IRB Member Orientation
Stanford University
Administrative Panel Year 2009- 2010

Bertha deLanda
Training Specialist
Research Compliance Office

Objectives

- **Understand** Stanford IRB
- **Introduce** ethical principles and regulations
- **Present** STANFORD *Human Research Protection Program* (HRPP)
- **Criteria** for Approval and Informed Consent
- **Discuss** protocol review and reviewer role
- **Identify** resources

The Institutional Review Boards at Stanford

Binder Tab 1

Stanford IRBs

This section will cover:

- Intro to IRB (general)
- IRB Composition
- IRB at Stanford
- RCO Management

IRB Intro –why are you here?

The Institutional Review Board is a functionally independent research review unit engaged in human subject protection

- **Ensure** the rights and welfare of participants involved in human research are adequately protected
- **Ensure** all activities are compliant with Federal, State and applicable laws
- Are **appointed** by the Vice Provost and Dean of Research
- **Composed** of faculty, students, staff, and members of the community

IRB Composition

- At least 5 members with diverse backgrounds
- At least one member who is
  - Scientific
  - Nonscientific (needed for quorum)
  - Unaffiliated or "Public"

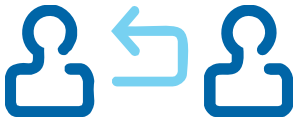
- "*Members must be sensitive to community attitudes, knowledgeable about institutional policies, regulations, and applicable laws*"

OHRP 45 CFR §46.107 and OHRP 45 CFR §46.108

IRB Composition (cont.)

- No member may participate in IRB review if they have a **conflicting interest**

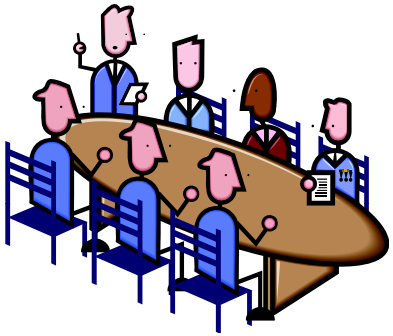
- Research involving vulnerable subjects should include individuals **knowledgeable of that subject population**



- Can invite **expert consultation**; however consultants cannot vote

(OHRP 45 CFR §46.107)

IRBs at Stanford



- Eight IRBs
  - Seven medical IRBs
  - One nonmedical IRB (Social and Behavioral Research)
- Convened meetings and ad hoc meetings
- *Administrative Panel for Human Subjects in Medical (or Nonmedical) Research*
- Approximately 130 IRB members

IRB's at Stanford, cont.

- Convened meetings meet once a month (for example, every 2nd Tuesday)
- Schedule on Human Subjects website
- Panel 6 and 8 do not convene
- Meetings at 12 noon, RCO conference room

IRB Management

Support for IRB: RCO Staff

IRB Manager – Initial review/modifications

IRB Associate – Continuing review

IRB Training Specialist – Educational items

HRPP Senior Staff

Stanford University
Research Compliance Organization Chart

Director
Kathy McClelland

HRPP Assoc. Director
Alice Haskett

Sr. IRB Coordination Mgr.
Kevin Murphy

Sr. IRB Lead
Celia Molvin

Sr. IRB Mgr. 1
Anastasia Doherty

IRB Mgr. 2

IRB Mgr. 3

Sr. IRB Assoc.
For Coo
Jan L

IRB A
Carme

IRB A
Elizab

IRB A
Gloria

IRB A
Ashima Goel

Barbara Ho

IRB Assoc. 8
Monica Castillo

IRB Assoc. 7
Carol Hill

IACUC
Mgr.
Missy Howard

Sr. IACUC Mgr.
Valerie Fratus

Sr. IACUC Assoc.

Victor Valencia

Arturo Retana

CQI Assoc. Director
Mahshid Parsi

Sr. Compliance Analyst
Karen Corday

Training Specialist
Bertha deLanda

ecords Mgr.
Shulaker

umentation
ecialist
Aldeguer

Vice Provost & Dean of Research

Ann Arvin, MD

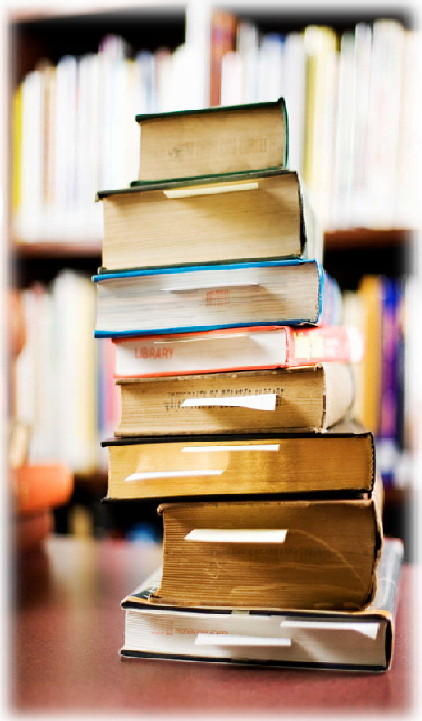
Lucile Salter Packard Professor in Pediatrics and Professor of Microbiology and Immunology

- Institutional Official
- Head of HRPP

Ethical Principles & Regulations

Binder Tab 2

Ethical Principles & Regulations - Outline

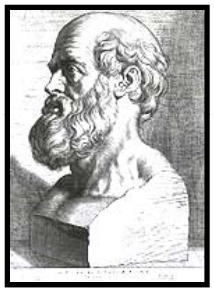


- The Belmont Report
- OHRP & *The Common Rule*
- FDA regulations
- HIPAA Privacy Rule
- California State/VA regulations
- AAHRPP Accreditation

The Belmont Report

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

Three Basic Principles



1. Respect for Persons

Treat subjects as autonomous agents, protect those who have diminished autonomy

2. Beneficence

Do not harm, maximize possible benefits, minimize possible harms

3. Justice

Equitable distribution of burdens and benefits

OPRR Reports; The Belmont Report 1979

Belmont Report - Application

Respect for persons

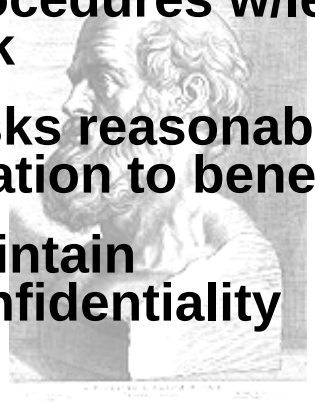
Informed Consent

- Obtain and document
- Voluntariness/ no coercion
- Protect privacy

Beneficence

Risks/Benefits

- Procedures w/least risk
- Risks reasonable in relation to benefits
- Maintain confidentiality



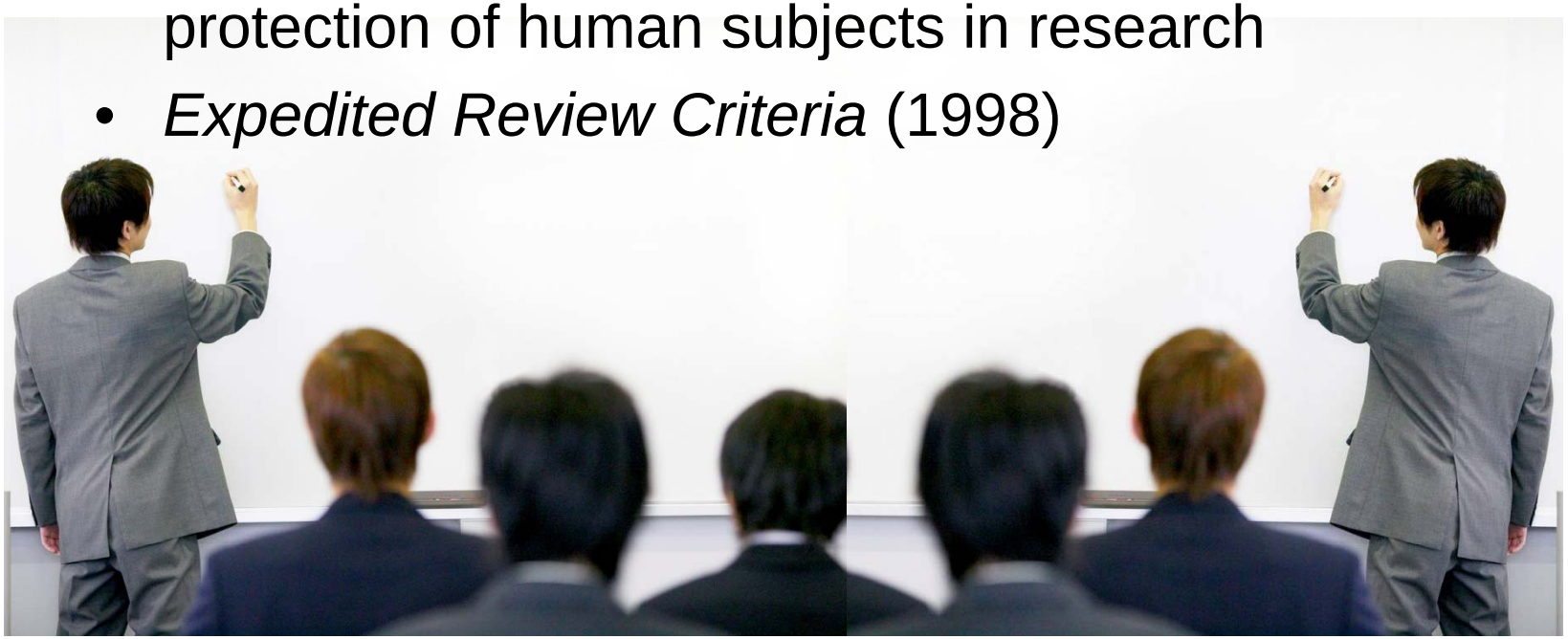
Justice

Enrollment

- Select participants equitably
- Avoid exploitation of vulnerable populations

Office for Human Research Protections (OHRP)

- Established after Belmont Report
- Created 45 CFR 46 or “The Common Rule” for the protection of human subjects in research
- *Expedited Review Criteria* (1998)



Federalwide Assurance (FWA)

"Any institution engaged in…HHS-supported human subjects research must provide written assurance that it will comply with the… protection of human subjects regulations"

OHRP 45 CFR 46.103(a)

The five STANFORD institutions each have an FWA; each of the IRB's is registered and has its own number

SU, LPCH, SHC, PAIRE and VA

Food and Drug Administration

Federal monitoring entity for all drug and device research on humans; relevant regulations include:

- 21 CFR 50 Protection of Human Subjects
- 21 CFR 56 Institutional Review Boards **(IRB)**
- 21 CFR 600 Biological Products: General
- 21 CFR 312 Investigational New Drug Application **(IND)**
- 21 CFR 812 Investigational Device Exemptions **(IDE)**

Note: All significant and non significant risk **(SR/NSR)** devices, Emergency Use, Sponsor-investigator, “Off-label” use fall under FDA regulations

HIPAA

- Health Insurance Portability and Accountability Act
- *45 CFR 164,* HIPAA Privacy Rule for Research
- Protect the privacy & security of an individual's protected health information (PHI)
- Governs the way PHI is:
  - » Collected
  - » Maintained
  - » Used
  - » Disclosed

Stanford IRB = Privacy Board for University

Additional Regulations

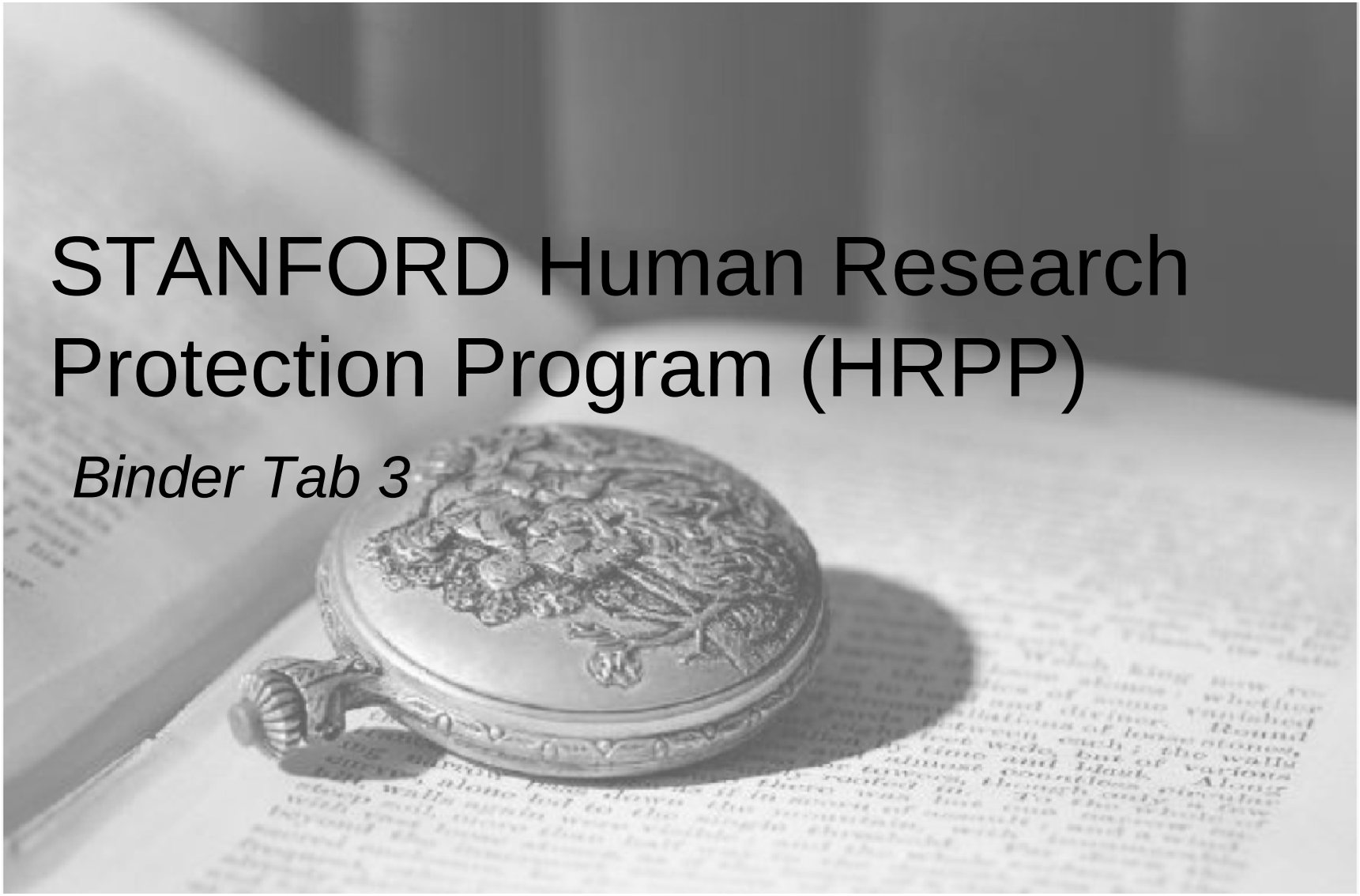
California State

- Person obtaining consent (POC)
- *Experimental Subjects Bill of Rights*
- HIPAA – follow State and Federal requirements

Veterans Administration

- Data security
- Special consent form header and footer
- HIPAA – Federal requirements

Stanford University – Re-accreditation : March 2009

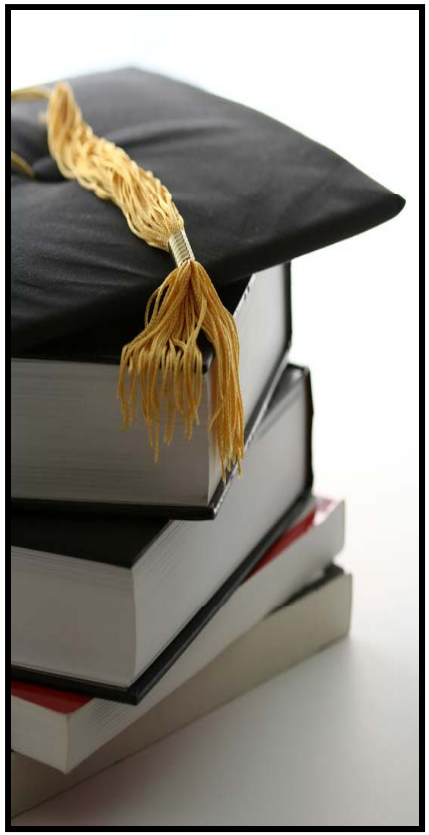


STANFORD Human Research Protection Program (HRPP)

Binder Tab 3

STANFORD HRPP

"Human Research Protection Policy"



In this section, we will cover:

- Definition/objective
- Entities covered/organization
- HRPP policies and procedures

Available to entire research community on RCO website (http://humansubjects.stanford.edu)

STANFORD HRPP Manual

- **Definition:**
  - Embodiment of Federal Laws, regulations, and legislation as Stanford interprets and applies them to human subject research
- **Contains** documentation of IRB Policies; **20 chapters**

Chapters of particular significance:

- ✓ **Informed Consent (Ch. 12)**
- ✓ **Privacy and Confidentiality (Ch. 11)**
- ✓ **Structure and Composition of IRB (Ch. 6)**
- ✓ **Systematic Review (Ch. 7)**

STANFORD HRPP

Goal :

- *To protect the rights and welfare of human research participants*
- *Guided by ethical principals (e.g., The Belmont Report)*
- *Compliance with applicable laws*

Objective:

- *Establish a formal process to monitor, evaluate, and improve HSP*
- *Exercise oversight*
- *Intervene when necessary*
- *Educate investigators and staff*

Components of the HRPP-covered entities

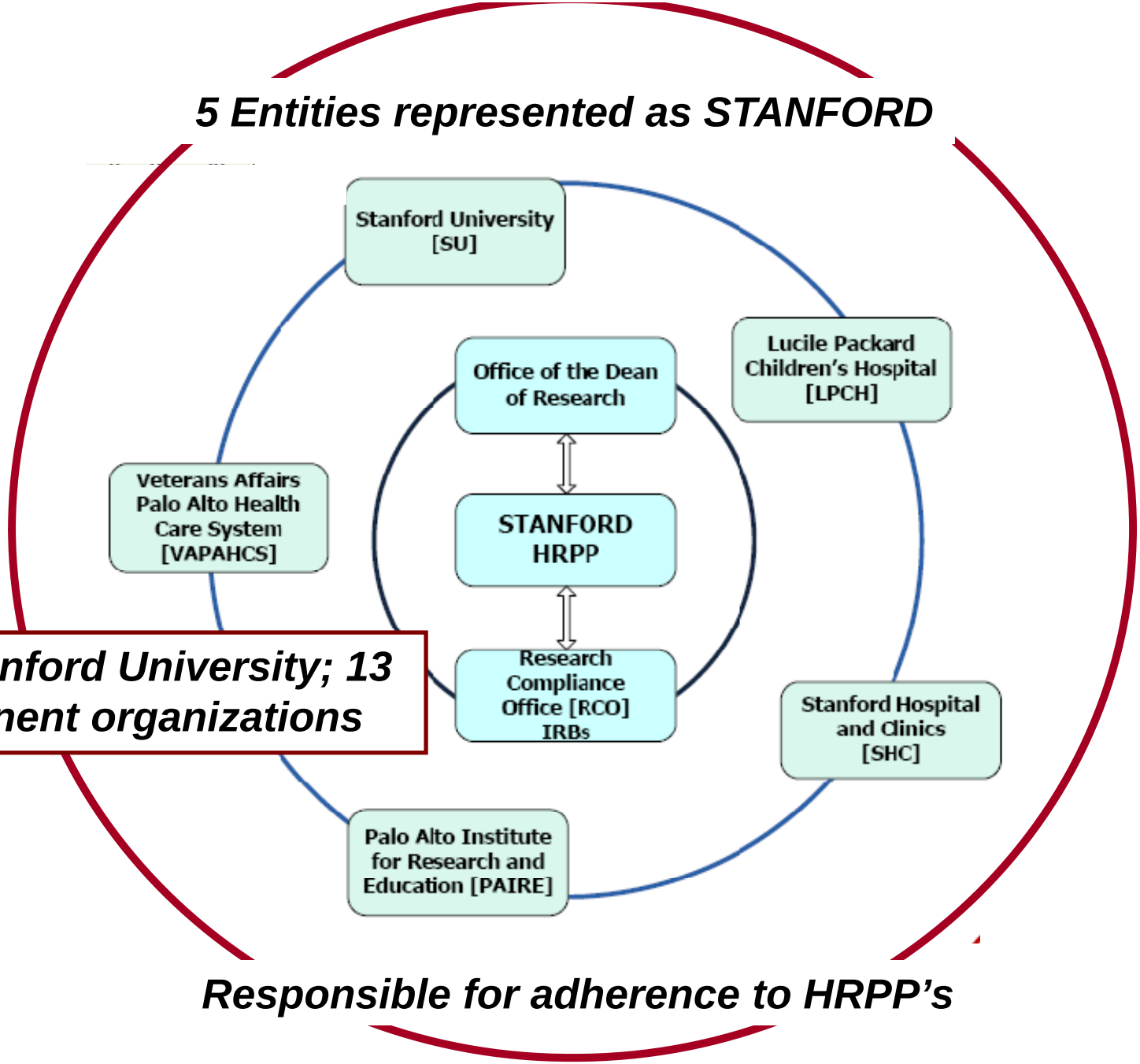
Ann Arvin; Institutional Official

Head of the HRPP; responsible for overseeing its implementation

IRB staff, CQI, Panel Members

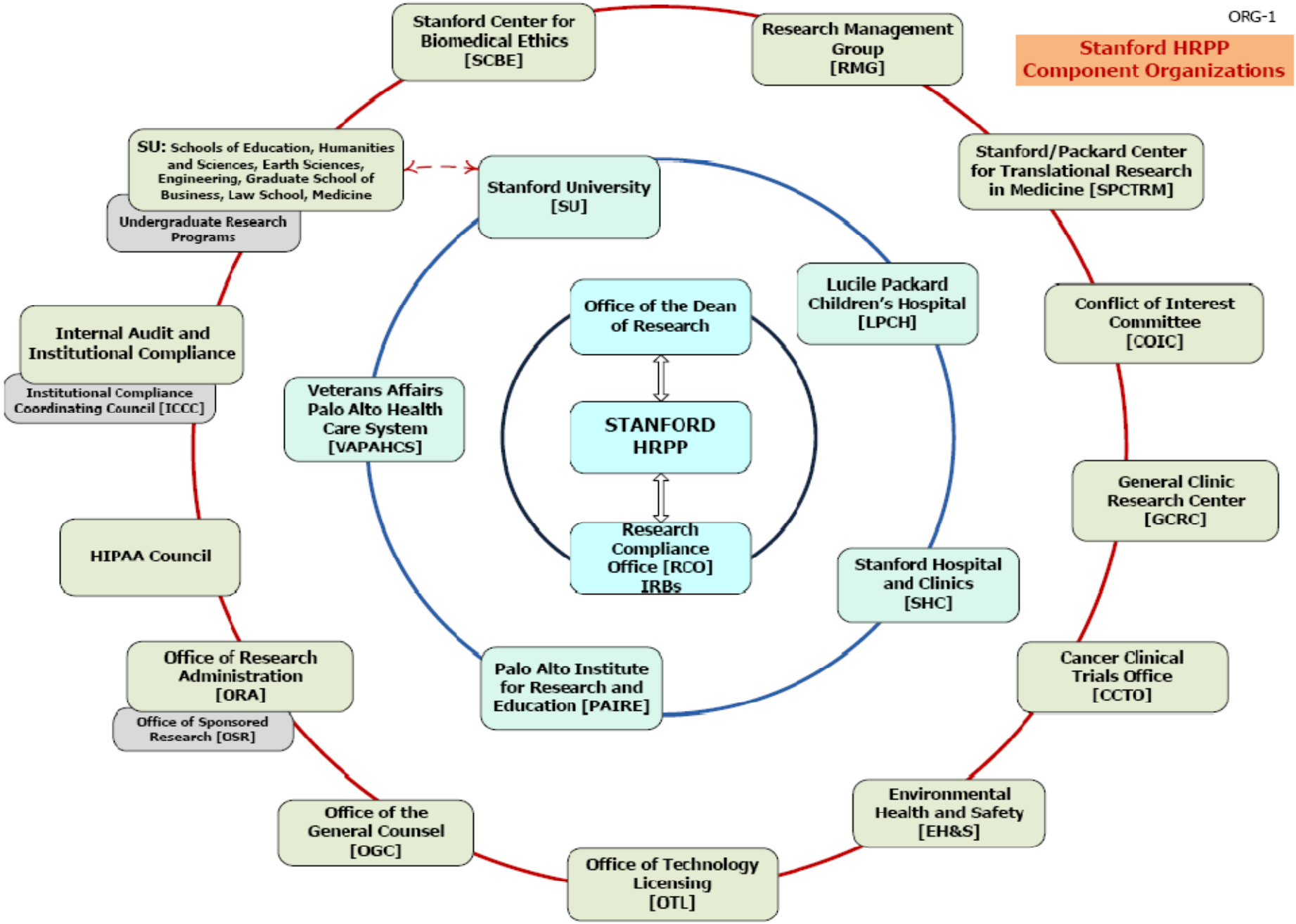
Maintenance and implementation of day to day operations of those affected by HRPP

5 Entities represented as STANFORD



From Stanford University; 13 Component organizations

Responsible for adherence to HRPP's


ORG-1
Stanford HRPP Component Organizations
Stanford Center for Biomedical Ethics [SCBE]
Research Management Group [RMG]
Stanford/Packard Center for Translational Research in Medicine [SPCTRM]
Conflict of Interest Committee [COIC]
General Clinic Research Center [GCRC]
Cancer Clinical Trials Office [CCTO]
Environmental Health and Safety [EH&S]
Office of Technology Licensing [OTL]
Office of the General Counsel [OGC]
Office of Research Administration [ORA]
Office of Sponsored Research [OSR]
HIPAA Council
Internal Audit and Institutional Compliance
Institutional Compliance Coordinating Council [ICCC]
SU: Schools of Education, Humanities and Sciences, Earth Sciences, Engineering, Graduate School of Business, Law School, Medicine
Undergraduate Research Programs
Stanford University [SU]
Veterans Affairs Palo Alto Health Care System [VAPAHCS]
Lucile Packard Children's Hospital [LPCH]
Stanford Hospital and Clinics [SHC]
Palo Alto Institute for Research and Education [PAIRE]
Office of the Dean of Research
STANFORD HRPP
Research Compliance Office [RCO]
IRBs

Criteria for Approval & Requirements for Informed Consent

Binder Tab 4

Criteria for IRB Approval of Research

Are <u>all</u> of the following requirements satisfied?

1. Risks **minimized**, research design sound
2. Risks **reasonable** vs. benefits
3. Subject selection **equitable**
4. **Informed consent** from subject or legally authorized representative
5. Informed consent **documented**

Are vulnerable subjects included?

6. Data **monitoring** when available
7. Plan for **privacy/confidentiality**, when appropriate
8. Additional safeguards for **vulnerable** population

Adapted from §45 CFR 46.111

Basic Elements of Informed Consent

1. Study involves research; purposes; duration; procedures; experimental procedures
2. Risks/discomforts
3. Benefits (if any or if none)
4. Alternative procedures
5. Confidentiality of subjects' records
6. Compensation, medical treatments if injury
7. Contact information for questions about research, participants' rights, injury event
8. Voluntary participation: Refusal OK, Stop OK

Adapted from §45 CFR 46.116 (a)

Additional Elements of Informed Consent

1. Risks are unforeseeable
2. Participation may be terminated by investigator
3. Additional costs
4. Consequences of decision to withdraw from research
5. Significant new findings to be provided to subject
6. Approximate number of subjects

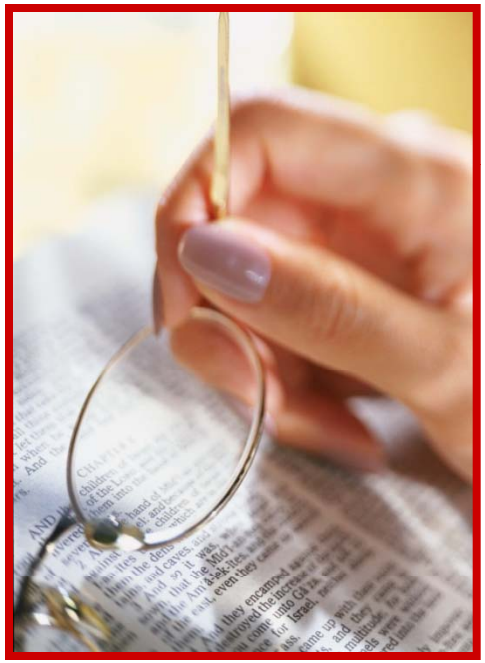
Adapted from §45 CFR 46.116 (b)

Protocol Review Process & Reviewer Role

Binder Tab 5

Protocol Review/Reviewer Role

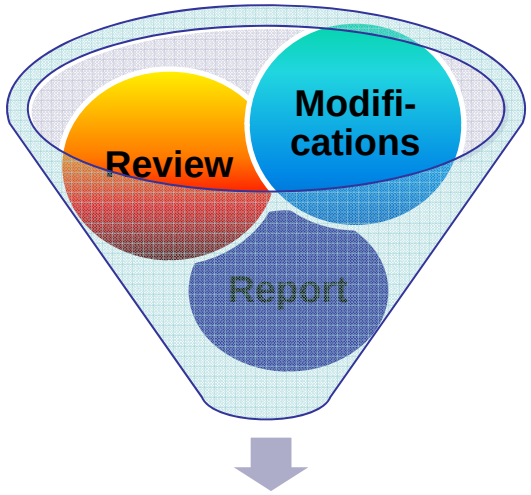
In this section we will cover:



- Protocol Events
- Protocol Review Types
- eProtocol Review Process
- Reviewer Role
- Special Classes of Participants

Protocol Events

- **Initial Review** — New protocols
- **Modification** — Changes in procedure, risk level, personnel
- **Continuing Review** — SAE's, AE's, frequency set by IRB
- **Final Report** — Completion of research
- **Report** — Unanticipated Problems (UP)
  Deviations or violations
  Complaints



Protocol Review Types

Review types are defined by regulations and determined by staff before protocols are assigned to reviewers

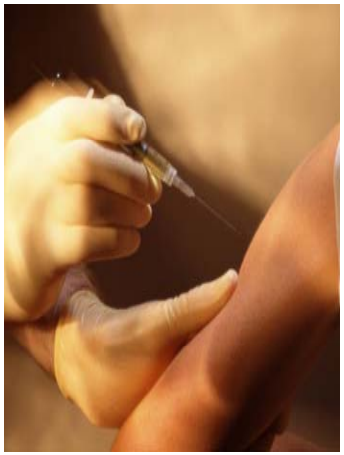
Regular – more than minimal risk; reviewed at panel meeting

Expedited – no more than minimal risk; not presented

Exempt – implied minimal risk; not presented (determined not to need continuing review)

Definitions of Minimal Risk

- **Minimal Risk:**



"the probability and magnitude of **harm or discomfort**…

not greater …than those ordinarily **encountered in daily life**

or during the performance of **routine** physical or psychological **examinations** or tests"

45 CFR §46.102(i)

“Regular” Review

- **Initial** review at convened meeting
  - 2 primary reviewers (*pink* and *yellow*)
  - approved by full panel (**blue** reviewers included)

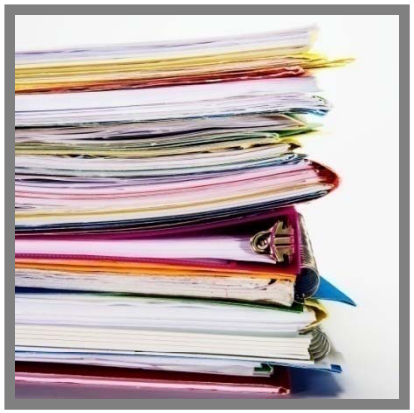
- **Continuing** review required (at least annually)

- **Examples**
  - Studies using FDA investigational **devices**
  - Studies involving **drugs or biologics**
  - Studies with **vulnerable populations**

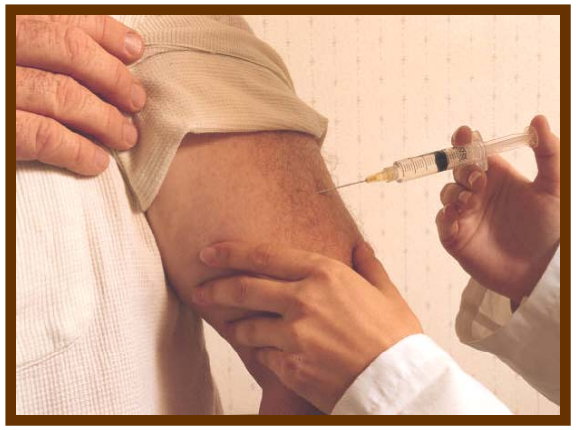
Risk : more than minimal

“Expedited” Review

- **No more than** minimal risk
- Assigned to **one IRB member** for review (not presented at a convened meeting)
- “*Expedited Review **Categories**” - 9*
- **Continuing review** required (at least annually)



Examples:
chart reviews
or simple
blood draw studies

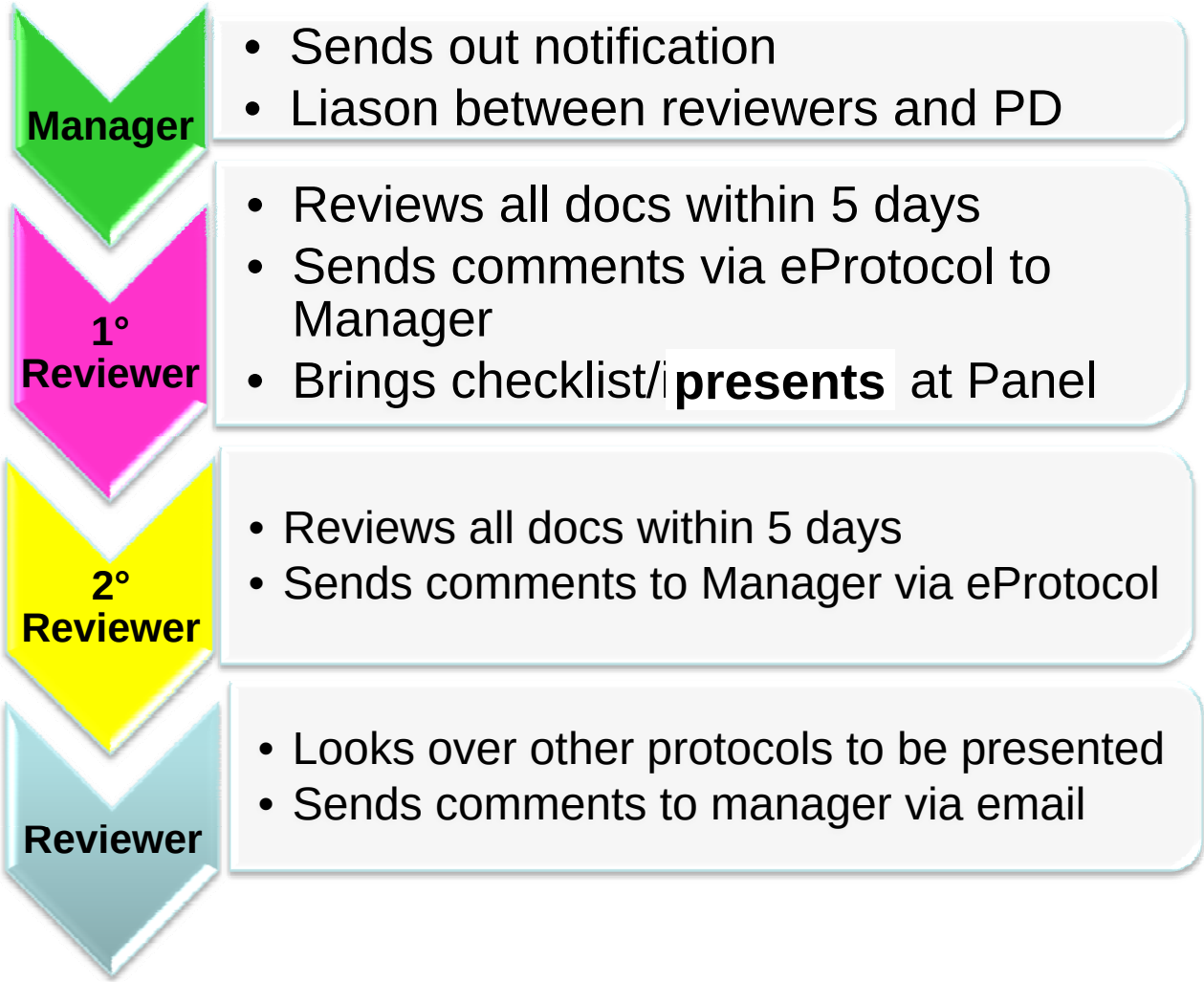


“Exempt” Review

- **Minimal** risk (not presented)
- Exempt **categories** - 6
- **Uncommon** in medical research because of HIPAA considerations
- Exempt from **continuing review**
- **Reviewed** by one panel manager (6 or 8)

Examples :
mostly social &
behavior studies

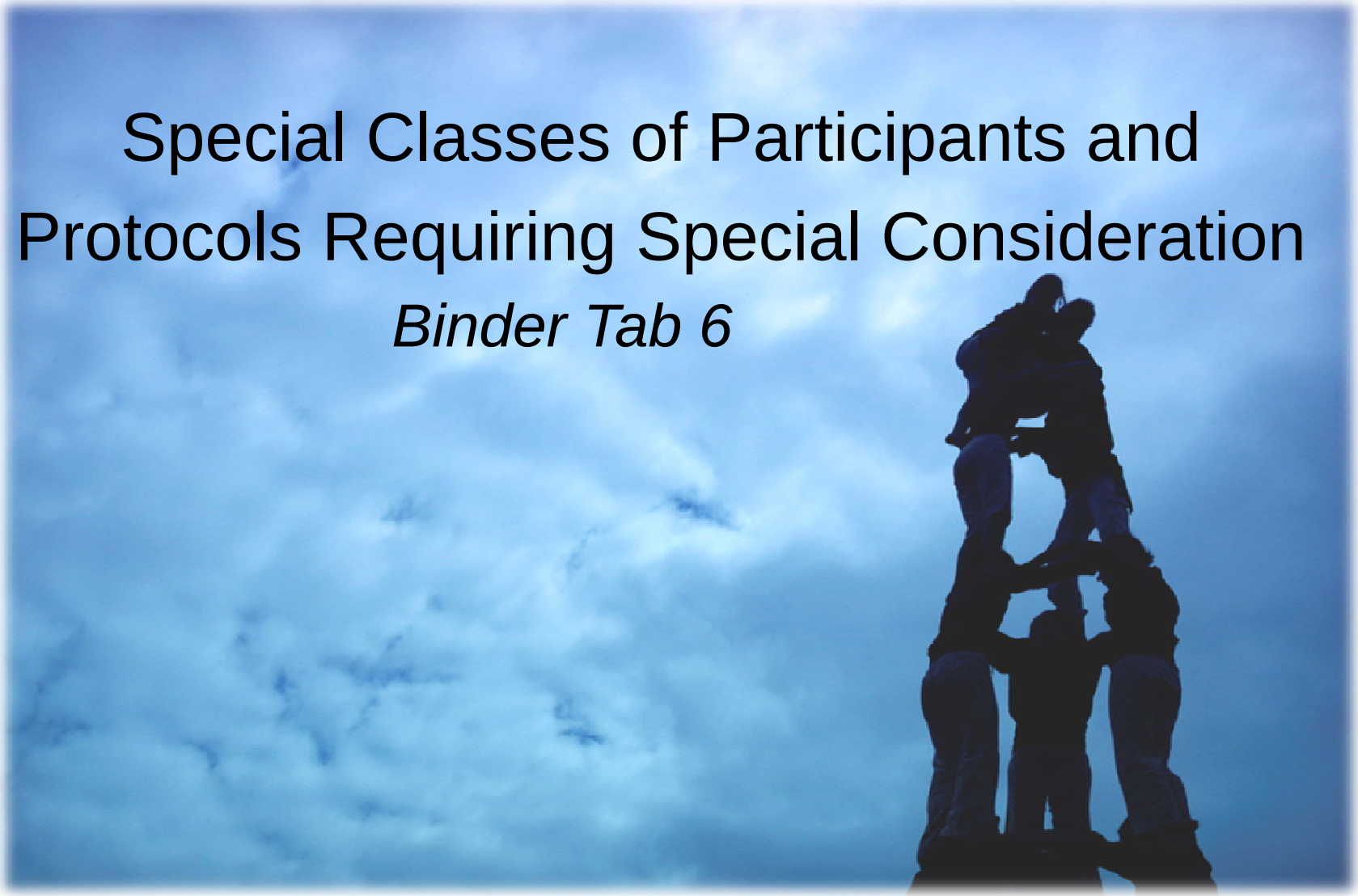
Protocol Review Process *– Reviewer/Manager Responsibilities*



All information and discussion at panel goes into decision regarding protocol

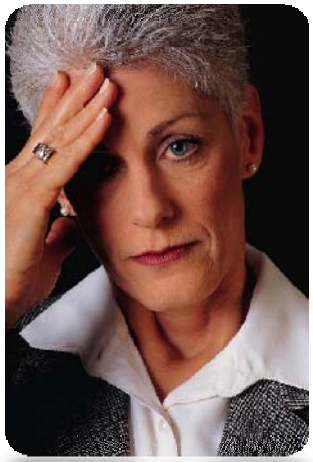
Special Classes of Participants and Protocols Requiring Special Consideration

Binder Tab 6



Special Classes of Subjects

- Children
- Pregnant women, fetuses and neonates
- Prisoners
- Other vulnerable subjects (persons with impaired decision making)
- Students, employees



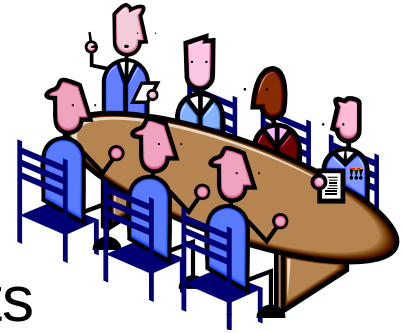
Protocols Requiring Special Consideration or Procedures

- Sponsor-investigator research
- Stem cell research
- Gene transfer research
- Device Studies
- Emergency Use
- Federally Funded research

IRB Related Issues

Binder Tab 7

Convened Meeting Procedures



- **Green** folders
  - » Roster
  - » Agenda
  - » Conflict of Interest documents
  - » “Laminates”
- Name tents
- Confidentiality & Conflict of Interest statements
- Minutes from previous meeting
- Education Items

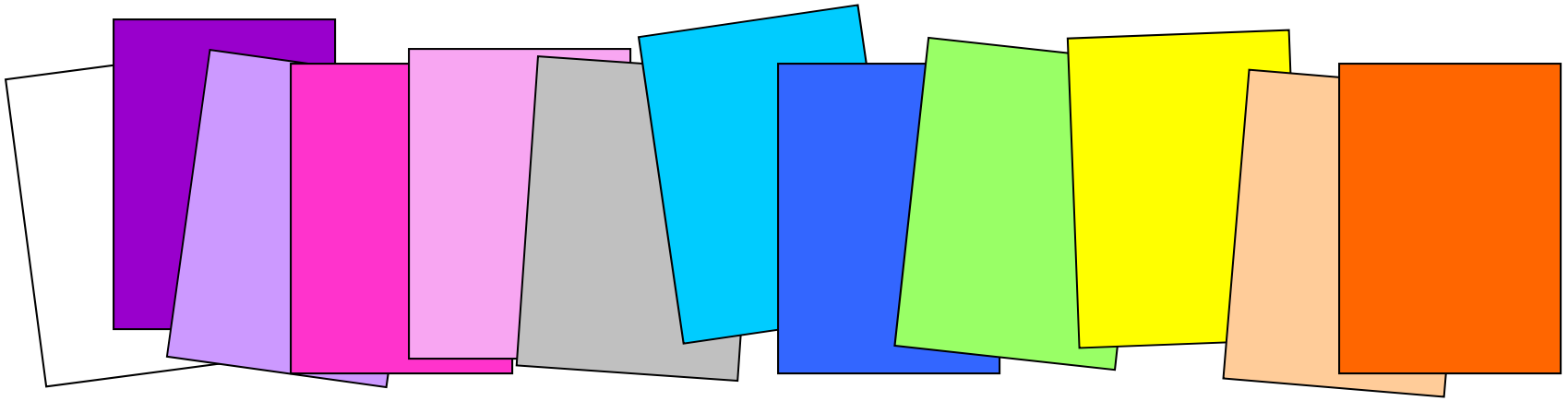
*Occasionally there will be an **early agenda item***

IRB Guidance “Laminates”

Provided at each meeting for reference use

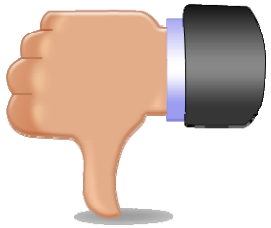
Give regulations and guidance pertaining to research criteria

Examples of topics: children’s findings, exempt categories, requirements for waivers



IRB Findings

- **Additional regulations** associated with a protocol characteristic or a special population
- Example: children's findings (orange laminate)



  - Presenter explains justification
  - IRB Chair summarizes
  - IRB Manager highlights

- **Vote** on the approval includes the "finding"
- **Documented** in IRB minutes

IRB Related Issues

Forms:

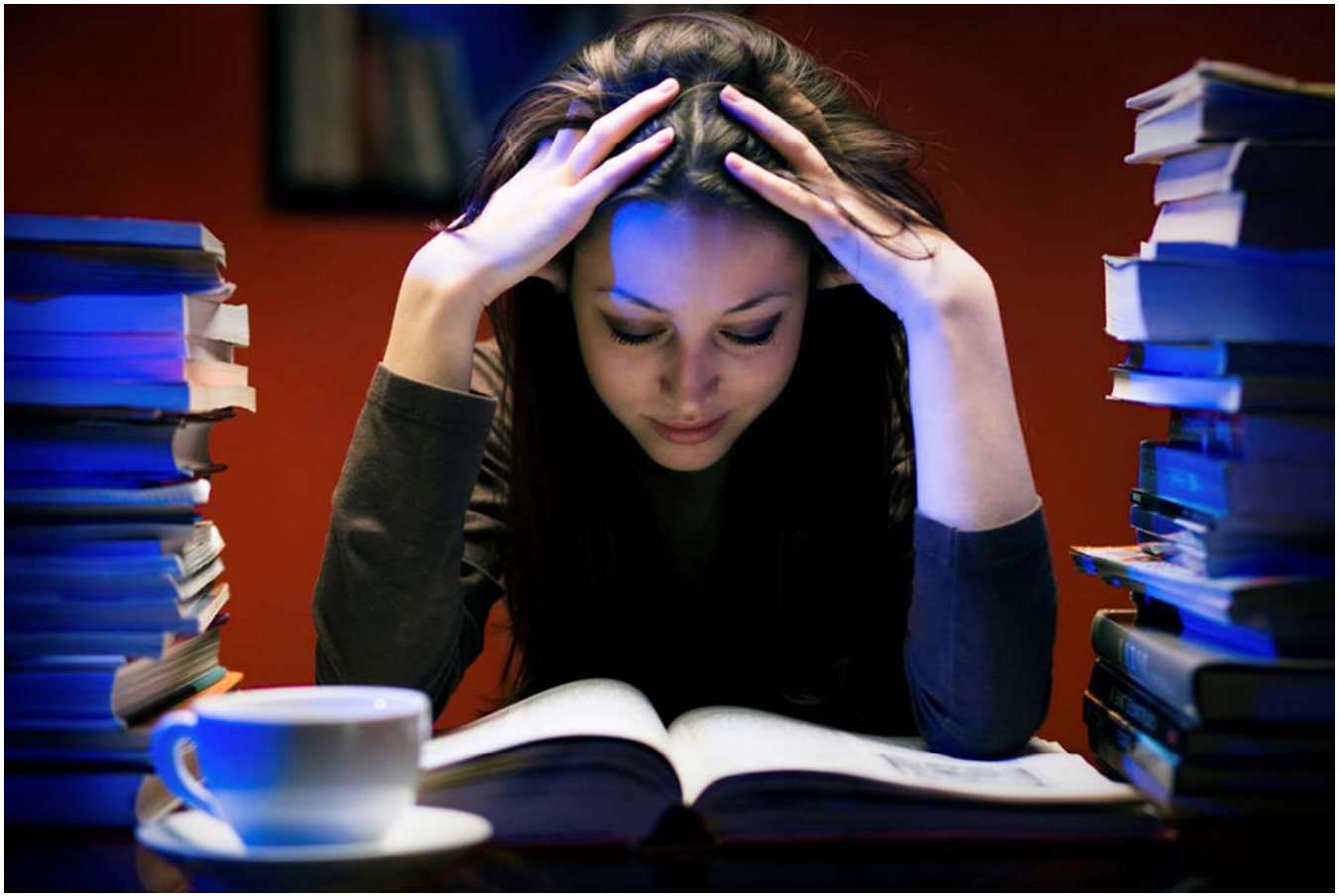
- Confidentiality of IRB process (meetings and documents)
- Conflict of Interest

*If you will be late, **please call your panel manager** or associate before noon the day of your meeting.*

Resources and IRB Member Continuing Education

Binder Tab 8

What do you think so far?



Education Items

Training:

- HIPAA Awareness (STARS)
- CITI Training (www.citiprogram.org)

Education

- 10 minutes at the beginning of panel
- contact information:
  - Bertha deLanda
  - Educ. Line: 650-724-7141
  - Direct line : 650-736-2686

Resources & IRB Member Continuing Education

- RCO Web Site:
  - http://humansubjects.stanford.edu/
- RCO Staff Contact Page:
  - http://humansubjects.stanford.edu/general/contact.html
- Collaborative IRB Training Initiative (CITI):
  - http://www.citiprogram.org
- eProtocol Help:
  - http://humansubjects.stanford.edu/general/eprotocol/help.html