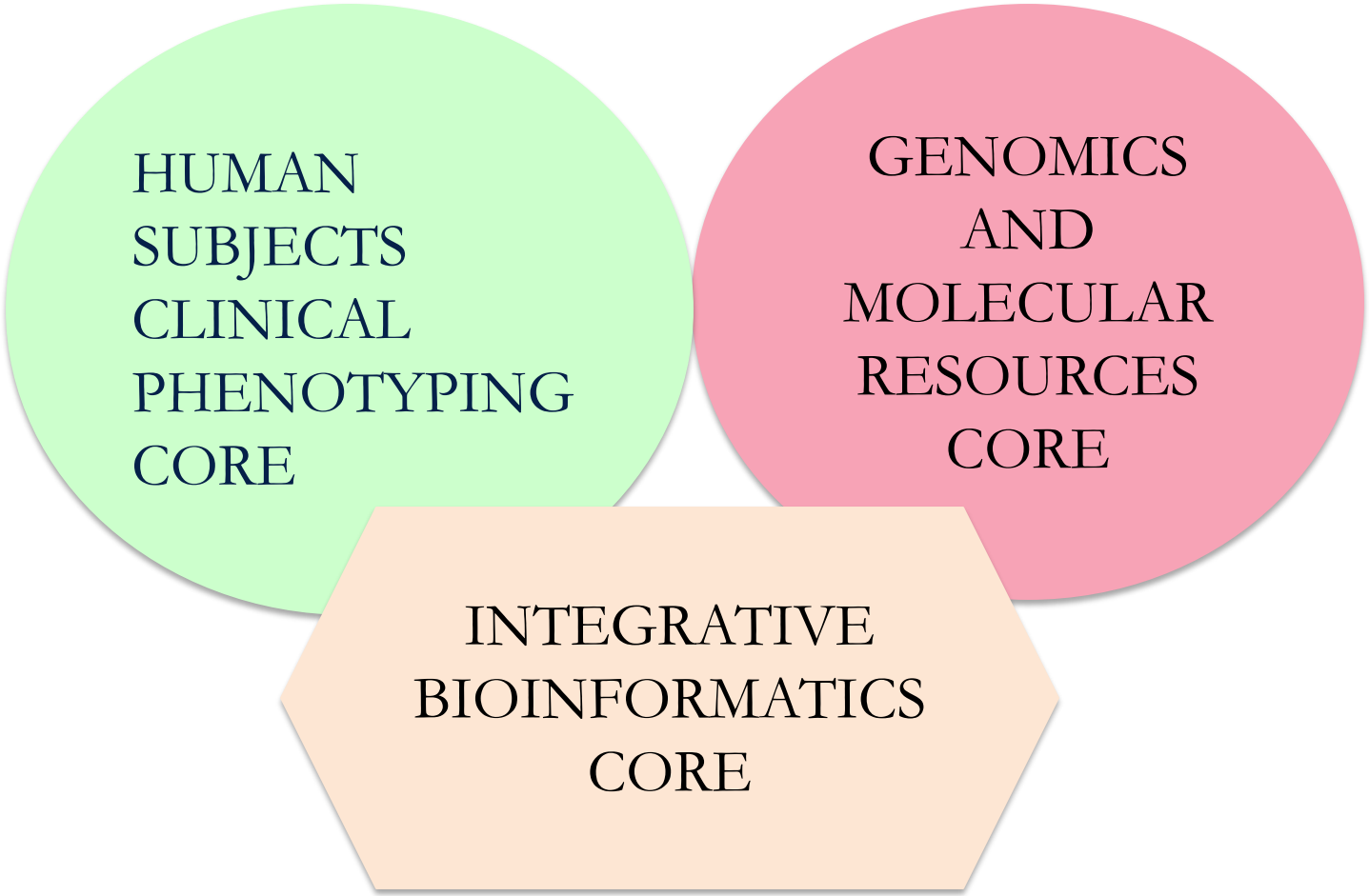
PREMIER Precision Medicine in Rheumatology



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Human Research Protections Program

From bench to bedside: Partnering with the IRB

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Today's Topics

- Brief history of Institutional Review Boards
- Do you need IRB review?
- What level of Review?
- What does the IRB look for?
- Submission process
  - Common errors
- Bench ⟶ Bedside considerations

Where it began…

- Before WWII, there were no specific laws, regulations, or codes governing research on humans.
- Historical abuses of human research participants prompted the development of ethical codes and guidelines.

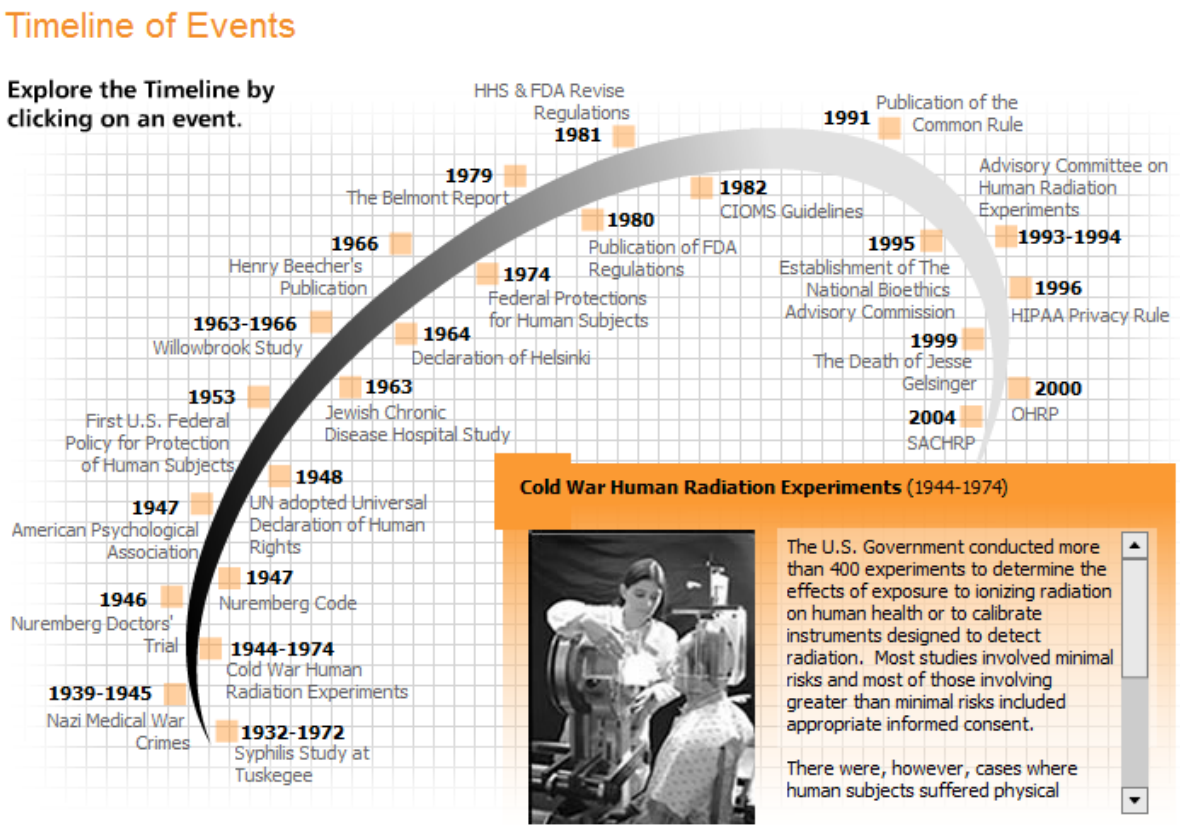
Examples

- Nazi Medical Experiments (1939-1945)
- Cold War Radiation Experiments (1944-1974)
- Tuskegee Syphilis Study (1932-1972), US Public Health Service.
- Willowbrook Hepatitis Study (1963-1966)

Historical Foundations of Research Regulation

Recommended Resource: NIH Timeline of Events

https://phrp.nihtraining.com/history/07_history.php



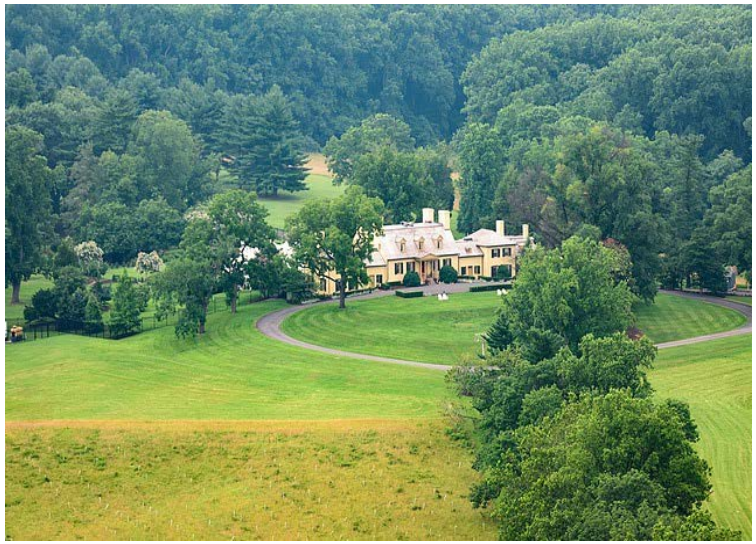
Milestones in Protections

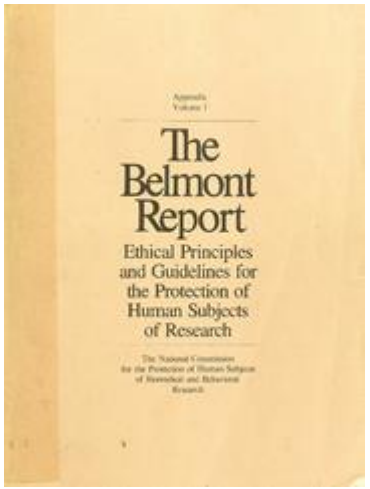
- 1947-Nuremburg Code
- 1966- Policies for the Protection of Human Subjects
- 1971- Establishment of UCSF IRB
- 1974- National Research Act- Formation of the Commission
- 1979- Belmont report

Belmont Report, 1979

Three ethical principles that govern research on human subjects:

- Respect for persons (autonomy)
- Beneficence
- Justice





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Do I need IRB review?

The saddest words:
"But I was only…"

- looking at patient records
- using tissue that would be thrown away
- working with my own patients
- using an FDA-approved drug/device
- asking a few questions

Risks of Inadequate IRB review

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Is your project human subjects research?

- Research =
  - A systematic investigation
  - Designed to develop or contribute to generalizable knowledge

- Human Subject = Living individual about whom an investigator conducting research obtains
  - Data through intervention or interaction with the individual, **or**
  - Identifiable private information

Examples of Activities That Do Not Require IRB Approval

- If the Investigator obtains de-identified or coded data or biological samples under the following conditions
  - A PI gets de-identified specimens from a UCSF tissue bank that has approval for the collection and dissemination of the tissue.
  - A PI analyzes coded data from Johns Hopkins. The PI never sees identifiable information, such as name, date of birth, or medical record #.

Points to Consider

Consider whether the investigators receive <u>any</u> identifiers or can break the code, <u>even theoretically.</u>

CALL IRB IF YOU'RE UNSURE!

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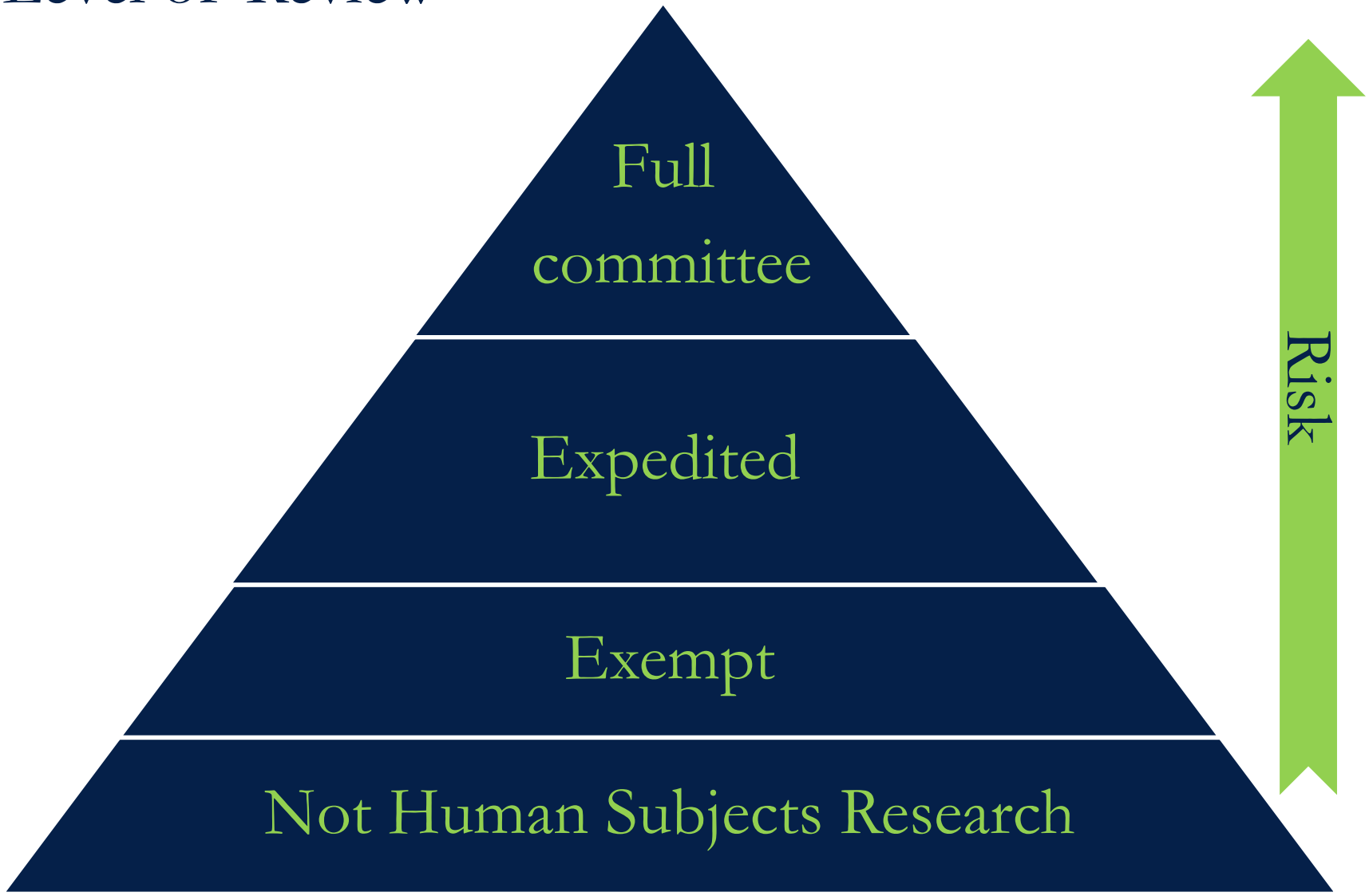
What kind of review?

Level of Review



Exempt Certification

Involves human subjects, but IRB *approval* is not required.

- IRB must *review* the application and *certify* that the project qualifies for the exemption.
- Exempt research must
  - Be minimal risk and
  - Fit into one of several federal categories

Example of Exempt Research

- Use of existing data or specimens
  - Publicly available or
  - Not identifiable

Education

Anonymous surveys

Taste tests

Exempt Application Process

- Click “Exempt” bubble
- Truncated Application
- Approval time of 1-2 weeks
- No Continuing Review required

Expedited Review

Research that

- presents no more than minimal risk to the subjects ***and***
- fits into one of the federal expedited review categories.

Note: Expedited = minimal risk

Expedited ≠ fast (sometimes)

Expedited Review Categories

- Category 1 - Studies of approved drugs being used for their approved indications
- Category 2 – Blood sampling*:* specified volumes and time period
- Category 3 – Non-invasive specimen collection (cheek swabs, urine or hair samples)
- Category 4 – Non-invasive clinical procedure (MRI, EKG, ultrasound, moderate exercise testing – NOT X-ray)
- Category 5 – Use of data/specimens collected for non-research or research purposes (includes medical record reviews)

Full Committee Review

- Required for studies that
  - May present greater than minimal risk to subjects or
  - Are minimal risk, but do not fit in an expedited review category

Examples:

- Studies using investigational drugs or devices
- Radiation exposure
- Behavioral studies involving risky interventions, observations of illegal behavior, or very sensitive data/questions

Resources

- HRPP Website
- Office of Research Integrity: The Research Clinic
  https://ori.hhs.gov/the-research-clinic
- OHRP on YouTube-
  https://www.youtube.com/view_play_list?p=5965CB14C2506914
- iRIS training https://iris-help.ucsf.edu/irb-iris
- Clinical Research Resource Hub https://hub.ucsf.edu/
- CITI Training: https://about.citiprogram.org/en/homepage/

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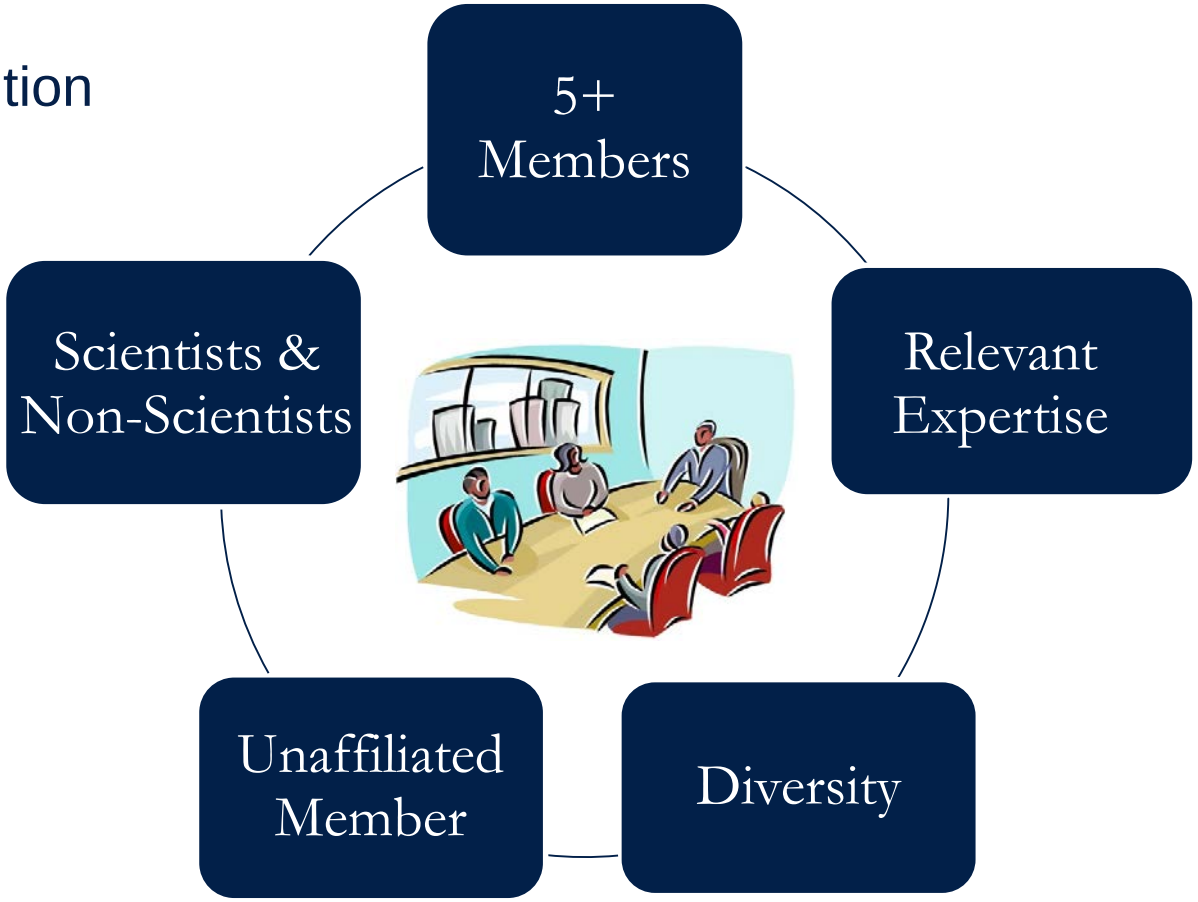
What do IRBs do?

Mandate of the IRB

Provide independent ethical review of all research involving human subjects performed by UCSF faculty, staff and students regardless of funding and location

Institutional Review Board (IRB)

Composition



- UCSF has **four** IRBs panels that meet on a bimonthly basis
- Approximately 6,600 research studies are open at UCSF

What do IRBs talk about?

- **Risks to subjects are minimized (Beneficence)**
  - Procedures consistent with sound research design
  - Do not unnecessarily expose subjects to risk
- **Risk/benefit ratio**
- **Equitable subject selection and fair recruitment (Justice)**
- **Consent sought and documented appropriately (Autonomy/Respect)**
- **Protection of privacy and confidentiality**
- **Extra protections for vulnerable populations**

IRB Actions

- Approved as submitted
- Stipulations that must be met
- Suggestions
- Denial of approval

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Submitting to the IRB

Approval Process:

Submit in iRIS →  → Approved!

Review Process

Study team submits the study

↓

IRB administrative pre-review screening ⟷ Stipulations

↓

Review by Committee, Chair, or IRB member

↓

Post-review correspondence ⟷ Stipulations

↓

This process takes time, so plan accordingly!

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Top IRB Submission Tips

Tip #1:
Complete Human Subjects Protection Training

- Key Study Personnel need to take UCSF's human subjects training through the CITI Program (https://about.citiprogram.org/en/homepage/)

- Key Study Personnel = individuals who contribute in a substantive way to the execution and monitoring of the study, including individuals who obtain consent

Tip #2 – Submit a Complete Packet

- Study protocol
- Human Subjects Section of grant, if applicable
- Investigator Brochure, if applicable
- Consent forms in UCSF format

Tip #3 Submit a thoughtful application

- Formulate careful responses to all questions – don't overlook providing a discussion of risk, privacy and confidentiality, even if just doing interviews
- Provide a thorough discussion of the background and goal of study
- Clearly spell out the procedures in a way they can be reproduced

Tip #4:

- Procedures in application must match the protocol
- All documents (consent forms, questionnaires, ads) and sections of the application should be internally consistent
- Check the purpose, significance, procedures, benefits and alternatives in both the application and consent form
- Define groups with clear labels and use consistent terminology throughout

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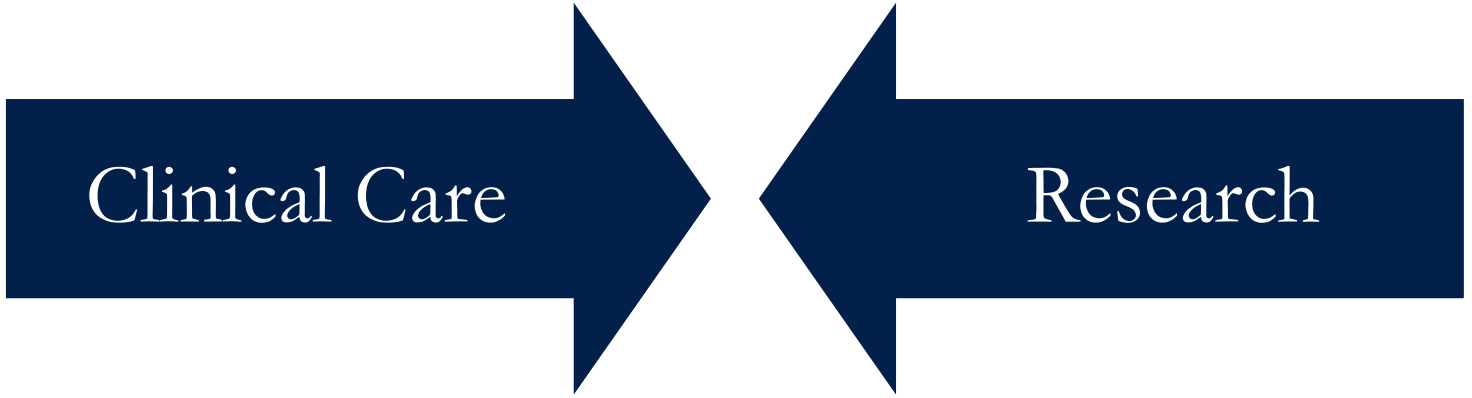
Tip #5:
Explain What Is Research v. Clinical Care



- Need to know what the participant would be doing if **not** in the research study
- **One of must common reasons for a return and delay of approval**

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Tip #6: Ask for assistance

- Use ‘Help’ buttons on Application
- HRPP Website
- Call or email the IRB and ask for the Analyst of the Day
- Main IRB Line: 415-476-1814
- Main IRB Email: IRB@ucsf.edu

- The HUB: http://hub.ucsf.edu – lots of research resources for investigators and study staff

Other Resources

- **Research Ethics:** Office of Research Integrity: The Research Clinic https://ori.hhs.gov/the-research-clinic
- **Consenting:** OHRP on YouTube- https://www.youtube.com/view_play_list?p=5965CB14C2506914
- **Tools, Templates, Guidance:** Research Resource Hub: https://hub.ucsf.edu/

iRIS training https://iris-help.ucsf.edu/irb-iris

Initial Application: "Review Ready"

- All attachments
  - Non-standardized questionnaires
  - Recruitment materials
  - All consent documents
  - Scientific protocol
  - NIH grant
- All questions answered
- Answers are
  - clear
  - on point
  - consistent: internally and externally

Recruitment Guidance

In-house: PREMIER Cores

HRPP Website

CTSI Participant Recruitment Program

Consent Guidance

- Templates
- Instructional videos
- Watch someone- apprenticeship
- Don’t oversell benefits

Privacy Guidance

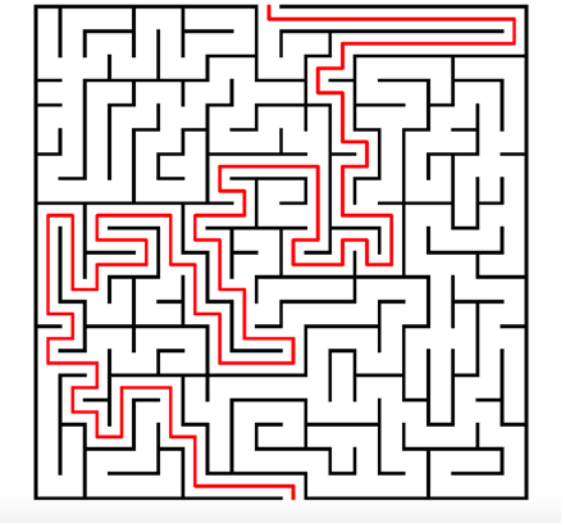
- PREMIER Cores for data and specimen storage
- IT Security
- Genomic Data Sharing on HRPP website
- Privacy Office: HIPAA Authorization

In closing

Understanding the regulatory landscape is challenging

The IRB can guide through the process

Partners in discovery



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For more information go to:

http://premier.ucsf.edu