goal:

Centralized infrastructure to support rare disease data registry that includes/or at least interacts with bio-specimen repository.

Development requires understanding of basic banking construct:

It is easier to have a **Data/tissue source** on a single site. As more basic issues arise, the **Bank** must be simple and the **Data/tissue recipient** must be on a single site.

The data/tissue source – the regulatory oversight will vary as a function of specific characteristics;, for example:

- Clinical vs research source
- Identifiability of the data/specimen
- Obtained with informed consent/authorization
 - If yes, is the banking the primary or secondary use
 - What did the consent include in terms of the down-stream uses? Sharing?
 - Who obtained consent? Banking personnel? Individual investigators?

The bank itself – specific characteristics that must be considered:

- Will the bank passively hold the data/specimens – or process them in some way; e.g., abstract DNA
- Will the bank maintain identifiable specimens/data? Or not?
- Who 'owns' the bank – who is responsible for the governance
- Rules of the bank:
 - For example, does the bank have any rules re: return of research results

Data/tissue recipients – for consideration

- Are there eligibility criteria for obtaining materials from the bank?
 - Any limitations? E.g., only those who deposit? Commercial entities?
- What can recipients obtain?
 - Data: identifiable? Aggregate only etc
 - Specimens: identifiable?
- Who determines if the recipient should get the material?
 - IRB approval required

- Internal bank review?
- Return to the bank
 - Must recipients return research results to the bank for others to use?
- Can recipients return research results to individuals? If so, does the bank determine the process?

These are just examples of details that merit attention for a single bank.

What additional complexities would a centralized infrastructure introduce?

1. What materials: would different diseases have different requirements re:
 - a. Clinical vs research materials
 - b. Identifiability – and ability to up-date
 - c. Type and handling of tissue
2. Could the various disease groups agree on:
 - a. Governance of the repository/bank
 - b. Rules for depositing and accessing materials
 - c. Policies re: sharing – who can access?
 - d. Policies re: return of research results?
3. Who would provide the funds?
 - a. Equal commitment or sliding scale
4. Who would be in charge?
 - a. Single owner? Versus committee



Uniting Rare Diseases

Advancing Rare Disease Research: The Intersection of Patient Registries, Biospecimen Repositories and Clinical Data

Session V

Human Subjects: Bioethical & Legal Issues for Clinical Studies

Ethical and legal Issues/Government Regulations

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Human Subjects: Ethical & Legal Issues (45 CFR 46)

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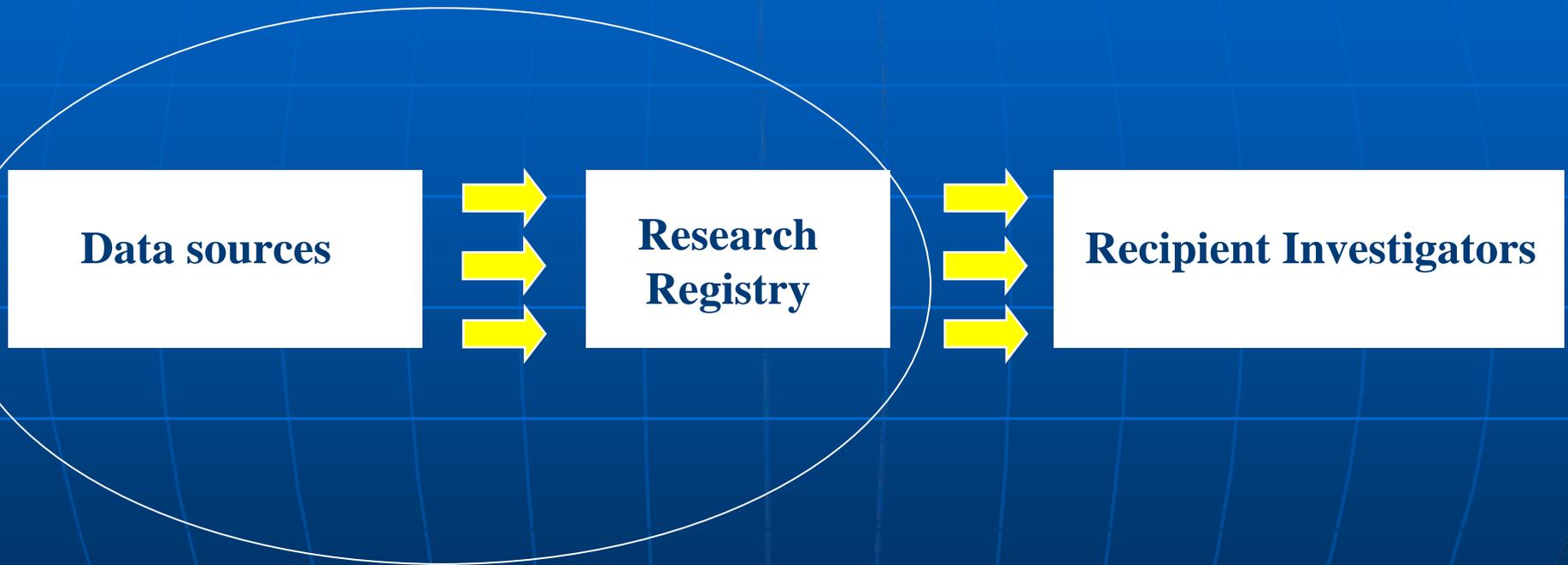
Presumed goal

- Centralized infrastructure to support rare disease data registry that includes/or at least interacts with bio-specimen repository
- Must understand the basics

The Basic Model



The Basic Model



Basic Concerns of the First Circle

- Someone must 'own' the repository/registry and be responsible for the:
 - Rules of operation
 - Addressing regulatory issues
 - Addressing ethical issues
 - Addressing business issues

The Regulatory Issues

- When does 45 CFR 46 Apply?
- When does HIPAA apply?

When does 45 CFR 46 Apply?

- **Apply to human subject research conducted or supported by U.S. Department of Health and Human Services**
- **If U.S. institution chooses to apply to all human subjects research through a Federalwide Assurance—apply regardless of source of support**

Applicability of HHS Regulations

Research [45 CFR 46.102(d)]?



Human subjects [45 CFR 46.102(f)]?



Exempt [45 CFR 46.101(b)]?

Applying 45 CFR 46 to a Research Registry (or Biospecimen Repository)



Applying 45 CFR 46 to a Research Registry (or Biospecimen Repository)



Research Registry Study

Research?

- Yes

Human subjects?

- Research intervention/interaction?
(e.g. health data obtained for registry from research survey)
- Identifiable private information?
(e.g. identifiable health information obtained from medical record)

Applying 45 CFR 46 to a Research Registry (or Biospecimen Repository)



Research Registry Study

If Human Subjects Research:

- IRB review – at least one institution is “engaged.”
- Informed consent or waiver

Applying 45 CFR 46 to a Research Registry (or Biospecimen Repository)

Data sources



Research
Registry



Recipient Investigators

Research Registry Study

Informed consent considerations:

- If data obtained for clinical purposes, is consent for inclusion in bank needed or is a waiver permissible?
- If data obtained from prior research study, is inclusion in registry consistent with prior consent, if any? Is specific consent for inclusion in bank needed?
- If consent is to be obtained for registry, how specific should consent be about future research? Will “tiered” consent be an option?
- What will be said about confidentiality of data? Will registry provide investigators with de-identified, identifiable, or coded data? Under what conditions?

Plus:

- Are subjects children? Is child assent needed?
- Does HIPAA’s or GINA’s protections apply?

HIPAA Issues

- There is no single answer
- Questions to ask:
 - Which components are covered by HIPAA?
 - The Registry itself?
 - Data source institutions
 - What data is involved?
 - Is it PHI (personal health information)
 - Is it identifiable?
 - Is it clinical PHI? Is it research PHI?

More Issues

- Differences between informed consent and authorization
 - N.b., permission for broad future uses
- How to determine identifiability
- The logistics of consent
 - By whom?
 - When?
 - Where?

The Basic Model



Basic Concerns of the Second Circle

- Who is allowed to access data/material?
- Who makes that decision?
- Which regulations apply?
 - 45 CFR 46
 - HIPAA
- Are there other ethical issues that should be addressed?

Applying 45 CFR part 46 to a Research Registry (or Biospecimen Repository)



Research Study

Research?

- Yes

Human subjects?

- Identifiable private information?
- Coded?

Applying 45 CFR part 46 to a Research Registry (or Biospecimen Repository)



Research Study

If human subjects research:

- IRB review—at least 1 institution is engaged
- Informed consent or waiver

Applying 45 CFR part 46 to a Research Registry (or Biospecimen Repository)



Research Study

Informed consent considerations:

- Is currently proposed research consistent with prior consent, if any?
- Does prior consent fulfill informed consent requirements for the current study?
- If data obtained for registry when subject was a child, is consent needed from now-adult subject?

WHAT ABOUT FUTURE CONSENT?

Can original consent fulfill the informed consent requirements for a current study?

- **Yes – if the prior informed consent meets the informed consent requirements of 45 CFR 46.116 for the current research study.**

Note: HIPAA Authorization must be research study specific

Reminder

- **45 CFR 46 establish the federal “floor” for human subject protections**
- **Local law may create additional requirements (including international standards)**
- **Regulatory requirements do not address all relevant ethical considerations**

Complexities of a centralized infrastructure

- What would the registry look like?
 - All data placed into a common-use bank?
 - Separate 'rooms' for separate diseases?
- Would every disease group agree on:
 - Types of data going into the bank?
 - Clinical vs research
 - Definition of identifiability?

Complexities of a centralized infrastructure

Would every disease group support:

- A single governance structure?
- Rules for depositing and accessing
- Policies regarding:
 - Return of research results
 - Withdrawal of data upon request of subject/s
 - Etc.

Complexities of a centralized infrastructure

- Who would be in charge?
(who 'goes to jail' for noncompliance)
 - Single 'owner'
 - Committee
- Financial support
 - Equal commitment from all involved?
 - Sliding scale?

Complexities of a centralized infrastructure

- What if:
 - A group wants to discontinue collaboration?
 - A new group wants to join?
 - The money runs out?

OHRP RESOURCES

- 45 CFR part 46:

<http://www.dhhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>

- Human subject regulations decision charts:

<http://www.dhhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm>

- Repositories and databases:

<http://www.dhhs.gov/ohrp/humansubjects/guidance/reposit.htm>

- Coded guidance: <http://>

- Engagement:

<http://www.hhs.gov/ohrp/humansubjects/guidance/engage08.pdf>

- Informed consent FAQs:

<http://www.hhs.gov/ohrp/informconsfaq.html>