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• Brief discussion of regulations
• IRB Structure
• Levels of Approval
• Informed Consent
• HIPAA/HITECH
Federal Regulations

DHHS

FDA

21 CFR 50, 56

OHRP

45 CFR 46 – The Common Rule

Institutional Review Board
The regulations established to oversee the ethical behavior of research is encapsulated in the Department of Health and Human Services (DHHS), Code of Federal Regulations (CFR) 45 CFR 46 divided into four subparts A, B, C and D.

The “Common Rule,” subpart A is the baseline standard that all academic institutions are held to in conducting research.

These regulations have been adopted by other federal departments which regulate human research such as the Department of Defense (DOD), National Institutes of Health (NIH), etc..

A similar set of rules was established from the Food and Drug Administration (FDA) several years later, Title 21 CFR 50.
Federal Wide Assurance (FWA)
- Establish a fully operational compliance program
- Develop policies and procedures that comply with CFRs
- Develop a monitoring and auditing process
- Enforcement and penalties for failure to observe federal regulations
- The University of Arizona is currently under one FWA

• Review of research by an Institutional Review Board.
• Ensure informed consent of subjects participating in a research study.
What is under the IRB umbrella?

Research and involves Human Subjects
Human Subject Definitions

• Common Rule
  – “A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information (PHI).”
    45 CFR 46.102(f)
  – That means: surveys, chart reviews, some observations, blood draws, etc. involve human subjects
Human Subject Definitions

- **FDA Definition**
  - “an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A subject may be either a healthy individual or patient.”

  21 CFR 56.102(e)
Research + Human Subjects = Institutional Review Board
IRB Function and Composition

• IRB Purpose:
  – to review research and to ensure the rights and welfare of human subjects involved in research are adequately protected.

• The IRB is comprised of at least 5 members
  ▶ At least 1 scientist
  ▶ At least 1 non-scientist
  ▶ At least 1 community member
  ▶ Men and women both represented
  ▶ Diverse in expertise

• University of Arizona has 4 IRB’s
  – All in Tucson
  – Each meet once a month
IRB Review Process
IRB Review

Type of Review

- Exempt
- Expedited
- Full Committee

Level of Risk

- Low
- Minimal
- High
Exempt from *further* IRB Review

- Involves little or no risk to human subjects.
- Even if you believe your project is Exempt, you will need to complete either the:
  - F200: Application for Human Research or
  - F203: Application for Retrospective Records Review
  - [http://orcr.vpr.arizona.edu/irb/forms](http://orcr.vpr.arizona.edu/irb/forms)
- Only the IRB can make the determination of Exempt. This cannot be determined by PI.
Exemption Categories

• **6 Categories, defined by 45 CFR 46.101(b)(1-6)**
  – (1) Research involving educational practices
  – (2 and 3) Research involving the use of educational tests, surveys, interviews or observation of public behavior
  – (4) Research on existing public or anonymous data or specimens that are de-identified
  – (5) Research and demonstration projects which are conducted by or subject to the approval of federal department or agency heads, and are designed to study or evaluate
  – (6) Taste and food evaluation

• **Absolute exceptions to exemptions**
  • Does NOT apply to prisoners
  • Some categories do not apply to children
  • (1) – (5) do not apply to FDA-regulated research
IRB Review

Type of Review
- Exempt
- Expedited
- Full Committee

Level of Risk
- Low
- Minimal
- High
Expedited Review

- Expedited does NOT mean “fast” it is a federal term used for research that must meet specific criteria
  - 9 categories
  - Rigor is same as full review only the number of reviewers is different

- No more than minimal risk
Eligible for Expedited Review

• Clinical studies: IND/IDE NOT required
• Blood sample collection (routine methods – small amounts)
• Prospective collection of biological samples
• Data collected through noninvasive means (routinely practiced in clinical settings)
• Materials (data, documents, specimens, etc.) have been collected or will be collected for non-research purposes
• Collection of voice, video or digital data for research purposes
• Individual or group behavior, surveys, interviews, oral histories
• Specific types of continuing review
IRB Review

Type of Review

- Exempt
- Expedited
- Full Committee

Level of Risk

- Low
- Minimal
- High
Full Review

- One or more IRB member(s) are assigned to review the complete protocol or amendment, consent form, Investigational Drug/Device Brochure and any other protocol materials.

- These Primary & Secondary Reviewers summarize the protocol or amendment to the full IRB Committee at a convened meeting and answer questions during the discussion.

- All other committee members are provided with summary information, for example the Protocol Cover Form and informed consent document. *This stresses the importance of the accuracy and details provided in these documents, since the majority of voting members only see these 2 documents!*
IRB Application Elements

• Setting of Human Research
• Resources available to conduct research
• Study population
• Vulnerable populations
• Recruitment methods
• Consent/Assent/Permission process
• Procedures involved in the research
• Risks to subjects
• Potential benefits to subjects
• Provisions to protect the privacy of subjects
• Other items as applicable:
  – Compensation to subjects, medical care or compensation for injury, cost to subjects, withdrawal of subjects, data monitoring, information management
IRB Application Process

Where do I send the application?
– Send the completed application to Phoenix Research Administration and they will submit it to UA IRB.

What happens after submission?
– The IRB will determine the level of review.
– The IRB will take one of the following actions:
  – Approval of Research
  – Stipulated minor changes or clarifications required prior to approval.
  – Deferral (full board action only)
  – Disapproval (full board action only).

IRB approval is required BEFORE research begins.
Deferral of IRB Oversight

The UA IRB will defer to:

- Western IRB (WIRB) for any multi-center, industry sponsored or non-federally funded clinical study where the University of Arizona is not the coordinating center.

- ASU IRB or NAU IRB when ASU or NAU is the primary grantee agency and a co-investigator of the project is at the University of Arizona.

- Another organization’s IRB if:
  - the University of Arizona investigator is a collaborator on Human Research conducted by that organization;
  - the PI of the organization will have direct oversight of the University of Arizona investigator; and
  - the organization agrees to take responsibility for the University of Arizona investigator.
Deferral of IRB Oversight

Step 1: Obtain IRB approval from primary research site. Ex. hospital

Step 2: Work with RAO at the COM-PHX to complete necessary IRB deferral application and support. RAO will submit the application to UA IRB.

Step 3: UA IRB approves the application for deferral of IRB oversight to primary research site.
Continuing review is required no less than annually for expedited and full board review within 45 days prior to the end of the approval period.

Amendments are required if you make any change in the protocol. Requires approval before implementing the change.

Adverse events and unanticipated problems. Submit to the IRB within 10 business days after the event occurs.

Other Items for IRB Review

Complete form F212: Continuing Review Progress Report

Complete form F213: Modification of Approved Human Research
IRB Closing Procedures

• Only required for research that received Expedited or Full Board IRB oversight
• Complete a Continuing Review Form F212
• Check the box:
  “Research is permanently closed to enrollment AND analysis of private identifiable information is completed”
Informed Consent
Informed Consent

It is a PROCESS in which….

– Investigator discloses all relevant information
– Potential subject has opportunity to ask questions
– Investigator answers questions
Informed Consent

• Is informed consent necessary?
  – The standard expectation is that all subjects will sign a document containing all the elements of informed consent.
  – The informed consent process gives potential subjects a description of the study that is clear and complete enough for the individual to judge whether she or he wants to participate.
  – The consent form should provide readily understandable information in an amount appropriate to the level of risk in participating.
  – Some or all of the elements of consent, including signatures, may be waived under certain circumstances.

• Does the UA IRB have a consent form template?
  – Yes. Templates can be found at http://orcr.vpr.arizona.edu/irb/forms
Informed Consent Elements

- Purpose of the research
- Participation is voluntary
- Description of the procedures
- Risks and benefits to the participant
- Alternative treatments
- Confidentiality of information
- Medical treatment if injured and who to contact if injured
- Contact name for research subjects’ rights
- Duration of participation
- No coercion
- Understandable language: 6th to 8th grade reading level
Informed Consent Elements (continued)

- Subject’s participation may be terminated by investigator
- Any additional costs to subject
- Consequences of withdrawal from research
- Statement that new findings will be provided
- No language that appears to waive subject’s rights or releases anyone from liability for negligence
How do I obtain consent from Non-English speaking participants?

- Researchers should be fluent in the subject’s language or an official interpreter should be available during the consent process and throughout the subject’s participation as needed.

- Consent forms should be prepared in the language understandable to potential subjects.

- Consent forms can be developed in languages other than English by a certified translational service only.
Waiver of Consent

What are the exceptions to informed consent requirements?

– The IRB may waive the requirement for written consent if the consent document is the only link between the subject and the research and the principal risk of harm would come from a breach of confidentiality.

– The IRB may waive consent if:
  • The research involves no more than minimal risk to the subjects;
  • The waiver will not adversely affect the rights and welfare of the subjects;
  • The research could not practicably be carried out without the waiver;
  • If appropriate, the subjects will be provided with additional information after participation.

– Consent may also be waived for some types of research regarding public service programs.
Biological Specimens

HIPAA/HITECH

Human Subject Training
Are there special requirements for use of biological specimens?

- Yes. Storage of research data and/or specimens for future research is allowed at the University of Arizona and is done through a repository or bank. Whenever possible, subjects should consent to their participation in the repository.

- Recommended that the repository have a separate IRB approval.

- Whenever possible, all information should be de-identified or a coding system should be in place to prevent secondary researchers from obtaining the identity of the subject.
Privacy and Security

• HIPAA:
  Health Insurance Portability and Accountability Act

• HITECH:
  Health Information Technology for Economic and Clinical Health
A covered entity may not use or disclose an individual’s protected health information (PHI) unless authorized in writing by the individual.
Security Rule

- The HIPAA Security Rule establishes national standards to protect individuals’ electronic personal health information that is created, received, used, or maintained by a covered entity.

- The Security Rule requires appropriate administrative, physical and technical safeguards to ensure the confidentiality, integrity, and security of electronic protected health information.
HIPAA – a new language

- Covered Entity; Covered Component
- PHI
  - Individually identifiable health information transmitted or maintained in any form or medium, including paper or electronic records
  - Relates to past, present, or future health, healthcare or payment for healthcare
- Use and Disclosure
  - Use = sharing within the entity or component
  - Disclosure = sharing outside the entity or component
- Types of Data
  - De-identified
  - Coded
  - Limited data set
  - Identified

HIPAA patients have a right to request a complete listing of all disclosures of their PHI for 6 years
<table>
<thead>
<tr>
<th>PHI: Eighteen Identifiers</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Names</td>
</tr>
<tr>
<td>• Geographic subdivisions smaller than a state including city, ZIP code</td>
</tr>
<tr>
<td>• Any dates (except year); age &gt;89</td>
</tr>
<tr>
<td>• Telephone number</td>
</tr>
<tr>
<td>• Fax number</td>
</tr>
<tr>
<td>• Email address</td>
</tr>
<tr>
<td>• Social Security number</td>
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<td>• Medical Records number</td>
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<tr>
<td>• Health Plan Beneficiary number</td>
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<tr>
<td>• Account Numbers</td>
</tr>
<tr>
<td>• Certificate/license numbers</td>
</tr>
<tr>
<td>• VIN</td>
</tr>
<tr>
<td>• Device identification or serial number</td>
</tr>
<tr>
<td>• Web URL</td>
</tr>
<tr>
<td>• Internet Protocol (IP) address</td>
</tr>
<tr>
<td>• Biometric identifiers, including finger and voice prints</td>
</tr>
<tr>
<td>• Full face photographic images</td>
</tr>
<tr>
<td>• Any other unique identifying number, characteristic, or code</td>
</tr>
</tbody>
</table>
Limited Data Set

• De-identified except
  – Dates
  – Zip Codes and City
  – Any other unique identifying number, characteristic, or code that are not expressly excluded

• Minimum Necessary

• Data Use Agreement
  – Limits use and disclosure of PHI
  – Agreement not to re-use or re-disclose
HITECH

- Spells out tougher data security requirements for all health care organizations as well as their business associates.

- Breach notification rule
  - Covered entities, as well as their business associates, must notify individuals within 60 days if protected health information is breached.
  - More than 500 subjects involved requires notifying subject, media and DHHS.
  - Penalties now can be levied against individuals within a healthcare organization as well as the organization itself. Penalties for breaches of personal healthcare information or other HIPAA violations range up to $1.5 million per violation. This is separate from any criminal penalties that might apply.
Training for Human Subject Research

• All applicants must have human subjects research training. Renewed every 3 years at COM-PHX.
• Online course
• Go to Collaborative Institutional Training Initiative Program (CITI Program) at http://www.citiprogram.org/
• Select the University of Arizona College of Medicine – Phoenix as your institution.
• Create a Username and Password and take the following modules with a passing grade of 80%.
  – Biomedical Research Investigators: Basic Course
Resources

• Research Administration Office
  – Rachel Langhofer
    rlanghof@email.arizona.edu
    602-827-2228

• Websites
  o U of A Human Subjects Protection Program-
    http://orcr.vpr.arizona.edu/irb
  o HHS Office of Human Research Protections-
    http://www.hhs.gov/ohrp/
  o CITI Training- www.citiprogram.org