Human Subjects Researchers/Staff: Prepare to be Interviewed! for AAHRPP Site Visit

As an Investigator/Researcher, you are an integral part of the Human Subject Protection Program (HSPP) at USC. USC is preparing for re-accreditation of its HSPP. Achieving accreditation publicly affirms USC as a top-tier academic institution in its ethical and regulatory conduct of human subjects research.

USC’s HSPP accreditation largely depends on these interviews. You will be expected to:

- Know your role(s) in the Human Subjects Protection Program (HSPP) and the roles of the HSPP (e.g. IRBs, OPRS, Office of Compliance)
- Know where to obtain answers to ethical/regulatory questions about conducting research duties (e.g. IRB Chair/Director/staff/members, , human subjects policies and procedures, HSPP website: oprs.usc.edu)
- Know how to access HSPP Policies and Procedures: oprs.usc.edu/rules
- Know how to report non-compliance, adverse events, unanticipated events, etc.
- Know how to maintain compliant research records and documentation, and be able to explain your research submission and rationale
- Know the regulatory standards that pertain to your research/discipline (e.g. OHRP, FDA, regulations for experimental drugs or devices)
- Know the ethical aspects and regulatory details applicable to research: what you are reviewing/performing is sound, purposeful, and has value
- Understand what constitutes a conflict of interest at all levels (e.g. staff, IRB, institution, administration)
- Familiarize yourself with the terminology contained in the iStar: https://oprs.usc.edu/review/istar/glossary/
- Describe the Human Subjects Education you’ve had: HSR, GCP, HIPAA training
- Know how to recruit subjects ethically and justly while adhering to inclusion/exclusion criteria

To obtain accreditation, all interviews must be successful. These materials and OPRS staff are available to help you succeed. The following guidance is intended to prepare you for the interview.

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1. What is AAHRPP accreditation and why is it important to USC?

AAHRPP accreditation is a gold standard recognizing adherence to a rigorous set of human subjects protection standards that surpass state and federal requirements. The accreditation process involves an evaluation of the USC Human Subjects Protection Program (HSPP) and a site visit focused on interviews with critical members of the HSPP, including IRB members. Accreditation largely depends on these interviews which involve tough questions about research policies, process, and training.

2. What are the components of the USC Human Subjects Protection Program (HSPP)?

The USC Human Subjects Protection Program (HSPP) is a team effort. It includes all the University Park and Health Sciences IRB staff, directors, chairs, vice chairs, members, as well as Office of Compliance officials, Office for the Protection of Research Subjects members and the Vice President of Research. IRB staff and reviewers are responsible for review and administration of IRB issues. OPRS is responsible for policy, education and outreach efforts. The Office of Compliance serves as a legal and ethical resource for OPRS and the IRBs.

3. What does the IRB do?

There are four Institutional Review Boards at USC (one at University Park Campus, and three at the Health Sciences Campus). The main mission of the Institutional Review Boards at USC is to protect the rights, safety and welfare of research subjects. The IRBs review and approve research in accordance with Department of Health and Human Services (HHS) regulations in 45 CFR 46. For studies involving products regulated by the Food and Drug Administration (FDA), the IRBs review research according to the requirements in 21 CFR 50, 21 CFR 56, 21 CFR 312, 21 CFR 812. The IRBs also comply with HIPAA and the regulations in 45 CFR 160 and 164.

4. What education have you taken to be qualified to complete a human subjects project?

The answer is person-specific but can include CITI Human Subjects Protection course, Good Clinical Practices, Responsible Conduct of Research, and HIPAA training if applicable. All individuals involved in or supervising human subjects research projects at USC must be licensed, certified, or possess a degree appropriate for their field.

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5. Do you know the kinds and levels of risk?

Risks can be categorized as physical, psychological, sociological, economic, and legal. Risks to subjects must be reasonable in relation to anticipated benefits, if any, to subjects and to the importance of knowledge that may reasonably be expected to result from the research.

- **Greater than Minimal Risk:** The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- **Minimal risk:** The probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. An example of minimal risk is the risk of drawing a small amount of blood from a healthy individual for research purposes (because the risk of doing so is no greater than the risk of doing so as part of a routine physical examination).

6. Who should you contact for help with regulatory or ethical issues?

The first point of contact is normally the IRB and/or the Office for the Protection of Research Subjects. Additional follow-up may be necessary with the Office of Compliance, USC General Counsel, the FDA, or the Health and Human Services Office for Human Research Protections (OHRP).

7. What is the difference between privacy and confidentiality?

- **Privacy is related to setting:** it relates to control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.
- **Confidentiality is related to information/data:** it pertains to the steps taken to protect an individual’s personal information (limited access, password-protection) including the assurances made to a subject in the consent form that his/her information will not be divulged to unauthorized personnel without their permission.
- The IRB must decide on a case-by-case (e.g. study by study) basis whether there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. The IRB must take into account the degree of sensitivity of the information that may be obtained in the research and the protections offered the study and study population. As with other aspects of IRB review, these determinations will be dependent on the circumstances of the study and subjects.
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IRB review of privacy and confidentiality protections is required under the Common Rule and the FDA regulations as well as state and local statutes. Protocols submitted to the IRB must include mechanisms to protect subject privacy and confidentiality. The IRB will review what is promised to subjects on informed consents, what protections are in place during recruitment and follow-up, and what methods will be employed to protect data and samples. Sponsor access and any legally authorized access to subject information must be described in the consent form. Subjects should be informed whether the data collected will be retained, and if so, for what purpose, what period of time, or whether and when data will be de-identified and destroyed. Studies that obtain particularly sensitive information (e.g. HIV status, drug abuse) may be required to obtain an NIH Certificate of Confidentiality.

8. What is the “process” of consent? Do you know how to properly obtain consent?

Obtaining informed consent is a basic ethical obligation for researchers. The process of consent should ensure that potential subjects are provided with information about the study in a way that is understandable to them (written in “lay language” and in the subject’s language) allowing them to make an informed and voluntary decision about participation. The amount of information and the manner of presentation can vary depending on the complexity and risk involved in the study. The consent form serves to document that the subject agreed to participate in the study and also serves for the subject’s future reference.

Subjects should sign the consent form after the investigator has verbally explained the purpose and procedures involved in the study, answered questions, and provided information that permits the subject to make an informed decision. The consent form must be signed before any study data collection procedures begin. The consent process should be an ongoing educational interaction between the investigator and the research subject that is ongoing throughout the study.

Only legally competent adults can give legally effective informed consent. Minors and those individuals who are not competent to provide consent should be given the opportunity to assent to participate in the research project. Assent is an affirmative, knowledgeable agreement to participate in the project. Adequate provisions should be made for soliciting the independent, non-coerced assent from minors or cognitively-impaired persons who are capable of a knowledgeable agreement. In general, the IRB recommends that children ages seven and older, and most cognitively-impaired adults, be given the opportunity to assent. In cases where assent is obtained from a minor or cognitively-impaired subject,
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permission must also be obtained from an authorized representative. In studies involving minors, the authorized representative may be:

- a parent
- court-appointed guardian
- the court

9. What is ethical research?

- Research must have sound design and not unnecessarily expose subjects to risk (45 CFR 46.111)
- It is unethical to put subjects at risk or even to inconvenience them in a flawed study.
- Research should advance scientific understanding and promote human welfare.

10. What are expedited and exempted categories? When are they used?

The categories of exempt and expedited are mutually exclusive. If the study is minimal risk, the designated reviewer considers whether the research falls into an exempt category. If the research does not meet criteria for one of the exempt categories, then the expedited review categories are considered.

Exempt Review

Only the IRB may determine which activities qualify for an exempt review. Investigators do not have the authority to make an independent determination that research involving human subjects is exempt.

Research may be granted exempt status by the IRB if all research activities involve procedures listed in one or more of the specific categories under 45 CFR 46.101(b).

NOTE: The exempt categories do not apply to research involving prisoners and categories 1-5 do not apply to FDA regulated research.

- Exempt categories:
  i. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as classroom management methods.
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ii. Research involving the use of educational tests (cognitive, diagnostic,
aptitude, achievement), survey procedures, interview procedures or
observation of public behavior, unless subjects can be identified, directly or
through identifiers linked to the subjects; and disclosure of the subjects’
responses could place the subjects at risk of criminal or civil liability or
damage to the subjects’ financial standing, employability, or reputation.

iii. Research involving the use of educational tests (cognitive, diagnostic,
aptitude, achievement), survey procedures, interview procedures, or
observation of public behavior that is not exempt under 45 CFR 46.101(b)(2) if
the subjects are elected or appointed public officials or candidates for
public office; or Federal statutes require confidentiality of the personally
identifiable information will be maintained throughout the research and
thereafter.

iv. Research involving the collection or study of existing data, documents,
records, pathological specimens, or diagnostic specimens, if these sources are
publicly available or the information is recorded by the Investigator in such
a manner that subjects cannot be identified, directly or through identifiers
linked to the subjects.

v. Research and demonstration projects, which are conducted by or subject to
the approval of Federal Department or Agency heads, and which are
designed to study, evaluate, or otherwise examine public benefit or service
programs; procedures for obtaining services or benefits under those
programs; changes in or alternatives to those programs or procedures; or
changes in methods or levels of payment for benefits or services under those
programs.

vi. Taste and food quality evaluation and consumer acceptance studies;

Expedited Review

Federal regulations allow the IRB to review certain applications on an expedited basis if they
meet specified criteria (45 CFR 46.110, 21 CFR 56.110 and 38 CFR 16.110). Expedited review
categories applies to research that involves no more than minimal risk. All expedited
protocols are reviewed by the IRB at least once per year.

NOTE: The expedited categories do not apply to research involving prisoners. Also,
expedited review procedures may not be used where identification of the subjects

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and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

- Expedited review categories:
  - i. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
    - A. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.
    - B. Research on medical devices for which an investigational device exemption application (21 CFR Part 812) is not required; or the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
  - ii. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
    - A. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
    - B. From other adults and children, when the age, weight, and health of the subjects, the collection procedure, the amount of blood to be considered. For these participants, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week. Children are defined in the federal regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted" (See 45 CFR 46.402(a)).
  - iii. Prospective collection of biological specimens for research purposes by noninvasive means. For example, hair and nail clippings in a non-disfiguring manner; mucosal and skin cells collected by buccal scrapping or swab, skin swab, or mouth washings; and/or
iv. Collection of data through noninvasive 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. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications). Examples include: physical sensors that are applied either to the surface of the body; weighing or testing sensory acuity; magnetic resonance imaging;

v. 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).

vi. Collection of data from voice, video, digital, or image recordings made for research purposes.

vii. 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.

11. What is the difference between exempt human subjects research and not-human-subjects research?

Certain activities have characteristics of research but do not meet the regulatory definition of human subjects research. Some studies fall in gray areas and it is difficult to determine if in fact they are human subjects research and require IRB review. To be considered research, a study must involve human subjects and be research. Below are the federal definitions of each.

Does the study involve Human Subjects?

To involve human subjects, the study must involve a living individual about whom an investigator conducting research **obtains data through intervention or interaction with the individual OR** the study must involve a living individual about whom an investigator conducting research **obtains identifiable private information**.

Is the activity Research?

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To be Research, the activity must be a **systematic investigation** including research, development, testing and evaluation **AND** the activity must be designed to **develop or contribute to generalizable knowledge**.

If a study does not meet both definitions, it is “not-human-subjects research” and does not require IRB review. However, this is different from exempt human subjects research. See question XX for more information about exempt research (which requires IRB review).

Examples of research that may not require IRB review include:

1. Data collection for internal departmental purpose such as “customer service” survey
2. Surveys issued by USC personnel with the intent of improving USC services and programs, as long as the privacy of subjects is protected, confidentiality of individual responses is maintained and participation is voluntary. *Note: if at a future date, an opportunity arose to contribute previously collected identifiable or coded survey data to a new project producing generalizable knowledge, application of IRB review would be required before the data could be released to the new project.*
3. Fact-collecting interviews of individuals where questions focus on things, products, or policies, rather than on people or their opinions such as canvassing librarians about inter-library loan policies or rising journal costs.
4. Course-related activities designed specifically for educational or teaching purposes, where data is collected from and about human subjects as part of a class exercise or assignment that is not intended for use outside of the classroom such as research methods exercise.
5. Searches of existing literature
6. Research involving a living individual, such as a biography, that is not generalizable beyond that individual.
7. Procedures carried out under independent contract for an external agency.
8. Research about things or expertise, rather than “about whom” (i.e. questions not about the individual providing the information).
9. Quality Improvement projects are generally not considered research unless there is a clear intent to use the data derived from the project to improve the quality of patient care or efficiency of a healthcare operation and also contribute to generalizable knowledge via publication in professional journals and/or presentation at national or regional meetings.
10. Case histories which are published and/or presented at national or regional meetings are not considered research if the case is limited to a description of the clinical features and/or outcome of up to three patients.

12. What is the Nuremberg Code? the Belmont Report? the “Common Rule”?

**Nuremberg Code**
Modern human subjects protections began with the Nuremberg Code which was developed for the Nuremberg Military Tribunal as standards by which to judge human experimentation conducted by the Nazis. The Code captures many of what are now considered basic principles governing the ethical conduct of research involving human subjects. The first provision of the Code states that “the voluntary consent of the human subject is absolutely essential”, which is the cornerstone of ethical experimentation involving human subjects.

The Nuremberg Code also discusses capacity to consent, freedom from coercion, and comprehension of the risks and benefits involved. Other provisions include: minimization of risk and harm, favorable risk/benefit ratio, qualified investigators using appropriate research designs, and freedom for the subject to withdraw at any time.

**Belmont Report**

In 1978, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research presented *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. The Report sets forth three basic ethical principles: respect for persons, beneficence, and justice. These principles are now accepted as the three quintessential requirements for the ethical conduct of research involving human subjects. The Report describes how these principles apply to the conduct of research. Specifically, the principle of *respect for persons* underlies the need to obtain informed consent; the principle of *beneficence* underlies the need to engage in a risk/benefit analysis and to minimize risks; and the principle of *justice* requires that subjects be fairly selected.

The Report also provides a distinction between “practice” and “research”:

- **practice** is described as medical or behavioral interventions to diagnose, treat, or provide therapy to particular individuals.
- **research** is described as an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge.
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The Report recognizes that “experimental” procedures do not necessarily constitute research, and that research and practice may occur simultaneously.

The “Common Rule”

In 1991, 16 federal departments and agencies adopted a common set of regulations (hence the term “Common Rule”) governing human subjects research sponsored by the federal government. The Rule is designed to create a uniform human subjects protections system for all relevant federal agencies and departments. The Rule consists of Subpart A of the Department of Health and Human Services (DHHS) regulations for the protection of human subjects. The authority and function of the IRB are defined in the Common Rule.

Additional protections for vulnerable populations have also been adopted by DHHS:

- Subpart C, “Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects”
- Subpart D, “Additional Protections for Children Involved as Subjects in Research”

13. What is OHRP, FDA, and HIPAA?

OHRP

The Office for Human Research Protections (OHRP) is the federal office overseeing the system that protects the rights, welfare, and well-being of subjects involved in research and helping to ensure that research is carried out in accordance with Department of Health and Human Services (DHHS) regulations.

FDA

The Food and Drug Administration is responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, US food supply, cosmetics, and products that emit radiation. FDA regulations for research with drugs, devices, and biologics are contained in Title 21 Parts 50 and 56 of the Code of Federal Regulations. Additional FDA regulations that are relevant to IRB review of research are Parts 312 (Investigational New Drug Application), 812 (Investigational Device Exemptions) and 860 (Medical Device Classification Procedures).
HIPAA

The Health Insurance Portability and Accountability Act (HIPAA), also known as the “Privacy Rule” (effective April 14, 2003), establishes minimum Federal standards for safeguarding the privacy of individual’s identifiable health information. The law generally prohibits health care providers such as health care practitioners, hospitals, nursing facilities and clinics from using or disclosing “protected health information” without written authorization from the individual.

14. What is a waiver of consent? What is a waiver of documentation of consent? What justifies each? How do they differ?

Waiver of Documentation of Consent

In some situations, the IRB may waive the requirement for obtaining a signed informed consent document (45 CFR 46.117(c)). Waiver of signed consent is allowed if:

- The only record linking the subject and the research would be the consent document and potential harm may result from a breach of confidentiality (the subjects would be placed at risk by documents linking them with an illegal or stigmatizing characteristic or behavior). For example, survey or interview studies that contain highly sensitive (e.g., criminal behavior, sexual behavior) questions.
- The research presents no more than minimal risk of harm to the subjects and involves no procedures for which written consent is normally required outside of the research context. For example, online surveys about topics that could not reasonably damage a participant’s reputation or employability or be otherwise stigmatizing.

In cases where the documentation requirement is waived the IRB may require the investigator to provide subjects with a written statement regarding the research (the documentation may also be referred to as an info, fact sheet or similar title).

Waiver of consent or elements of consent

Some research projects would not be possible if informed consent were required. The IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent, or may waive the requirements to obtain informed consent.
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(45 CFR 46.116(d)). The regulations state that informed consent may be waived in full or in part if the IRB determines that:

- the research involves no more than minimal risk to the subjects; and
- the waiver or alteration will not adversely affect the rights and welfare of the subjects; and
- the research could not practicably be carried out without the waiver or alteration; and
- whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Examples of types of studies in which all of the elements of consent have been waived include retrospective chart reviews. If the study can be classified as minimal risk and adequate provisions for protecting data confidentiality are in place, the IRB chair generally finds that obtaining consent is not impracticable (not possible).

Examples of types of studies in which some of the elements of consent have been waived include certain types of ethnographic research or studies that require deception. Studies involving deception require a debriefing statement that would be provided to the subjects (written and oral) at the conclusion of the study procedures.

If the investigator seeks a waiver of any or all of the elements of consent, the IRB application should justify the request by showing the research could not be conducted without the waiver.

15. Are there additional requirements for DOD-sponsored studies? NSF-sponsored research? DOE-sponsored research?

Studies funded by NSF, DOD or other non-HHS sponsor are subject to additional requirements. Consult the sponsor’s website, the project officer, or the IRB for additional information.

16. What are your research topics?

This is researcher-specific.

17. What methods do you use to protect human subjects in your research?

This is researcher-specific, should include confidentiality, consent, etc.