

Human Research Protections

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Objectives:



1. Discuss the history & basis for human subjects protections
2. Discuss core ethical principles and the purpose of the IRB
3. Determine what studies require IRB review
4. Identify the IRB and investigator responsibilities for approval of research
5. Discuss the IRB structures and types of IRB reviews

IRB = Institutional Review Board

Objective 1:

Discuss the history &
basis for human
subjects protections

History of Research Ethics



- WWII Nazi medical research/experiments
- 1932-1972 Tuskegee Syphilis Study
- 1970 Humphrey's "Tearoom Trade" Study
- 1999 Death of Jesse Gelsinger – UPenn gene therapy clinical trial
 - 1946 Nuremburg Doctor's Trial
 - 1964 Declaration of Helsinki
 - 1979 Belmont Report
 - 2011 DHHS proposal to improve rules protecting human research subjects
 - 2015 Proposed changes out for review
- Nuremburg Code, Declaration of Helsinki, International Conference on Harmonisation
- DHHS OHRP Title 45 Code of Federal Regulations Part 46: "The Common Rule"
- DHHS HIPAA Privacy & Security Rules
- FDA Title 21 Code of Federal Regulations Part 50
- International, National, State, Local, and Institutional

Ethics violations in research

Responses

Regulations, Codes, & Guidelines



Objective 2:

Discuss the core ethical principles and the purpose of the IRB

The Belmont Report: Ethical Principles

1. Respect for Persons

Respect for persons incorporates at least two ethical convictions:

- that individuals should be treated as autonomous agents,
- that persons with diminished autonomy are entitled to protection (vulnerable populations).

Informed Consent - process

The Belmont Report: Ethical Principles

2. Beneficence

Two general rules have been formulated as complementary expressions of beneficent actions:

- do good, not harm
- maximize possible benefits and minimize possible harms.

Risk-Benefit Analysis - who is doing the assessment?

The Belmont Report: Ethical Principles

3. Justice

Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved."

Fair Subject Selection

Objective 3:

Determine what studies
require IRB review

What is the purpose of the IRB?

The IRB - an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the institution with which it is affiliated.

Authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction as specified by both federal regulations and *local institutional policy*.

Boundaries Between Practice and Research

The term “practice” refers to interventions that are designated solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success.

The purpose of medical or behavioral practice is to provide diagnosis, preventative treatment or therapy to particular individuals.

The Belmont Report: Ethical Principles and Guidelines for the
Protection of Human Subjects of Research, 1979

Boundaries Between Practice and Research

By contrast, the term “research” designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

The Belmont Report: Ethical Principles and Guidelines for the
Protection of Human Subjects of Research, 1979

Human Subject Research

Research

A systematic investigation (including research development, testing, and evaluation) designed to develop or contribute to *generalizable knowledge*

Human Subject

A living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual or through identifiable private information

Responsibilities of the IRB

The primary responsibility of the IRB is to protect the rights & welfare of research subjects.

The IRB also serves to protect the investigators and institution through compliance with regulatory & ethical standards.

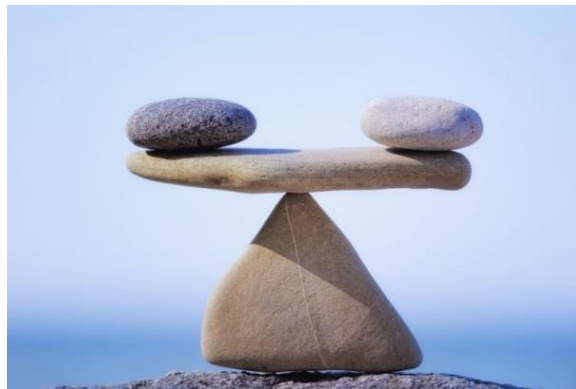
The IRB is required to follow defined standards (codes, rules, & regulations) and to establish policies and procedures for IRB operations.

Objective 4:

Identify IRB responsibilities
and investigator responsibilities
for approval of research

Federal Regulations

Risk: Minimal Risk generally means that the probability and magnitude of physical or psychological harm anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life, or in routine medical, dental, or psychological examinations.



IRB: 3 levels of Review

1. Exempt

Less than minimal risk

One or two primary reviewers



2. Expedited Review

- Minimal risk
- One or two primary reviewers

3. Full Board Review

- Greater than minimal risk
- Vulnerable populations
- Two primary reviewers
- Majority decision by convened IRB



Exempt Review

Certain types of human subject research are exempt and must meet criteria:

- Categories of exemption
 - research in educational settings on instructional strategies or effectiveness of technique
 - research using educational tests, survey, interview, observation of public behavior if no identifiers
 - research using existing data if it is recorded in such a way that participants cannot be directly or indirectly linked to the data (de-identified)

- Categories of exemption
 - research designed to study, evaluate, or otherwise examine: (i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs
 - research using educational tests, survey, interview, observation of public behavior if no identifiers
 - research involves a taste and food quality evaluation and consumer acceptance studies

IRB may still require informed consent

NOTE: Only the IRB (not the researcher or anyone else) can make the determination whether or not research is exempt

Expedited Review Categories

- Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis).
- Collection of data from voice, video, digital or image recordings made for research purposes.
- Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Expedited Review Categories

- Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows...
- Prospective collection of biological specimens for research purposes by noninvasive means...
- Collection of data through non invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing...
- Clinical studies of drugs and medical devices only when condition (a) or (b) is met...

Full Committee Review

- Greater than minimal risk (or proposed as minimal risk but sent to full committee at reviewer's discretion)
- Vulnerable populations
- Assigned to two primary reviewers
- Reviewed at next available scheduled IRB meeting
- The protocol and reviews are discussed, then the entire committee makes a determination
- Majority vote
- Returns to committee annually, at minimum
- Can be determined Expedited for continuing review

Other review types

- Emergency Use
- Outbreak Investigation



Application Packet

- Application
- Protocol
- Grant application (NIH)
- Biosketches (for all key personnel)
- Informed Consent Forms/Assent Forms
- Questionnaires, Surveys, Scripts, Ads
- Conflict of Interest (for all key personnel)
- HSP Training (for all key personnel)
- Letters of support, approval



Principal Investigator

The person who takes direct responsibility for completion of a project, directing the research, and reporting directly to the funding agency. This typically includes:

- Designing the research
- Initial application
- Response to findings
- Conduct of research
- Annual reports/updates to the IRB
- Reporting unanticipated events
- Reporting any changes of protocol to the IRB
- Closing out project once completed

A student PI is required to have a responsible faculty member designated on their IRB application.

New Study Submissions

All research activities involving humans must be reviewed and approved by the IRB.

Review board members need to be given enough detailed information about a proposed study in order to effectively make their determination. The Principal Investigator should submit a new study application, protocol, and any other relevant documents as required.

Initial Reviews

Research activities cannot begin until the Principal Investigator receives an official letter of approval from the IRB.

Amendment: Change to IRB Approved Research

When any document or procedure within an IRB approved research study is revised, the Principal Investigator needs to submit an Amendment Request form and all relevant documents to the IRB for review and approval.



Amendments

This process needs to occur prior to implementation of the proposed changes.

Adverse Events and Unanticipated Problems

After approval, if any adverse events or unanticipated problems occur during the course of the research, these issues need to be promptly reported to the IRB.

Adverse Events &
Unanticipated
Problems

Post-Approval Monitoring (Audit)

Post Approval
Monitoring

Approved research procedures and data can be audited by the IRB to ensure that the study is being conducted according to the approved protocol.

Continuation of IRB Approved Research

Previously approved Full Committee and Expedited research must undergo annual continuing review.

Continuing
Reviews

Approval must be granted prior to the study expiration date to avoid a non-compliance closure.

The Principal Investigator needs to submit a progress report and all relevant documents to the IRB review and approval at least 30 days prior to the study expiration date.

Closure of IRB Approved Research

A study can be formally closed with the IRB when data analysis has been completed OR data analysis continues on de-identified data only.

The Principal Investigator needs to submit a closure report and all relevant documents to the IRB for review and approval for closure prior to the study expiration date.



Closures

Reactivation of IRB Approved Research

A study that has either expired or closed can be reactivated within 6 months of the expiration date.



Reactivations

The Principal Investigator needs to submit a reactivation request and all relevant documents to the IRB for review and approval.

Studies closed longer than 6 months must be submitted as a New Study.

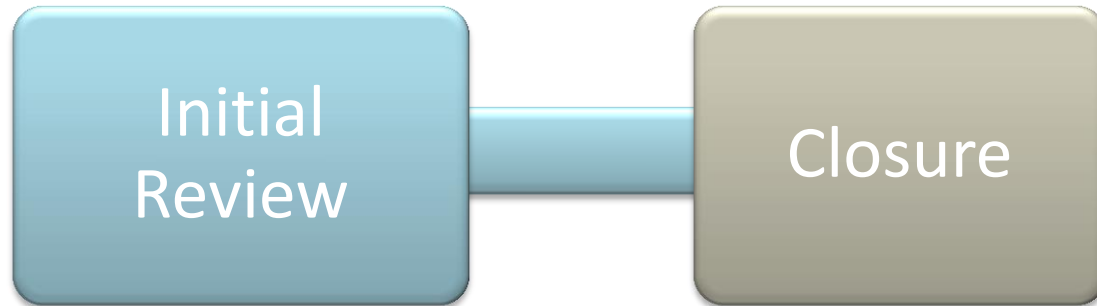
Institution Authorization

- Deferral to an IRB to be the IRB of record

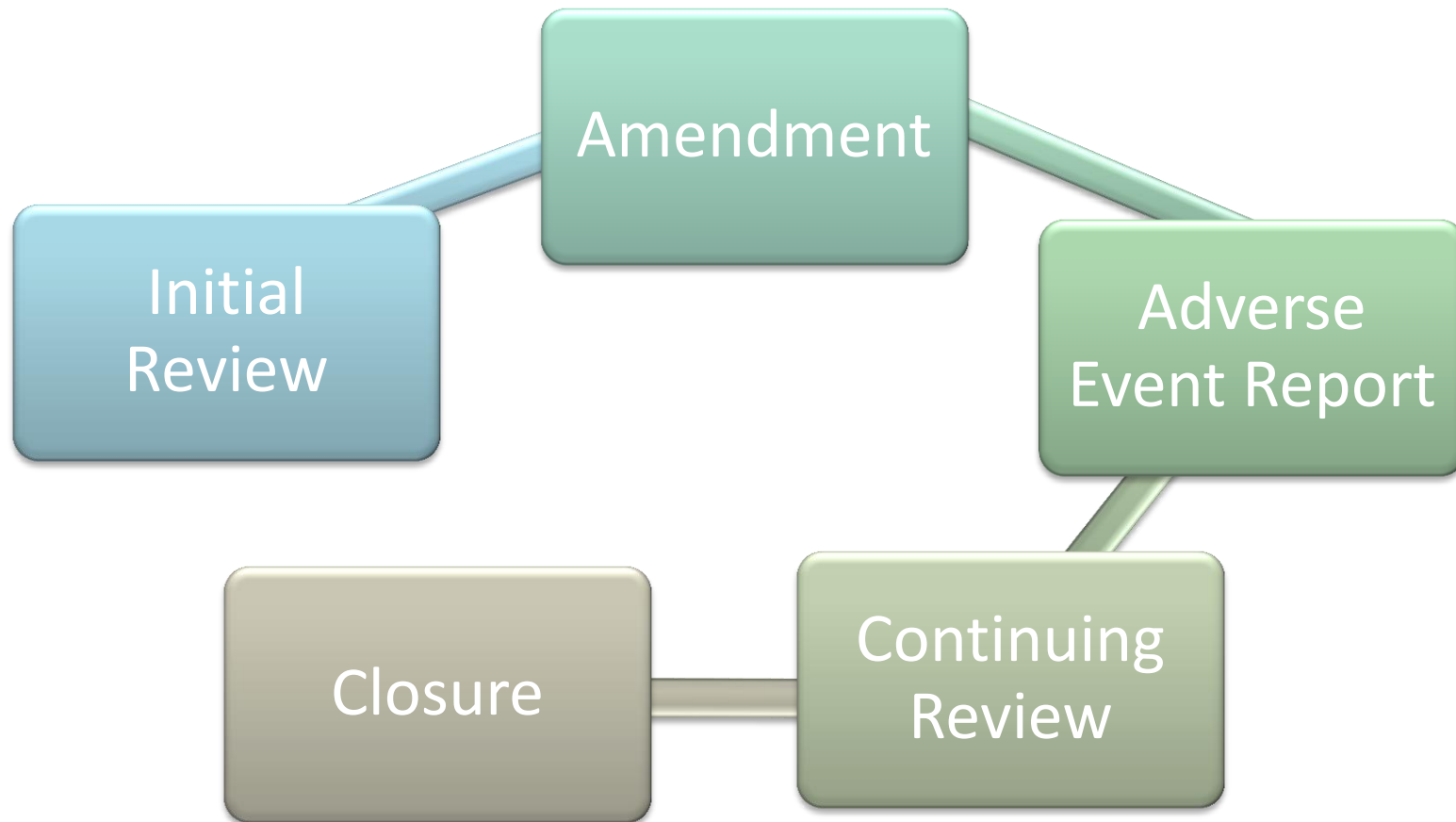


Institution
Authorization

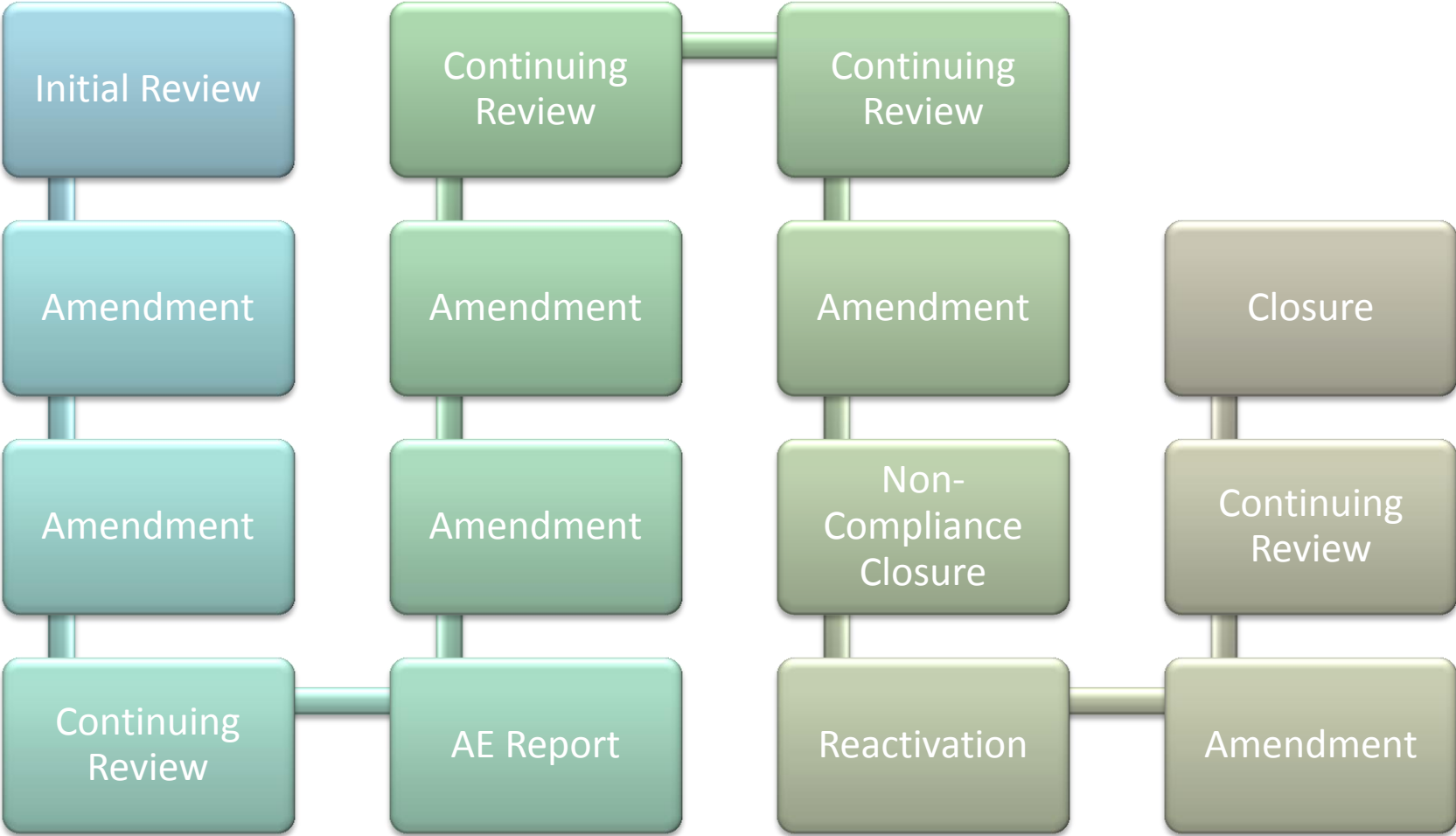
Life Cycle of a Study



Life Cycle of a Study



Life Cycle of a Study



Objective 5:

Discuss the IRB structure
and the types of regulations

Basic Concepts - Functions

45 CFR 46

Title 45 Public Welfare, Department of Health & Human Services, Part 46, Protection of Human Subjects

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>

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

Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains

IRB membership, functions and operations, review of research, records, requirements

Basic Concepts - Functions

21 CFR 50

Title 21 Food and Drugs, Chapter 1, Food & Drug Administration,
Department of Health & Human Services, Subchapter A, General, Part 50,
Protection of Human Subjects

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50>

Clinical Investigations means drugs for human use, medical devices for human use, biological products for human use

IND – Investigational New Drug

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm>

IDE – Investigational Device Exemption

<http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/InvestigationalNewDrugINDorDeviceExemptionIDEProcess/default.htm>

Basic Concepts - Functions

21 CFR 160

Title 45 Public Welfare, Subtitle A, Department of Health & Human Services, Subchapter C, Administrative Data Standards and Related Requirements, Part 160, General Administrative Requirements

http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title45/45cfr160_main_02.tpl

HIPAA – Health Insurance Portability and Accountability Act

HIPAA Privacy Rule - requires appropriate safeguards to protect the privacy of personal health information (**PHI**), and sets limits and conditions on the uses and disclosures that may be made of such information without patient authorization.

<http://www.hhs.gov/ocr/privacy/hipaa/administrative/privacyrule/index.html>

- Health Insurance Portability and Accountability Act Privacy Rule, 1996
 - Requires that each authorization by the patient for release of protected health information includes **a specific research purpose**
 - PHI includes 18 variables: names, zip code, dates, phone numbers, fax numbers, SSN, medical record numbers, account numbers, VIN, URLs, IPs, full face photographic images, e-mail addresses
- Health Information Technology for Economic and Clinical Health (HITECH) Act, enacted as part of the American Recovery and Reinvestment Act of 2009, was signed into law on February 17, 2009, to address privacy and security associated with electronic transmission of health information



Basic Concepts - Responsibilities

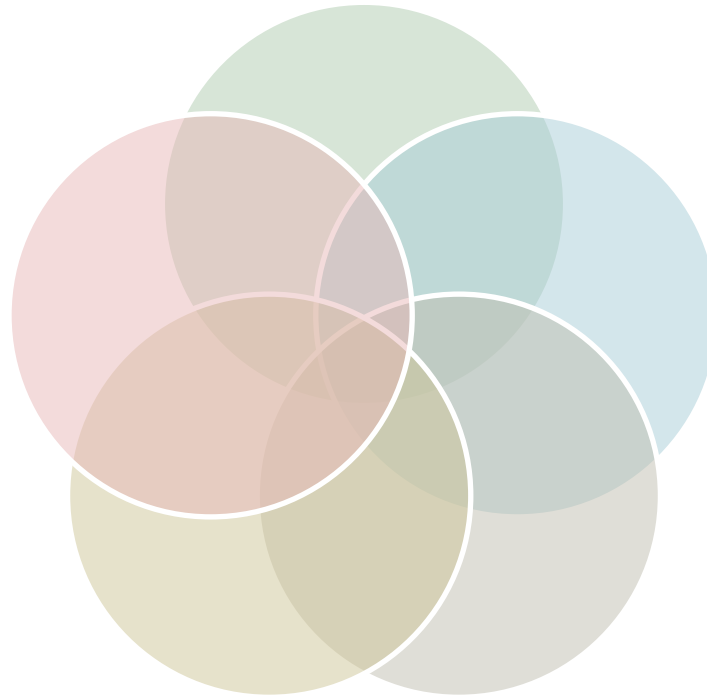
OHRP – Office of
Human Research
Protections

SACHRP – Secretary's
Advisory Committee
on Human Research
Protections

AAHRPP –
Association for the
Accreditation of
Human Research
Protection Programs

PRIM&R – Public
Responsibility in
Medicine and
Research

CIP – Certified IRB
Professional



Institutional Assurance

(Title 45 CFR 46.103)

- Federal Wide Assurance (FWA)
 - If federally conducted or supported, research must have written Assurance of Compliance
 - A contract with U.S. DHHS to review ALL human subject research, Approved by OHRP
 - Individualistic FWA
- Designation and identification of IRB members
- Written procedures
 - Initial & Continuing Review
 - Proposed Changes
 - Reporting of unanticipated problems
 - Reporting of suspension or termination

The IRB

The members of the IRB volunteer their time to serve on these committees

Members are expected to:

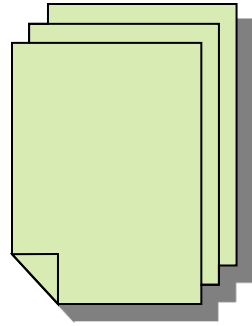
- Attend meetings
- Thoroughly review study documents prior to meeting
- Participate in meeting discussions
- Declare any conflicts of interest and abstain from voting on studies where they have a conflict of interest
- Serve for a minimum of 3 years

Members undergo training prior to having voting privileges.

IRB Membership

- At least 5 members
 - majority must be present (quorum)
- Diverse: community members, not entirely men or women, various experience and expertise
- Scientific member
- Non-scientific member
- Non-affiliated member
- Pediatric Representative
- Prisoner Representative

IRB Processing (Suggestions)

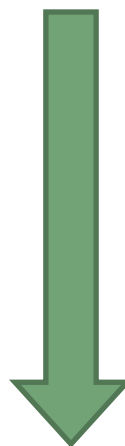


- Prior guidance and mentoring provided on how to conduct reviews
- Assign primary and secondary reviewers
- Ideal to assign protocols according to areas of expertise of reviewers
- Provide all reviewers with review sheets to complete, prepopulated with study information

IRB Processing (Suggestions)



- Allow at least 1 week for review
- Return completed review sheets with decision
- Communicate decision to PI
- Keep metrics of turnaround times by steps



– Submission to review



– Reviewer turnaround time, first look



– If back to PI, how long with PI



– Reviewer turnaround time, second look



– Decision to PI



IRB Processing (Suggestions)

- All IRB members confirmed to attend a meeting, be familiar with proposals
- At least 1-2 weeks allowed for review
- Primary mentor provides
 - Brief description and overview of the proposed study
 - Discusses any issues, comments, questions



IRB Processing (Suggestions)

- Secondary mentor provides
 - Additional issues, comments, questions
- All IRB members get to add additional issues, comments, questions
- Discussion ensues
- Both reviews recommend a decision
- Decision is opened to members; vote
- Letter communicating decision sent to PI



IRB Processing (Suggestions)



- If studies are reviewed outside committee, the reviews and decisions are communicated to IRB members at the next meeting
- Typically IRB meetings are closed meetings and permission granted to guests
- If a protocol is outside the scope of expertise, individuals with expertise need to be invited to assist with review
- IRB members should be provided ongoing continuing education

State Regulations

State genetic privacy statutes

State and Statute	Personal Access to Genetic Information Required	Consent Required to				Define as Personal Property		Specific Penalties for Genetic Privacy Violations
		Perform/Require Genetic Test	Obtain/Access Genetic Information	Retain Genetic Information	Disclose Genetic Information	Genetic Information	DNA Samples	
New Mexico §24-21-1 to §24-21-7	x	x	x	x	x			x
Alaska §18.13.010-100		x	x	x	x	x	x	x
Arizona §20-448.02		x			x			
Arkansas §20-35-101 to 103					x			
Montana								
Wyoming								

National Conference of State Legislatures, Genetic Privacy Laws: <http://www.ncsl.org/issues-research/health/genetic-privacy-laws.aspx>

- Scientific Advisory Committee
- Biosafety & Biosecurity Committee
- Tissue Repository Committee
- Radiation, Chemical & Biological Safety Committee
- Export Control
- Conflict of Interest



University Regulations

- Informed consent – each biospecimen resource should have documentation of informed consent
- Equipment monitoring, calibration, maintenance and repair
- Control of biospecimen collection supplies (reagents)
- Biospecimen identification and labeling conventions
- Biospecimen collection and processing methods
- Training and security (physical and informatics)
- Storage and retrieval
- Shipping and receiving
- Biospecimen quality control
- Biosafety

Laboratory SOPs



Recap

Why do IRBs exist today?



The Belmont Report (1979)

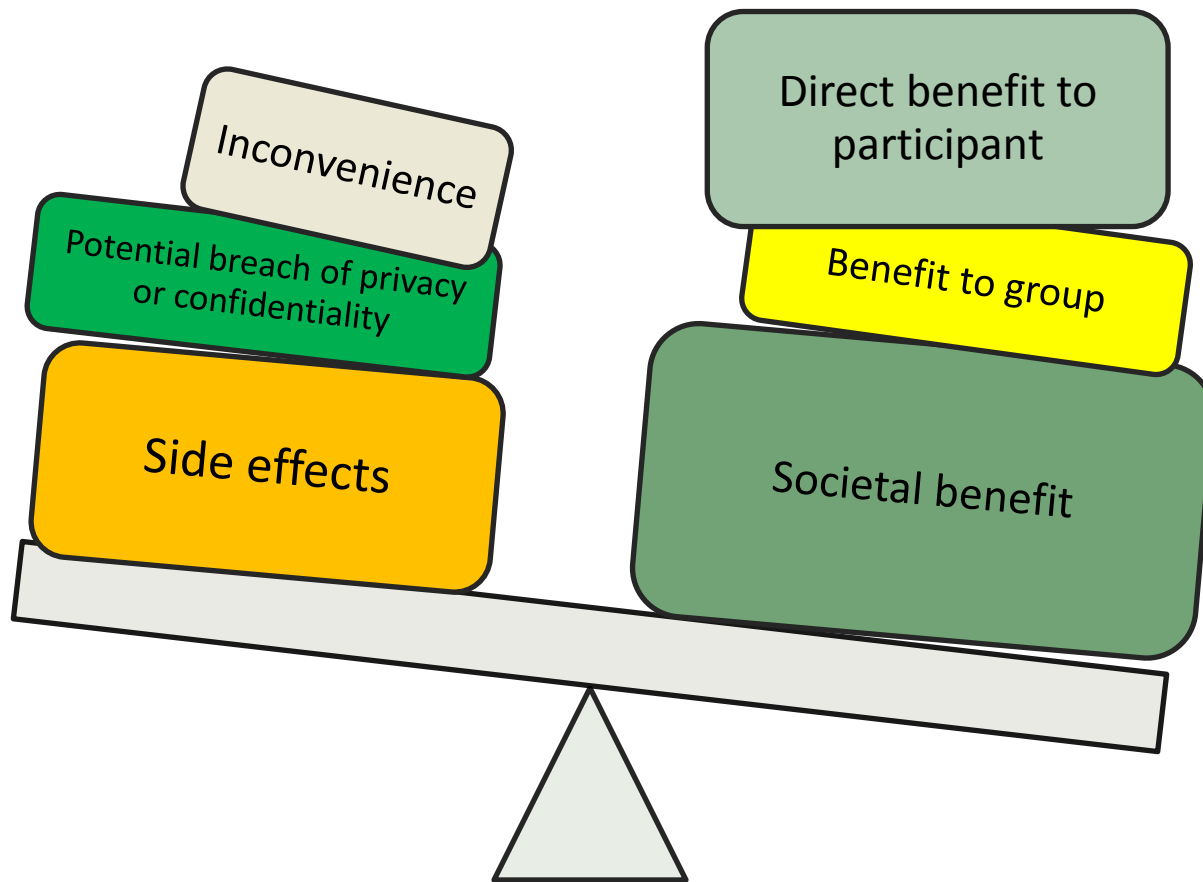
Ethical Principles of conducting human subjects research:

1. Respect for Persons
2. Beneficence
3. Justice



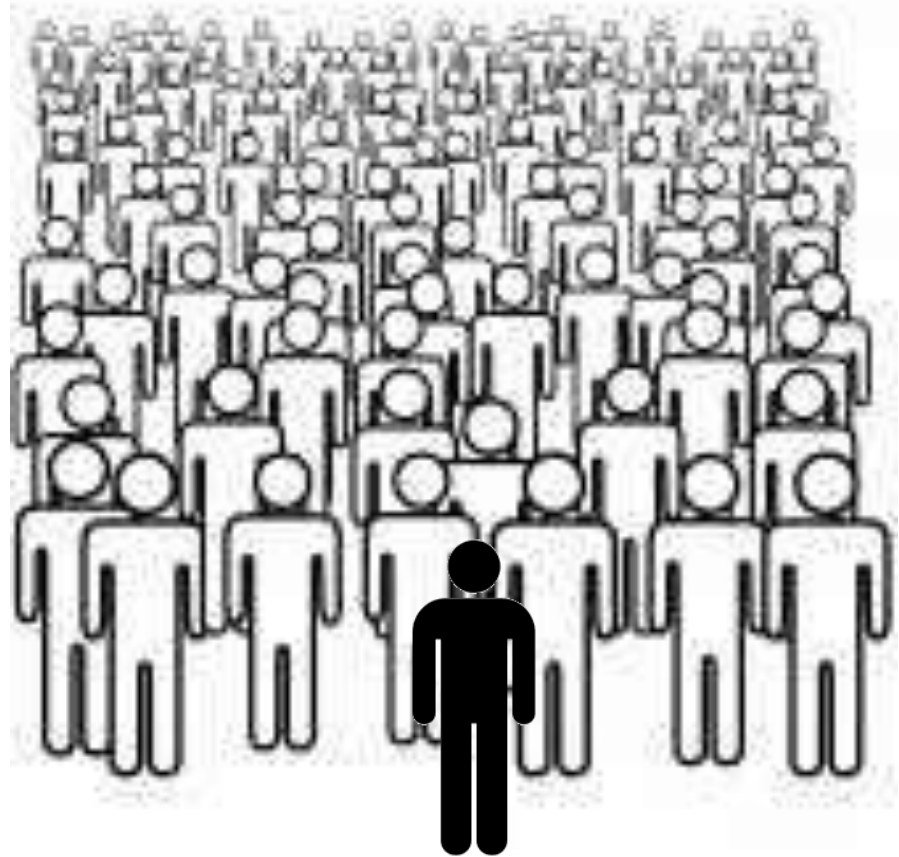
Maximize possible benefits and minimize possible harms.

Risk-Benefit Analysis



What risks can occur in human subjects research?

Harm to a community or group



Harm to the individual participant



Questions?

