Education & Training

Post Approval Monitoring

UCSF
Human Research
Protection Program

IRB Review Process

UCSF
University of California
San Francisco

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Human Research Protection Program Training

Preparing a New CHR Application

UCSF
University of California
San Francisco

Outline for Today

- **When to submit to CHR**

- **How to complete the CHR Application**
  - Considerations for Different Types of Research

- **What attachments to submit**

- **Demystifying the CHR review process**

- **Tips for speeding up CHR approval**

- **Getting answers after this class**

**Human
Research
Protection
Program**

Mandate of the CHR

- **Review and make decisions on all research involving human subjects performed by UCSF faculty, staff and students regardless of funding and location**

    - Over 5,700 active studies at UCSF!

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Step 1: Are you conducting research?

Research = A systematic investigation that

- Involves development, testing and evaluation
- Designed to develop or contribute to generalizable knowledge

Step 2: Does your research involve human subjects?

Human Subject = Living individual about whom an investigator conducting research obtains

– Data through intervention or interaction with the individual, or

– Identifiable private information

Not Human Subjects Research

- **PI obtains <u>de-identified</u> or <u>coded</u> data or biological samples under these conditions:**

    1. The research is not regulated by the FDA; and
    2. The researcher <u>never obtains identifiable information</u>.

- **Example: You analyze coded data from Johns Hopkins. You never see identifiable information, such as name or date of birth.**

- **Confirm using the Self-Certification Form**

CHR Levels of Review/Applications

- *Greater Than Minimal Risk:*
  - Full Committee

- *Minimal Risk:*
  - Expedited Review (7 review categories)
  - Exempt Certification (4 review categories)

- *Not Human Subjects:*
  - Self-Certification Form

- **See the "<u>Determining the Level of CHR Review</u>" handout for categories and examples**

Step 2: What level of review is needed?

- **<u>Risk</u> to the subject determines the level of review required and the type of application**

- **"Minimal risk" =** The probability and magnitude of harm or discomfort you think the subject will experience in the research is not greater than the harm or discomfort the subject would normally encounter in

  - daily life or

 - during *routine* physical or psychological examination or tests.

Step 3: Filling Out the Application

- **Submit via iRIS, the CHR's online submission and review system**

- **iRIS also used by:**

  - Research Management Services (RMS)

    -eProposal

  - Human Gamete, Embryo, and Stem Cell Research (GESCR) Committee

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Filling Out the Application

- **Once you are logged in to iRIS: Click "Add a New Study" button**

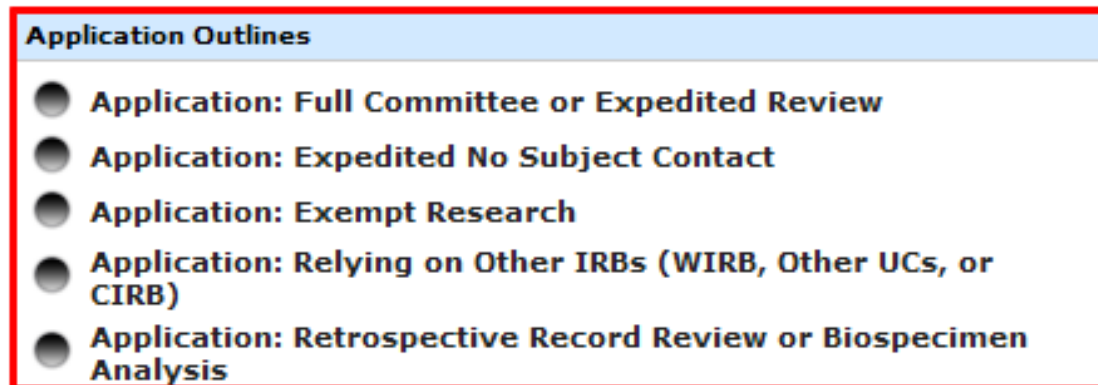- **The electronic CHR Application will build based on how you answer key questions**

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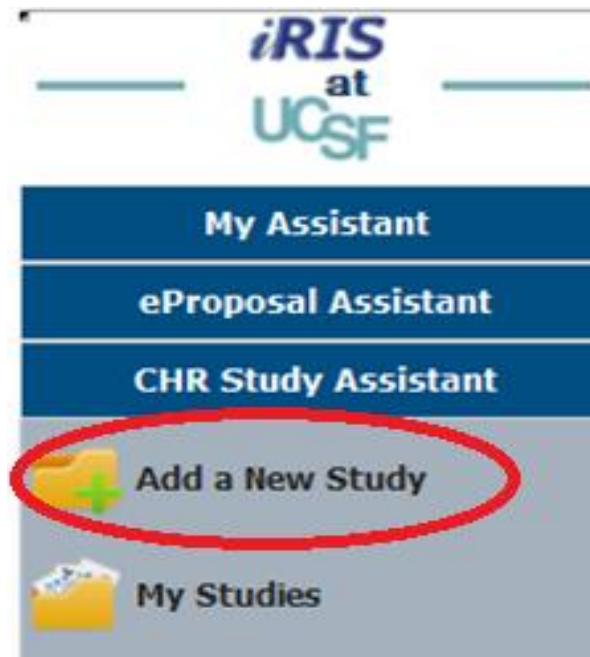
Filling Out the Application

- **For technical help, look at the quick guides in iRIS "Help" section**

- **Application outlines in iRIS "Help" menu can be helpful**

Application Sections: Assign Key Study Personnel (KSP) Access to the Study

- **Add PI, Other Investigators, Research Support Staff, and Study Contacts from UCSF or affiliate institutions (e.g. the SFVAMC, Gladstone, BSRI)**

- **Do not list unaffiliated collaborators *unless* they need iRIS access.**

Roles and Qualifications of Key Study Personnel

- **Only list for KSP – people who have a substantial role in the design and conduct of the study, including obtaining informed consent**

- **Sample for Study Investigator:**

  - **Role:** Assists with recruiting, consenting, tracking and follow-up of participants, and collecting study data through interviews and lab measurements.

  - **Qualifications**: Jane Researcher, MD, PhD, is an Assistant Professor in the department of Laboratory Medicine. She has worked in this field of research for 5 years and has been involved in several projects like this one, including XX.

These individuals need human subjects training through CITI.

Application Sections:

- **Screening Questions**
  - Risk level?
  - Exempt, expedited, or full committee review?
  - Subject contact?
  - Funding?
  - Retrospective chart review?
  - Study Drugs/Devices?
  - Clinical Trial?
  - Stem Cell Research?
  - Relying on another IRB?

Application Sections: Funding

- **If funds are coming through UCSF, must have RAS Award or Proposal #.**

  - ➢ **Check with your financial administrator if you do not know funding details.**

- **When adding an *external sponsor*, if you can't find the sponsor name call our office for help.**

Study Sites (Affiliated and Outside Sites)

- **Check UCSF and any affiliate sites**

- **Are you *collaborating* with an unaffiliated institution?**
  - If yes, complete an **Outside Site Information Subform** for <u>each</u> site.

- **All sites for a *multicenter* study don't need to be listed, only the lead site/coordinating center.**

Study Design, Scientific Considerations, and Background

Why are you doing the research? What is the scientific validity of your study?

- **Design =** overall scientific design; do not list step-by-step procedures here

- **Hypotheses =** supposition or assumption for the study

- **Specific Aims =** specific study goals

- **Statistical Analysis =** types of analysis that will be applied

- **Background =** brief sketch of scientific background leading to the present study

- **Preliminary Studies =** Has anyone done research like this before? What were the results?

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Sample Size and Eligibility

- **Sample Size**

  - Number of subjects at UCSF (and affiliates)

  - Total number of subjects (including other research sites, if any)

  - Explain how the numbers were determined

- **Inclusion/Exclusion Criteria**

  - Be specific

  - Include all criteria for eligibility

Drugs and Device Details

- **List all drugs and devices that are being _studied_**

  - Includes approved drugs/devices under investigation

- **IND or IDE #**

  - Final approval can't be granted until you provide this # to CHR

- **Verification of IND / IDE #**

  - Listed on the sponsor's protocol   OR

  - Attach documentation from sponsor or FDA identifying the IND / IDE # for this study

Other Approvals and Registrations

- **Study taking place on patient care units?**

  - letter of support needed (some exceptions)

- **Radiation exposure?**

- **GWAS?**

- **Gene transfer?**

- **Approval needed from other regulatory committees?**

  - **Institutional Biological Safety (IBC)**

  - **Animal Care and Use (IACUC)**

  - **Radiation Safety (RSC)**

  - **Radioactive Drug Research (RDRC)**

  - **Controlled Substances (EHS)**

Procedures (Subject Contact)

- **What are subjects being asked to do for the purpose of the research study?**

  - Research vs. standard of care?

  - Write in a way that can be replicated and understood by someone not in your field.

  - Graphs or tables may be helpful (attach as study documents)

  - Generally, do not copy and paste from consent form – CHR members need details that subjects may not need.

	Week 1	Week 4	Week 8
Interview and Questionnaires	X	X	X
Blood Draw	X		X
Physical Exam	X		

Procedures (No Subject Contact)

- **Where are you getting the data and/or specimens? Did the source have IRB approval?**

- **Did subjects consent to have their data or samples used for research? If no, why not?**

- **What data do you want to abstract?**

- **What are the dates for the data you want to include?**

Alternatives

- **Is the study treatment available outside of the study?**

- **What is the standard of care where the research is being done?**

  - Is standard of care given as part of the research?

  - NOT acceptable to state that subjects who do not participate will receive "quality care."

- **What are other alternatives (e.g. any experimental treatments)?**

  - If the only alterative is to not participate, state this.

Risks and Benefits

- **Description of risks**
  - Physical risks, emotional risks, confidentiality risks
  - For greater than minimal risk studies, classify risks by likelihood and/or percentages – e.g. "Most Likely" or 25% of subjects

- **How will you minimize risks?**

- **Benefits to subjects and society**
  - Clearly state if no benefit to subjects
  - Payment and research procedures are <u>NOT</u> a benefit

- **Risk/benefit assessment**

BENEFIT

RISK

Data and Safety Monitoring

- **Greater-than-minimal risk, interventional studies need a data and safety monitoring <u>plan</u> to monitor the conduct and progress of the study to:**

  - Identify info that may affect the subjects' safety or welfare and act upon this info in a timely fashion, and

  - Review the validity and integrity of the data.

  - See *"DSMP Information Sheet"* handout

- **Data and Safety Monitoring Board or Committee**

  - Formal, <u>independent</u> committee that periodically reviews the study to assure safety, efficacy, relevance of the study intervention and data integrity.

  - Generally required for Phase III studies or high-risk/ multicenter, randomized Phase II studies

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Confidentiality and Privacy

- **Confidentiality = Data**

  - How are you collecting the data, what identifiers (PHI) will you collect, and how will you keep the data safe?

  - Will identifiable data be disclosed to anyone?

  - Encrypt portable devices that keep PHI

- **Privacy = Individuals**

  - Is there a private area to interview participants?

  - What are possible consequences to loss of privacy?

Subjects

- **Vulnerable Populations?**

  - Children   -Neonates

  - Pregnant Women or Fetuses   -Non-English Speakers

  - Cognitively Impaired or Incapacitated

  > Carefully look over consent requirements and regulatory or legal issues

- **Other Subjects Who *Might* Need Additional Protection**

  - Students or Staff, Economically Disadvantaged

- **Explain *why* you are enrolling these groups, how you'll protect their rights, and minimize coercion**

Recruitment

- **How, when, where, and by whom are potential subjects approached?**

  - Respect for privacy

  - Lack of pressure, unbiased presentation

  - Describe all methods for all subject populations

- **When possible, prospective research subjects should be contacted by people directly involved in their care, not by unknown researchers**

Waiver of Consent/Authorization for Recruitment Purposes

- **If PHI will be accessed before consent (e.g. charts will be screened), this section will appear.**

  - Explain why you need to access to PHI before obtaining consent

  - What will you do with info if subjects do not want to participate?

- **If satisfactory, CHR can waive HIPAA authorization and consent for recruitment purposes only.**

Consent

- **Signed consent**

  - Consent forms, parental consent forms, assent forms

  - Required for greater than minimal risk research

- **Waiver of signed consent**

  - Electronic consent, information sheets and/or verbal consent; allowed for some minimal risk research

- **Waiver of consent**

  - Must meet federal criteria: Minimal risk, impracticable, give subjects info after (if applicable), won't affect subjects' rights

Consent (con't)

- **How, where, when, and by whom will informed consent be obtained?**

- **How will researchers make sure potential subjects understand the study?**

- **Exempt Research**

  - Consent regulations do not apply, but UCSF requires some form of basic information sheet if interacting with subjects

  - Use templates from the HRPP website

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Financial Considerations

- **Will subjects be paid to participate?**

    - How will they be paid? Debit Card? Check? Cash? Gift Card?

    - Is the amount coercive?

    - What is the payment schedule? Will payments be prorated fairly?

- **Will subjects have to pay for any costs associated with the study?**

    - Generally, subjects should not be asked to pay for any experimental aspects of the study.

Initial Review Submission Packet

- **Provide contact information**

- **Include a lay summary**

- **Any special processing instructions?**

- **Attachments:** See "Submission Checklist" for complete list

  - Consent forms (see next slide for tips)

  - Recruitment and advertisement materials

  - Survey instruments/questionnaires

  - Sponsor's protocol

  - Investigator's brochure

  - Federal grant describing human subjects work

  - Graphs/charts (paste into a Word doc)

- **PI must sign off on study submission!**

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Consent Documents

- **Submit all consent/assent forms, verbal scripts, info sheets, etc.**

  - Use current UCSF consent form templates
    http://www.research.ucsf.edu/chr/Recruit/chrCFformats.asp

  - Remove instructional text from templates

  - No track changes!

- **Do not use language that is too technical**

  - Shorter sentences are easier to read

  - Graphs/charts can be helpful

  - Have someone else read your consent form

- **Keep 1.25" margin at top of each page for stamp**

Other Consent-Related Documents

- **If you are accessing or creating health info, subjects must sign a HIPAA authorization for research**

  - Do not submit to CHR (except for VA studies)

  - Review regulatory determinations on study approval letter

- **For biomedical studies, give subjects a copy of the Experimental Subject's Bill of Rights**

  - Do not submit to CHR

  - Translations found on HRPP website at
    http://www.research.ucsf.edu/chr/Recruit/chrRC.asp#Experimental

Step 4: The Review Process

➢ **Initial screening / pre-review stipulations**

CHR Analyst

Researcher

➢ **Review by CHR committee, CHR member(s) and/or Chair**

➢ **Post-review stipulations (if necessary)**

CHR Analyst

Researcher

➢ **APPROVAL!**☺

What happens during pre-review screening?

Is the submission complete?

- **CHR Application**
  - Have all necessary questions been answered fully?
  - Is the information consistent?

- **Consent and Assent Forms**
  - In UCSF format? Consistent with the CHR Application? In lay language?
  - Consent form for each subject group, when applicable?

- **Other Attachments**
  - Are all necessary attachments included?
  - Are recruitment materials coercive or incomplete?

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What do CHR members consider when reviewing a new study?

- **Risks to subjects are minimized**

    - Procedures are consistent with sound research design and do not unnecessarily expose subjects to risk

    - Study utilizes procedures already performed for diagnosis/treatment, whenever appropriate

- *"Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects and the importance of the knowledge that may reasonably be expected to result" – from DHHS regulations.*

- **Selection of subjects is equitable**

    - Inclusion/exclusion criteria are adequate

    - Research purpose and setting is appropriate

    - Recruitment process is fair

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What do CHR members consider when reviewing a new study? (cont.)

- **The research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects, when appropriate.**

- **Provisions to protect the privacy of subjects and to maintain the confidentiality of data are adequate.**

- **When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects.**

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Speeding Up Your CHR Approval: Top Tip #1

- **Determine the required level of review, or if review is even required**

- **Make sure the science is sound**

  - Interventional clinical trials require scientific and feasibility review before submitting to the CHR

- **Consider the audience when writing application**

  - Write application with understanding that not all CHR members are scientists, and few if any are experts in your field

  - Avoid acronyms, if possible. If needed, spell out before first use.

Top Tip #2

- **Strive for consistency within and among the various parts of the submission:**

  - Are CHR Application sections consistent with each other? (i.e., the purpose, benefits and subjects)

  - Are consent form sections clear and consistent?

  - Is the Application consistent with the sponsor's protocol and consent forms?

  - Use the same name for the subject groups and study activities throughout the application and consent documents.

- **Do not copy and paste from the sponsor's protocol without making revisions to suit the CHR version of the study.**

Top Tip #3

- **Provide a detailed discussion of the recruitment and consent process. Include the who, what, when, where, and how of each.**

- **Submit copies of all recruitment materials, including scripts, ads, and letters.**

Top Tip #4

- **Include "Special Processing Instructions" in the Initial Review Submission Packet to explain:**

  - Any particularly difficult or sensitive issues to show that you have thought them though ahead of time, or ask for CHR input

  - Special time constraints i.e., if study is being sent in "just in time" for NIH funding or you have a subject waiting.

  - If the study should be routed to a specific panel or analyst.

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Top Tip #5

- **Do a final review of CHR Application and study documents.**

- **If you are not the study PI, ask the PI to re-read the application before signoff.**

  - Important if the PI is your mentor.

- ***Bonus Tip*: Get a separate CHR approval for each discrete study. Do not group related studies into a complicated application.**

  - This can delay the review process and lead to multiple stipulation rounds

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Questions?

- **Contact the CHR Office and ask the Analyst of the Day**
  - Phone: 415-476-1814
  - E-mail: chr@ucsf.edu

- **Check our website for guidance and application tips:**
  www.research.ucsf.edu/CHR

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More Resources

- **UCSF Research Resource HUB**
  - Single portal resources, expertise, and best practices
  - http://hub.ucsf.edu/

- **UCSF CTSI's Consultation Services**
  - Consults in Biostatistics, Design, Ethics, Data Management, and Regulatory Knowledge
  - http://ctsi.ucsf.edu/about-us/programs/consultation-services
  - Contact ctsi.consulting@ucsf.edu or 415-514-8086
  - **Note:** Recharge rates may apply for these services

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