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Working With Other Institutions

Requirements and Types of Collaborations

Federalwide Assurance (FWA) of Compliance

What Defines Engagement in Human Subjects Research

"IRB Approval in the Context of Collaborative Research" Presentation (11/5/12) [1]

Requirements and Types of Collaborations

UCSF investigators who work with other institutions must fulfill requirements that may vary depending on the following factors:

- The role the collaborating organization plays;
- The type of regulatory infrastructure in place ? namely whether the institution has a governing Institutional Review Board (IRB) or Independent Ethics Committee (IEC); and
- The source of funding for the research. ??

Work may not begin at the new sites until the required approvals and assurances are complete.

General Requirements

IRB approval required at UCSF and often at the collaborating site

Research at collaborating institutions ?domestic and foreign ? requires review by the IRB at UCSF [2].

In addition, each institution that is conducting human subjects research [2] and is considered "engaged in the research" (per federal definition) must have its own IRB or Independent Ethics Committee approval before research can begin there. Approval is required regardless of the study's funding source. The UCSF IRB generally does not serve as the IRB [3] for non-UCSF researchers.

Reminder: The UCSF IRB serves as the IRB of record for several affiliated institutions [4], such as ZSFG (formerly SFGH), SFDPH, BSRI, SFVAMC, etc. Review the UCSF Affiliated Institutions [4] page.

Generally speaking, it does not matter which IRB approves the study first. However, research cannot begin at a site until its IRB approves the study. Approval from the lead/funding site also is required before research can begin. Ask collaborating sites if they have different requirements.

Letters of support vs. IRB approval [5]

A letter of support may be all that is needed from a site that is not engaged in minimal risk research. In such cases, UCSF investigators are responsible for all contact with participants and the additional site is simply allowing access to its clients. The letter should be signed by a responsible official at the site, granting access to the UCSF researchers. The letter must be on file before work can begin at that site. The site official should confirm that local IRB approval is not required and other local requirements are met. Contact the IRB with questions.

FWA needed if the study is federally funded/supported

For studies conducted or supported by any agency of the U.S. Department of Health and Human Services, each engaged institution also must have its own Federalwide Assurance (FWA).

Additional responsibilities for UCSF researchers who are the lead investigator, prime grant holder or serve as a coordinating center for a multi-center study

You are responsible for:?

- Obtaining UCSF IRB review for the overall project,
- Ensuring that other sites receive IRB review at their respective institutions, and
- Ensuring that relevant safety information is appropriately recorded and shared between engaged sites.

Types of Collaborations

Working with UCSF-affiliated institutions

Many UCSF investigators collaborate with researchers at UCSF-affiliated units [4]. The UCSF IRB serves as the IRB of record for these organizations, but the site may have local submission requirements [4] that must be met before the research begins (e.g. SFGH, SFDPH, SF VAMC).

Working with other U.S.-based academic institutions

Ensure that you and your collaborators meet your institution's respective IRB-review requirements. Most academic institutions within the U.S. that receive federal funding have already obtained assurance of compliance through the FWA program.

Working with U.S.-based non-academic hospitals, clinics and practices

Hospitals, clinics and practices that are not affiliated with academic medical centers may not have an IRB and or FWA program necessary for federally funded research to take place. If you are committed to working with these organizations, you may need to help find a local IRB to review the study or guide the site's pursuit of assurance of compliance through the FWA program.

Review When UCSF Can Serve as IRB of Record [3] for information on determining whether the UCSF IRB can serve as the IRB for an organization.

Working with international entities

You and/or your collaborator must obtain approval from the host country's or international site?s IRB or Independent Ethics Committee **and** from the IRB at UCSF. The IRB expects the standards for human subjects protection are no less than those that apply to U.S.-based research. Some international IRBs or ethics committees meet infrequently and/or have long review times, so plan accordingly.

If the study is federally funded, each engaged institution also must have an FWA, which the international entity may need to pursue.

More information can be found at the following sites:

- OHRP [6]'s International Compilation of Human Research Protections [6]
- ICH Good Clinical Practice (GCP) [7]
- International Conference on Harmonization (ICH) [8]
- Council for International Organizations of Medical Sciences [9]
- World Medical Association [10]
- International Association of Bioethics [11]

Additional topics to consider when conducting international research:

- Cultural differences that influence study design and the consent process.
- The rationale for conducting the study with an international population.
- A description of the host country?s ethics review and oversight mechanism for participant protection. (Note: In some countries, the review process can take a long time, so plan accordingly.)

Using Smart IRB

Use of the SMART IRB [12] platform is not yet available at UCSF. UCSF has signed the SMART IRB Agreement to enable study reliances, and is currently working to operationalize the process. An announcement will be made once the SMART IRB online platform is available to UCSF investigators.

Federalwide Assurance (FWA) of Compliance

If an institution is ***engaged*** in human subjects research that is conducted or supported by any agency of the U.S. Department of Health and Human Services (HHS), the institution must have assurance of compliance with the HHS regulations (45 CFR 46.103 [13]) for the protection of human subjects. Assurance of compliance and federal oversight are managed by OHRP under the provisions of the FWA program.

Obtaining an approved assurance from OHRP is a two-step process:

1. The IRB(s) designated under the Assurance must be registered with OHRP [14]. If not, submit the registration [15].
2. Complete the FWA application [16].

What Defines Engagement in Human Subjects Research

Current guidance from OHRP [17] defines engagement in human research by the type of research activities the institution conducts.

A. Institutions Engaged in Human Subjects Research

In general, institutions are considered engaged in an HHS-conducted or HHS-supported non-exempt human subjects research project when the involvement of their employees or agents in that project includes any of the following. If institutions are engaged in the research, they need to hold or obtain an OHRP-approved FWAs and certify IRB review and approval to HHS.

Reminder: At UCSF, IRB or Independent Ethics Committee approval is required regardless of the study's funding source.

(1) Institutions that directly receive funding from HHS (i.e. awardee institutions)

Institutions that receive an award through a grant, contract, or cooperative agreement directly from HHS for the non-exempt human subjects research (i.e. awardee institutions), even where all activities involving human subjects are carried out by employees or agents of another

institution.

(2) Employees/agents perform invasive or noninvasive research procedures

Institutions whose employees or agents intervene for research purposes with any human subjects of the research by performing invasive or noninvasive procedures.

Examples of invasive or noninvasive procedures include drawing blood; collecting buccal mucosa cells using a cotton swab; administering individual or group counseling or psychotherapy; administering drugs or other treatments; surgically implanting medical devices; utilizing physical sensors; and utilizing other measurement procedures.

[See scenarios B.(1), B.(2), and B.(3) below for limited exceptions.]

(3) Employees/agents manipulate the environment for research purposes

Institutions whose employees or agents intervene for research purposes with any human subject of the research by manipulating the environment.

Examples of manipulating the environment include controlling environmental light, sound, or temperature; presenting sensory stimuli; and orchestrating environmental events or social interactions.

[See scenarios B.(1) and B.(3) below for limited exceptions.]

(4) Employees/agents interact for research purposes with subject(s)

Institutions whose employees or agents interact for research purposes with any human subject of the research.

Examples of interacting include engaging in protocol dictated communication or interpersonal contact; asking someone to provide a specimen by voiding or spitting into a specimen container; and conducting research interviews or administering questionnaires.

[See scenarios B.(1), B.(2), B.(3), and B.(4) below for limited exceptions.]

(5) Employees/agents obtain consent

Institutions whose employees or agents obtain the informed consent of human subjects for the research.

(6) Employees/agents *obtain* identifiable private information or identifiable biological specimens for the research

Institutions whose employees or agents obtain for research purposes identifiable private information or identifiable biological specimens from any source for the research.

It is important to note that, in general, institutions whose employees or agents obtain identifiable private information or identifiable specimens for non-exempt human subjects research are considered engaged in the research, even if the institution?s employees or agents do not directly interact or intervene with human subjects. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:

(a) observing or recording private behavior;
(b) using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and
(c) using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

In general, OHRP considers private information and biospecimens to be **identifiable** if the identity of the subject is or may readily established by the investigator or linked with the information/biospecimen. 45 CFR 46.102(e)(5) and (6) (Common Rule).

B. Institutions*Not* Engaged in Human Subjects Research

Institutions would be considered **not** engaged in an HHS-conducted or -supported non-exempt human subjects research project if the involvement of their employees or agents in that project is **limited to one or more** of the following. Therefore, they would not need to hold an OHRP-approved FWA or certify IRB review and approval to HHS.

The following are scenarios describing the types of institutional involvement that would make an institution **not** engaged in human subjects research; there may be additional such scenarios:

(1) Employees/agents perform commercial or other services for investigators if **certain** conditions are met

Institutions whose employees or agents perform commercial or other services for investigators provided that **all** of the following conditions also are met:

(a) the services performed do not merit professional recognition or publication privileges;
(b) the services performed are typically performed by those institutions for non-research purposes; and
(c) the institution?s employees or agents do not administer any study intervention being tested or evaluated under the protocol.

The following are some examples, assuming the services described would not merit professional recognition or publication privileges:

- an appropriately qualified laboratory whose employees perform routine serum chemistry analyses of blood samples for investigators as a commercial service.

- a transcription company whose employees transcribe research study interviews as a commercial service.
- a hospital whose employees obtain blood through a blood draw or collect urine and provide such specimens to investigators as a service.
- a radiology clinic whose employees perform chest x-rays and send the results to investigators as a service.

(2) Employees/agents at non-research sites provide study-related medical services that would typically be performed as routine clinical monitoring and/or follow-up

Institutions (including private practices) not selected as a research site whose employees or agents provide clinical trial-related medical services that are dictated by the protocol and would typically be performed as part of routine clinical monitoring and/or follow-up of subjects enrolled at a study site by clinical trial investigators (e.g., medical history, physical examination, assessment of adverse events, blood test, chest X-ray, or CT scan) provided that **all** of the following conditions also are met:

(a) the institution?s employees or agents **do not** administer the study interventions being tested or evaluated under the protocol; (2) Institutions (including private practices) not selected as a research site whose employees or agents provide clinical trial-related medical services that are dictated by the protocol and would typically be performed as part of routine clinical monitoring and/or follow-up of subjects enrolled at a study site by clinical trial investigators (e.g., medical history, physical examination, assessment of adverse events, blood test, chest X-ray, or CT scan) provided that **all** of the following conditions also are met:

(b) the clinical trial-related medical services are typically provided by the institution for clinical purposes;
(c) the institution?s employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research; and
(d) when appropriate, investigators from an institution engaged in the research retain responsibility for:

(i) overseeing protocol-related activities; and
(ii) ensuring appropriate arrangements are made for reporting protocol-related data to investigators at an engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol.

Note: Institutions (including private practices) not initially selected as research sites whose employees or agents administer the interventions being tested or evaluated in the study?such as administering either of two chemotherapy regimens as part of an oncology clinical trial evaluating the safety and effectiveness of the two regimens?generally would be engaged in human subjects research (see scenario B.(3) below for a limited exception). If such an institution does not have an FWA, its employees or agents may be covered by the FWA of another institution that is engaged in the research through an Individual Investigator Agreement [18].

(3) Employees/agents at non-research sites administer the study intervention(s) being tested/evaluated on a one-time or short-term basis

Institutions (including private practices) not initially selected as a research site whose employees or agents administer the study interventions being tested or evaluated under the protocol limited to a one-time or short-term basis (e.g., an oncologist at the institution administers chemotherapy to a research subject as part of a clinical trial because the subject unexpectedly goes out of town, or is unexpectedly hospitalized), provided that **all** of the following conditions also are met:

(a) an investigator from an institution engaged in the research determines that it would be in the subject?s best interest to receive the study interventions being tested or evaluated under the protocol;
(b) the institution?s employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research;
(c) investigators from the institution engaged in the research retain responsibility for:

(i) overseeing protocol-related activities;
(ii) ensuring the study interventions are administered in accordance with the IRB-approved protocol; and
(iii) ensuring appropriate arrangements are made for reporting protocol-related data to investigators at the engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol;

and (d) an IRB designated on the engaged institution?s FWA is informed that study interventions being tested or evaluated under the protocol have been administered at an institution **not** selected as a research site.

(4) Employees/agents inform prospective subjects about the the research, but do not obtain consent or act as reps of the investigator

Institutions whose employees or agents:

(a) inform prospective subjects about the availability of the research;
(b) provide prospective subjects with information about the research (which may include a copy of the relevant informed consent document and other IRB approved materials) but do not obtain subjects? consent for the research or act as representatives of the investigators;
(c) provide prospective subjects with information about contacting investigators for information or enrollment; and/or
(d) seek or obtain the prospective subjects? permission for investigators to contact them.

An example of this would be a clinician who provides patients with literature about a research study at another institution, including a copy of the informed consent document, and obtains permission from the patient to provide the patient?s name and telephone number to investigators.

(5) Institutions (e.g., schools, nursing homes, businesses) permit use of their facilities for the research

Institutions (e.g., schools, nursing homes, businesses) that permit use of their facilities for

intervention or interaction with subjects by investigators from another institution.

Important Note: The UCSF investigator must provide a letter of support from the institution to the IRB.

Examples would be a school that permits investigators from another institution to conduct or distribute a research survey in the classroom; or a business that permits investigators from another institution to recruit research subjects or to draw a blood sample at the work site for research purposes.

(6) Employees/agents***release*** to investigators at another institution identifiable private information or biological specimens for the research

Institutions whose employees or agents **release** to investigators at another institution identifiable private information or identifiable biological specimens pertaining to the subjects of the research.

Note that in some cases the institution releasing identifiable private information or identifiable biological specimens may have institutional requirements that would need to be satisfied before the information or specimens may be released, and/or may need to comply with other applicable regulations or laws. In addition, if the identifiable private information or identifiable biological specimens to be released were collected for another research study covered by 45 CFR part 46, then the institution releasing such information or specimens should:

(a) ensure that the release would not violate the informed consent provided by the subjects to whom the information or biological specimens pertain (under 45 CFR 46.116 [19]), or
(b) if informed consent was waived by the IRB, ensure that the release would be consistent with the IRB?s determinations that permitted a waiver of informed consent under 45 CFR 46.116 (c) or (d) [20].

Examples of institutions that might release identifiable private information or identifiable biological specimens to investigators at another institution include:

(a) schools that release identifiable student test scores;
(b) an HHS agency that releases identifiable records about its beneficiaries; and
(c) medical centers that release identifiable human biological specimens.

Note that, in general, the institutions whose employees or agents **obtain** the identifiable private information or identifiable biological specimens from the releasing institution would be engaged in human subjects research. [See scenario A.(6) above.

(7) Employees/agents obtain coded private information or biological specimens from another institution and are unable to readily ascertain the identity of the subjects

Institutions whose employees or agents: (a) obtain coded private information or human biological specimens from another institution involved in the research that retains a link to individually identifying information (such as name or social security number); **and** (b) are **unable** to readily ascertain the identity of the subjects to whom the coded information or

specimens pertain because, for example:

- the institution?s employees or agents and the holder of the key enter into an agreement prohibiting the release of the key to the those employees or agents under any circumstances;
- the releasing institution has IRB-approved written policies and operating procedures applicable to the research project that prohibit the release of the key to the institution?s employees or agents under any circumstances; or
- there are other legal requirements prohibiting the release of the key to the institution?s employees or agents.

For purposes of this guidance, *coded* means that:

(a) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, and/or combination thereof (i.e., the code); and
(b) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

(8) Employees/agents access or utilize individually identifiable private information only while visiting an institution that is engaged in the research

Institutions whose employees or agents access or utilize individually identifiable private information **only** while visiting an institution that is engaged in the research, provided their research activities are overseen by the IRB of the institution that is engaged in the research.

(9) Employees/agent conduct study audits

Institutions whose employees or agents access or review identifiable private information for purposes of study auditing (e.g. a government agency or private company will have access to individually identifiable study data for auditing purposes).

(10) Employees or agents receive identifiable private information for purposes of satisfying U.S. Food and Drug Administration reporting requirements.

(11) Employees or agents author a paper, journal article, or presentation describing a human subjects research study.

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Links
[1] http://hrpp.ucsf.edu/sites/hrpp.ucsf.edu/files/collaboration-presentation.pdf

[2] http://irb.ucsf.edu/research-needing-irb-review
[3] http://irb.ucsf.edu/when-ucsf-can-serve-irb-record
[4] http://irb.ucsf.edu/ucsf-affiliated-institutions
[5] http://irb.ucsf.edu/#
[6] http://www.hhs.gov/ohrp/international/intlcompilation/intlcompilation.html
[7] http://www.ich.org/products/guidelines/efficacy/efficacy-single/article/good-clinical-practice.html
[8] http://www.ich.org/
[9] http://www.cioms.ch/
[10] http://www.wma.net/
[11] http://www.bioethics-international.org/
[12] https://smartirb.org/
[13] http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
[14] http://ohrp.cit.nih.gov/search/
[15] http://www.hhs.gov/ohrp/assurances/index.html#registernew
[16] http://www.hhs.gov/ohrp/assurances/assurances/file/index.html
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[18] http://hrpp.ucsf.edu/sites/hrpp.ucsf.edu/files/ucsf-individual-investigator-agreement.doc
[19] http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.116
[20] http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.116(c)