



Basics of Human Subjects Research

INSTITUTIONAL REVIEW BOARD
OFFICE OF RESEARCH CONTRACTS





Presentation Outline

- What is human subjects research?
- What are the reasons for IRB review?
- What is exempt from IRB review and how makes that determination?
- When is a protocol required?
- Subcontracts/awards supporting human subjects research
- Materials and data transfers
- What are your obligations?



What is an IRB?

The purpose of an IRB is to ensure, by conducting scientific and ethical review, that the rights and welfare of human subjects are protected. This is done by assuring that the proposed human subjects research meets the requirements of Federal regulations and institutional policies.

The Federal regulations and institutional policies used by the IRB provide the boundaries within which a consensus of scientists, ethicists, and patient advocates worldwide (and over time) have agreed, research with human subjects will:

- 1) be ethical**
- 2) be scientifically valid**
- 3) produce important knowledge**
- 4) have a reasonable risk/benefit ratio**



Basic Principles of IRB Review

The Belmont Report

- Respect for Persons (*informed consent process*)
 - » Individual autonomy (voluntariness, privacy)
 - » Protection of individuals with reduced autonomy
- Beneficence (*research designed for the greater good*)
 - » Maximize benefits; minimize risks
- Justice (*inclusion of all groups, even if it is “hard” to do*)
 - » Equitable distribution of risks and benefits

Remember:

It is a privilege, not a right, to conduct human subjects research!



How are IRBs Regulated?

IRBs are federally regulated by the Department of Health and Human Services, Office for Human Research Protections (OHRP)

- 45 CFR 46 (Common Rule) specifies:
 - The findings that an IRB must make
 - The composition of an IRB
 - The criteria for IRB approval
 - How an IRB must function and operate
- IRBs also must apply FDA regulations, HIPAA, state and local laws

IRBs are responsible for ensuring that research is designed in compliance with the regulations



What is Human Subjects Research?

A. Must be “**Research**”

(Does not include the practice of medicine, teaching, quality improvement)

B. Must include at least **one** of the following:

- Interacting with people to collect information or samples
- Using identifiable information or samples obtained from people in the past
Includes information obtained from medical records or prior research studies
- Testing a drug, device, or biologic on one or more individuals or on their samples



Human Subjects Research -Regulations

- **Common Rule:** A living individual about whom an investigator obtains:
 - 1) data collected through an interaction/intervention, or
 - 2) identifiable private information (broader than PHI)
- **FDA:** An individual who is or becomes a participant in research, either as a recipient of test article (drug, device, or biologic) or as a control.
 - A human who participates in a clinical investigation or on whose samples an investigational device is tested
- **HIPAA:** A living or deceased individual about whom identifiable protected health information (PHI) is obtained (health information that includes one or more of 18 identifiers listed under HIPAA regulations).

Any code derived from or related to information about the subject is a HIPAA identifier.



What “Research” May be Exempt?

- Not Human Subjects Research

- Doesn’t meet definition of “human subject” under the **Common Rule**

Use of only coded or anonymous existing (previously collected) data or samples if the subjects cannot be **readily identified** by the researchers.

HIPAA requirements, if applicable, must be satisfied (waiver, decedent notices)
FDA regulations must not apply

- Exempt Human Subjects Research

- one of 6 categories defined “Exempt” under the **Common Rule**

HIPAA requirements, if applicable, must be satisfied (waiver, decedent notices)

No human subjects research involving prisoners or FDA regulated testing of drugs/devices/biologics may be considered Exempt



Who May Declare Research Exempt?

“Requests for Exemption” submissions reviewed by the IRB

- At Duke, to avoid a potential conflict of interest (COI), a researcher cannot declare his/her own “Research” as “exempt”, **the IRB must make that declaration.**
- “Research” that may be “exempt” must be submitted to the IRB. “Requests for Exemption” are reviewed by a Chair. If exempt, no further IRB review is needed (unless protocol is amended). No annual review is required.
- If the protocol is “Not Research” no submission to the IRB is needed (quality improvement, teaching, practice of medicine).

Submissions to the IRB that do not involve “Research” would only be needed if required by a program, required by a journal, or if the protocol is in a “gray area” and the study team or CRU would like an independent review.



Exempt Human Subjects Research

Under the Common Rule:

1. Research conducted in educational settings on educational practices.
2. Research involving the use of educational tests, interviews or surveys.
3. Research involving educational tests, interviews, or surveys on public officials or required by federal statute.
4. Research involving existing data or specimens if publicly available or if information is recorded by researchers so that subjects cannot be identified directly or through identifiers linked to subject.
5. Research and demonstration projects involving public service programs.
6. Taste and food quality evaluation and consumer acceptance studies
(this is the only category of Exempt Research under FDA regulations)

*****Exempt Human Subjects Research is not exempt from the consent process when appropriate, such as with tests, surveys or interviews. The consent process may be written, verbal, or implied by participation.**



Subrecipients with Human Subjects Activity

- Responsibility of ORC to draft HS subagreements that cover:
 - Research related subject injury
 - HIPAA privacy and security issues
 - Data transfers/material transfers
 - Insurance/liability terms
 - FDA regulations on clinical trials
- To draft the appropriate sub we review:
 - HS answer on sub face page
 - SOW
 - Budget justification
 - eIRB information



Subrecipients with Human Subjects Activity

- Duke's Federal-Wide Assurance (FWA) requires that we provide oversight for all human research protection activities at all sub-sites, when a Duke investigator serves as the primary grant awardee on a multi-site study funded by the U.S. Government. Therefore a protocol is **required at Duke**, even if the HS activity is only happening at the sub institution. Please be sure to mark the Duke face page yes at pre-award stage.
- For subs with HS activity, eIRB should indicate “yes” to the multi-site study question in Section 5. A copy of the sub’s protocol approval should be uploaded in eIRB.



Subrecipients with Human Subjects Activity

- When submitting a SIR for a sub, please include the Duke Protocol number. A Duke project must have at least a blanket protocol in place in order to issue a sub with human subject activity.
- For federal and foundation subs, you may be asked for follow-up information on data transfers to complete the following information on the subaward template:

Human Subjects Data (Select One)	Human Subjects Data will be exchanged under this Agreement (check all that apply):	The PTE will set forth the terms of the exchange of human subjects data (Select One):
<input type="checkbox"/> Not Applicable	<input type="checkbox"/> From Subrecipient to PTE	<input type="checkbox"/> In the Additional Terms section below
<input type="checkbox"/> Applicable	<input type="checkbox"/> From PTE to Subrecipient	<input type="checkbox"/> Via a separate Data Use Agreement



Vendor Agreements

- Vendors with access to protected health information (PHI) or sensitive electronic information, are involved in patient care, or are provided access to Duke systems are excluded from the procedures under GAP 200.370 and require an RSSA.
- ORC will provide the appropriate Rider C for the RSSA when a vendor has access to PHI or Duke systems.



Data Transfer Agreements

- The term Data Transfer Agreement is a generic term for multiple types of transfers:
- De-identified data
- Limited Data Set
- Protected Health Information more than a Limited Data Set
- Technology, Know-How, Research Data, Data Sets (annotated, longitudinal, etc)



Data Transfer Agreements

- De-identified data-all 18 HIPAA identifiers removed
- A Limited Data Set - a class of Protected Health Information (PHI) that only includes indirect identifiers:
 - Dates of service (e.g. blood drawn on May 1, 2015)
 - Ages greater than 89
 - Geographical information (State, County, City, Zip Code)
- PHI- more than a Limited Data Set
- Technology, Know-How, Research Data, Data Sets - proprietary



Data Transfer Agreement IRB Process

- Study team completes Intake Form
- ORC sends Intake Form to the IRB
- IRB review to determine acceptability of transfer
- Upon IRB consideration and permission to move forward, ORC drafts the appropriate Data Transfer Agreement and works with study team to send to the other party
- Study team uploads the fully executed DTA into the eIRB once signed by both parties
- IRB approved data can be transferred to the other party



Material Transfer Agreement

- Governs the Recipient's use of a Provider's Material.
- Non-use and non-distribution terms
- Publication rights
- Intellectual property rights
- Confidentiality
- Liability



Why a Material Transfer Agreement

- Protect the rights of both the Recipient and the Provider.
 - Publication rights
 - Intellectual Property rights
- Prevents unrestricted use of Materials
 - Necessary for compliance with ICF and IRB approval
 - Subject samples and clinical data
- Facilitates compliance with federal regulations
 - HIPAA
 - Export Control



Material Transfer Agreement

- Human samples (e.g. whole blood, plasma, fluids)
- Human tissues (e.g. whole organ, tissue biopsies)
- Human-derived samples (e.g. extracted RNA, DNA, proteins)

- Animal models and Animal tissues
- Proprietary materials (e.g. unique Abs)
- Research Tools (e.g. plasmids)
- Reagents (e.g. unique chemical compounds)

- Plus information (clinical, technical, confidential)



Material Transfer Agreement ORC Process

- Incoming Materials
 - Provider usually provides the agreement
- Outgoing Materials
 - Recipients
 - Nonprofits
 - Service Providers
 - Industry
 - Intra-Duke
 - Material type
 - Human samples, tissues or human-derived materials
 - Generally, a MTA is required
 - Other material transfers
 - Contact ORC for determination



Material Transfer Agreement IRB Process

- Incoming Materials
 - Study team should enter an amendment to the relevant protocol
 - Uploaded the fully executed MTA into the eIRB
- Outgoing Materials
 - For completed studies (retrospective)
 - Enter an amendment to the relevant protocol
 - Upload the fully executed MTA into the eIRB
 - For active studies
 - Enter an amendment to the relevant protocol
 - IRB review of ICF to determine acceptability of transfer
 - Upload the fully executed MTA into the eIRB



Additional Resources

Duke IRB home page <http://irb.duhs.duke.edu/>

Duke HRPP policies

http://irb.duhs.duke.edu/modules/irb_pols/index.php?id=3

OHRP guidance documents, Common Rule

<http://www.hhs.gov/ohrp/policy/index.html#topics>



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