HRPP TOPICS (click on any topic to jump to that section)

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20. RESEARCH WITH EXTERNAL COLLABORATORS/MULTIPLE SITES
21. DATA AND SAFETY MONITORING

NOTE: If you are asked a direct question and unsure of how to respond: We refer to Stanford policies/procedures, regulations, guidances on Stanford website, IRB Chair and members, and other IRB staff. Consider responding only to the question and not providing additional information that was not asked.

1. RESEARCH OVERSEEN BY HRPP

| What regulations and policies are followed? | • We follow: Belmont Report (respect for persons, beneficence, justice); OHRP Common Rule (45 CFR 46); FDA; VA; HIPAA; Other Federal Agencies (DoD, etc. – as appropriate to the funding), CA State Laws, and Stanford policies, (e.g., the HRPP Policy Manual, Research Policy Handbook (RPH)), CARE-Q (certification for research ethics, quality). |
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<table>
<thead>
<tr>
<th><strong>• We have a FederalWide Assurance with DHHS/OHRP</strong>, which states that when Stanford engages in non-exempt human subjects research supported by any federal department or agency that has adopted the Common Rule, Stanford will comply with the terms of the FWA (basically, the requirements of the Common Rule).&lt;br&gt;  • We apply different but equivalent policies and procedures for non-DHHS sponsored research on occasion for flexibility without compromising on subject protection.&lt;br&gt;  ○ For example – International research: Researchers should ensure that participants outside the US have the equivalent protections that participants would be afforded in the US. Many countries have their own research ethics review processes. Stanford researchers must follow all relevant local laws.</th>
<th><strong>FDA or OHRP?</strong>&lt;br&gt;General rule: If studies involve test articles (drugs/devices/biologics) – apply FDA regulations and make FDA findings, otherwise OHRP (HHS). If FDA study is supported by HHS, apply both.</th>
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<tbody>
<tr>
<td><strong>How are updates communicated?</strong> Policy updates for the research community are highlighted on the Human Subjects Research website.</td>
<td><strong>What projects require IRB review?</strong>&lt;br&gt;• HS Research is defined under OHRP, FDA regulations; must meet definition of research/clinical investigation, and involve a ‘human subject’&lt;br&gt;• <strong>Guidances</strong> assist researchers in what must be submitted and processes to follow.&lt;br&gt;• <strong>Examples of what might not be research</strong>: QA/QI; pilot projects (except for VA); research practicum; case studies (~3-5); oral histories. Our RPH also has a section on Use of Human Subjects in Student Projects, Pilot Studies and Oral Histories (Nonmedical)</td>
</tr>
</tbody>
</table>
| **Determination of Human Subject Research?**<br>• If ANY doubt, researchers submit an application for **Determination of HS Research** to the IRB. This is reviewed by IRB Staff or member.<br>• IRB has authority to decide if activity meets the definition of human subject research. | **2. REVISED COMMON RULE**

| **What common rule revisions affect IRB review?**<br>• Key information/summary at beginning of consent<br>• Future use section of consent for all research collecting identifiable data and/or specimens<br>• Incidental findings section of consent (e.g., MRIs)<br>• Address whole genome sequencing and commercial profit in consent for specimen collection<br>• A waiver of consent will no longer be needed for screening activities (A waiver of HIPAA authorization is still needed to access PHI)<br>• New waiver or alteration criterion that research could not practicably be carried out without using the information or biospecimens in an identifiable form<br>• New waiver of documentation consent criterion: If the subjects or LARs are members of a distinct cultural group or community in which signing forms is not the norm, the research is minimal risk, and there is an appropriate alternative mechanism for documenting that informed consent was obtained<br>• Refer to **Key Common Rule Revisions** for additional information |
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## 3. PROTOCOL REVIEW PROCESS

| What does staff review? | Staff utilize checklists to guide their review of protocols for regulatory and policy requirements.  
- New Protocol Checklists: Medical, Expedited, Chart Review, Nonmedical  
- Consent Checklists: Medical (clinical studies), Medical (expedited/minimal risk), Nonmedical, Neonates  
- Continuing Review Checklist  
- siIRB Checklist  
- Research Involving VA Studies: see Reviewing Veterans Affairs (VA) Research for additional requirements  
- Exemption from IRB Review: Emergency Use of a Test Article  
- Single Patient IND/IDE  

Other Federal Agency Requirements:  
- Dept. of Defense (DoD)  
- Dept. of Education (ED)  
- Dept. of Energy (DOE)  
- Dept. of Justice (DOJ)  
- Environmental Protection Agency (EPA) |
|---|---|
| What resources are available to staff? | • Common Rule, or FDA or other regulations  
• HRPP Policy Manual  
• Guidances and AIDs  
• IRB Procedures Manual  
• Senior panel managers and senior staff  
• Discussions at managers’ meeting |
| When/how are protocols assigned? | • IRB Reviewers receive an email from eProtocol notifying them of the assignment via our electronic system, eProtocol  
• For convened review, Primary Reviewers are notified approximately 3 weeks prior to the meeting |

### Convened Review Process

- **Notification of Meeting Materials**  
  - Draft agenda list and draft minutes are distributed one week prior to the convened meeting for all members to review.  
  - Presented protocols are **accessible and available for review** prior to meeting.  

- **Presented Protocols**  
  - Protocols that involve greater than minimal risk (i.e., regular) or do not meet exempt or expedited criteria are reviewed at a convened IRB meeting  
  - An expedited IRB reviewer or exempt reviewer may refer a study to the convened meeting  

- **Discussion/Vote**  
  - **Reviewer Checklist** in eProtocol can be used as a guide for presenting protocols  
  - Reviewers discuss and IRB members vote on whether criteria for approval are met, elements of consent are present or waived, and any applicable additional findings/determinations  

- **Controverted Issues**  
  - Reviewers and staff conduct **robust pre-review** ahead of the convened meeting with comments documented in eP  
  - Reviewers discuss controverted issues with other IRB members at the convened meeting.
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<tr>
<th>What do IRB members review?</th>
<th>Discussion documented in minutes</th>
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<tr>
<td>• <strong>Reviewer Checklist:</strong> Reviewers can generate this in eProtocol; based on the criteria for approval (see also GUI-40) Checklist Includes:</td>
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<tr>
<td>o Risks are minimized and sound research design</td>
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<td>o Risks are reasonable compared to benefits</td>
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<tr>
<td>o Equitable selection of subjects</td>
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<tr>
<td>o Informed consent obtained or waiver criteria met</td>
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<tr>
<td>o Documentation of consent obtained or waiver criteria met</td>
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<tr>
<td>o Data and safety monitoring plan for greater than minimal risk</td>
<td></td>
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<tr>
<td>o Adequate measures in place to protect subject privacy and data/specimen confidentiality</td>
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<tr>
<td>o Additional safeguards for vulnerable subjects</td>
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<tr>
<td>• <strong>Reviewers need to ensure all elements of consent are present,</strong> see GUI-C41 General Rqmnts for Informed Consent</td>
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<tr>
<td>• <strong>Reviewers need to review findings for special populations, non-significant risk determinations, and any waivers</strong></td>
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<tr>
<td>o Waiver/Alteration of Consent Requirements</td>
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<tr>
<td>o Waiver/Alteration of HIPAA and PHI</td>
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<td>o Additional Protections - Inclusion of Children (FDA)</td>
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<tr>
<td>o Additional Protections - Inclusion of Children (OHRP)</td>
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<tr>
<td>o Research Involving Pregnant Women, Fetuses and Neonates</td>
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<tr>
<td>o OHRP Guidance on Involvement of Prisoners in Research</td>
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<tr>
<td>o Significant Risk and Non-Significant Risk Medical Devices Studies</td>
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</table>

| IRB Approval and Expiration dates | An IRB shall conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk, not less than once per year. Examples of when the IRB may perform review more often than annually include:  |
|----------------------------------|  |
| • first-in-human research |  |
| • when there is a high degree of uncertainty regarding the risks involved |  |
| • the vulnerability of the subject population |  |
| • other studies as IRB members deem appropriate. |  |
| Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances: |  |
| • Research eligible for expedited review in accordance with §46.110; |  |
| • Research reviewed by the IRB in accordance with the limited IRB review described in §46.104(d)(2)(iii), (d)(3)(i)(C); |  |
| • Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study: |  |
|   1. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or |  |
|   2. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care. |  |

| Contingency sign-off | IRB panel decides whether IRB staff or an IRB member should sign off on the contingency |
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### How does IRB conduct continuing review?

The IRB should consider the following when reviewing CR based on OHRP guidance:

1. **Criteria for IRB Approval of Research Undergoing Continuing Review** (working presumption that the research, as previously approved, does satisfy all of the above criteria so focus on new information)
2. **Risk Assessment and Monitoring**
3. **Evaluating the Adequacy of the Informed Consent Process** (verify that the investigator is using the most recently approved version and that the document contains the most accurate, up-to-date information about the research)
4. **Evaluating Investigator and Institutional Issues** (e.g., deviations, etc.) *
5. **Evaluating Research Progress**

*Based on continuing review of deviations reported, the IRB may request a review by the Continuous Quality Improvement team.

### Expedited Review Process

**Expedited reviewers?**

An IRB member may perform *expedited review* when the IRB Chair, in consultation with the IRB manager, determines that the member is "experienced" with regard to this purpose. A member may achieve sufficient experience by e.g., attendance at IRB meetings, targeted education, working with a mentor, independent study, and previous IRB service. *The IRB is notified of expedited reviews & approvals via the Agenda and Approval Lists that are emailed to the Panels.*

### Exempt Review Process

**Exempt reviewers?**

*Exempt review* is performed by IRB staff or IRB members who have the knowledge and authority to confirm exemption or refer protocol for expedited or regular review.

### 4. MINUTES PROCESS

**Drafting Minutes**

- IRB Managers write the Minutes – send out to members approximately 3 weeks after meeting.
- Minutes are confidential; access is restricted and secured; kept on secure internal server

**Minutes Content**

- Attendance at the IRB Meeting
- Controverted Issues and Their Resolution
- Actions, such as findings, determinations, changes to the protocol or disapproving research, taken by the IRB
- The Vote on IRB Actions (including when members are conflicted)

**Retention of minutes and IRB records**

Per HIPAA regs, IRB records containing PHI are retained for at least six years after the completion of the research (OHRP regulations state to retain records at least three years after the completion of the research). It is Stanford policy to retain records for the greatest amount of mandated time. Thus, RCO retains all research records for at least six years with the exception of social and behavioral research records which are retained for three years. This policy applies to all minutes, IRB correspondence to researchers, and research studies, whether or not participants were enrolled. Sponsored grants and contracts may require additional periods for record retention. (VA records are currently retained for six years.)
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### 5. SCIENTIFIC AND SCHOLARLY REVIEW

<table>
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<tr>
<th>Evaluation of scientific and scholarly review?</th>
<th>When evaluating the scientific and scholarly validity of a protocol, the IRB relies on the review provided by different entities, as follows:</th>
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<tr>
<td></td>
<td>• Federally sponsored, including VA-funded: peer review process by the sponsoring agency</td>
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<td>• Research subject to FDA review: FDA conducts rigorous scientific design review during IND or IDE evaluation.</td>
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<td>• Research occurring at the VA Palo Alto Health Care System (VAPAHCS), the VA Research and Development Committee (R&amp;D) and subcommittees</td>
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<td></td>
<td>• Cancer Center Scientific Review Committee (SRC): peer review of local and national research protocols involving cancer patients at Stanford University Clinical Cancer Center and LPCH</td>
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<td>• Departmental, gift or no funding, or has not otherwise gone through a scientific review as described above, the IRB requires Scientific review by:</td>
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<td>o In the School of Medicine: Clinical Research Unit (CRU), the Division Chief or Department Chair of the PD’s department, (or the School Dean or his designee when the Division Chief or Department Chair has a conflicting interest), or</td>
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<td></td>
<td>o In other schools: the School Dean or designee.</td>
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<tr>
<td>For all research conducted by students, including research that may undergo scientific review by awarding entity, confirmation is by Academic Sponsor</td>
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<tr>
<th>IRB review of scientific and scholarly review</th>
<th>When there is no external scientific and scholarly review, the review is completed by the Department Chair, Division Chief or designee, attached to the eProtocol application and provided at the convened meeting. The IRB reviews the scientific reviewer’s response to the below questions:</th>
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<tr>
<td></td>
<td>• Are the research procedures the least risks that can be performed consistent with sound research design?</td>
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<td></td>
<td>• Is the research likely to achieve its aims?</td>
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<td></td>
<td>• Is the proposed research of sufficient scientific important to justify the risks entailed?</td>
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<td></td>
<td>• Are there adequate resources to complete this study?</td>
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<tr>
<td>If the scientific review includes comments, the IRB reviews and discusses the scientific reviewers’ concerns.</td>
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</table>

| Consultant or Expert review | • On an as-needed basis, an IRB reviewer may request individuals with expertise in special areas to assist in evaluating specific issues. |
| | • The IRB Manager, in consultation with the IRB Chair, invites individuals with expertise in the specific areas needed after reviewing the proposed meeting agenda (or protocol if expedited) and determining whether the IRB has the required expertise to review the research. |
### 6. CONSENT PROCESS

| RESEARCHERS CONSENT PROCESS: How should I describe the consent process in my protocol? | Consider (discussion points):
| --- | --- |
| | • Who is delegated to consent participants?  
• When documentation is not waived, who signs the consent forms?  
• When do you have an assent form?  
• What oversight and training should the PD provide?  
• How do you assess participant competence (e.g., to consent)?  
• How do you assess participant understanding of the study?  
• Where will signed consent documents be stored? |
| Criteria to evaluate the consent process? | • Review for *adequacy of the consent process* (ref: Consent Templates)  
• Refer to General Requirements for Informed Consent: OHRP, FDA (Medical)  
 **General Requirements:**  
  o Prospectively obtain legally effective consent  
  o Provide opportunity to discuss, consider participation, and minimize coercion/undue influence  
  o Provide information understandable to subject population  
  o Provide information a reasonable person would want in order to make a decision about whether to participate, and opportunity to discuss  
  o Begin with concise/focused *key information* and present information in sufficient detail to facilitate understanding of why/why not to participate  
  o No exculpatory language  
 **Elements of Informed Consent:**  
  o Purpose, statement of research, duration, procedures  
  o Risks  
  o Benefits (may be no direct benefit, state societal)  
  o Any alternatives  
  o Confidentiality  
  o Compensation and treatment for research injury  
  o Contact info for questions, rights, injuries  
  o Participation is voluntary  
  o Whether data or specimens will be used for future research  
 **Additional Elements as applicable:**  
  o Unforeseeable risks  
  o Researcher may withdraw subject  
  o Additional costs |
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| Consent from non-English speakers? | Participants should be provided informed consent in a language they understand. If researchers know they will encounter participants who speak certain languages based on target population, the IRB will inform researchers that they should prospectively submit a consent in that language once the English version is approved.  
- **Medical:** If researchers are **uncertain whether they may encounter a participant who does not speak English** but want to enroll eligible participants, the IRB can approve a [Short Form Consent](#) process – the study team will need a fluent bilingual witness at time of consent, request waiver of alteration of HIPAA, include special signature lines in their consent, and request short form consent in their application. Several templates for common local languages are provided on the Human Subjects research website. |
|---|---|
| Observation of the consent process? | **Observation:** IRB may require that informed consent process situations be observed for selected protocols e.g., high risk; Studies involving particularly complicated procedures or interventions, potentially vulnerable populations (e.g., ICU patients, children), study staff with minimal experience in administering consent, or situations when the IRB has concerns that the consent process is not proceeding well.  
- Consent Observation can be done by IRB staff or other university party. |
| Waiver/alteration of consent; waiver of documentation | The IRB may approve [waiver or alteration of consent](#) or [waiver of documentation of consent](#) by following regulations for [Findings for Waiver or Alteration of Consent Requirements](#) and [Waiver of Documentation (waiver of signature) of Consent](#). |

### 7. PARTICIPANTS

**Research Participants and Recruitment**

- **Discussion point:** When reviewing protocols, how do you identify the participants of the research? For example, what about the families of participants, or caregivers? Tissue donors?
- • Review recruitment & selection sections in the study to ensure that strategies are fair, equitable, & not misleading.

### 8. VULNERABLE PARTICIPANTS

**Vulnerable populations**

- Refer to [Laminates](#) page for additional protections for children, pregnant women, fetuses, neonates, and prisoners
- Review for [adequacy of the consent process](#)
  - **If using LARs** follow the California LAR hierarchy (unless VA)
- **Children:** [Parental permission](#) – determine if 2 signatures are needed. **Children: Assent of children:** IRB may determine assent is required, adequate provisions are made for soliciting assent, and whether and how assent must be documented. Generally, children aged 7 and above may be asked to give their assent.
- **Prisoners:** IRB Member prisoner rep must attend and vote on research involving prisoners.
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- **Adults with Impaired Decision-making Capacity:**
  - Criteria before approving research involving adult participants with impaired decision-making capacity – includes CA H&S Code 24178(b)
  - Consider whether *adult assent* of the participants that are decisionally challenged should be obtained, and, if so, whether the plan for assent is adequate.
- **Additional safeguards for participants** such as:
  - Requiring the involvement of participant advocates
  - Requiring independent monitoring
  - Requiring waiting periods (e.g., first-in-human studies, etc.)
- **Appointing a monitor** to supervise the informed consent process.

### Resources
- **Legal Counsel** assists when needed (e.g., unfamiliar/special populations/state laws etc. in other jurisdictions, etc.).
- **University Privacy Office** for state or international privacy laws.

### 9. REPORTING: NONCOMPLIANCE, UPS, SUSPENSIONS AND TERMINATIONS

**What must be promptly reported to the IRB?**

See Guidance [GUI-P13 Events and Information that Require Prompt Reporting to the IRB](#):

- These items must be promptly reported:
  - Unanticipated Problems Involving Risks to Subjects or Others (*unexpected, related* to research participation, *harmful*)
  - New Information that indicates a change to the risks or potential benefits
  - Protocol Violation or Deviation if: Intended to eliminate apparent immediate hazard; or harmful; or **possible serious or continued noncompliance**
  - Complaint unresolved by the research team, or that indicates increased or unexpected risks.
  - Incarceration when in PD’s opinion it is in the best interest of participant to remain on study.
  - Unanticipated adverse device effect
- **Timeframe for prompt reports:** Generally, within 10 working days (note VA timeframes differ and sponsor timeframes may differ such as DOD); Unexpected deaths or life-threatening experiences related to the research (at Stanford, or when STANFORD is coordinating institution in multi-site study) must be reported to IRB within 5 working days (note VA timeframes differ and sponsor timeframes may differ such as DOD)
- **Not sure whether you should submit a report?** Refer to the Guidance [GUI-P13](#) or call the IRB.

**Noncompliance:**

**Serious or Continuing noncompliance**

We have a defined process for how and by whom serious or continuing noncompliance determinations are made:

1. All reports initially evaluated by IRB staff, and designated as not requiring further action, or escalated for review by RCO Director, Deputy Director, IRB Chair or delegate.
2. Instances of possible serious/continuing noncompliance are referred to convened IRB for determination; IRB has list of possible actions (e.g., suspension or termination of research, modifications, monitoring of the research or consent process).
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| 3. | Allegation of noncompliance found to be true based on preponderance of evidence becomes a determination of serious and/or continuing noncompliance at a convened meeting. |
| Unanticipated Problems | • Events as defined by guidance GUI-P13 *(unexpected + related or possibly related + suggests that research places subjects at greater risk of harm)* must be reported;  
• IRB staff evaluates → IRB Member reviews → IRB convened meeting for determination  
• If the IRB determination affects enrolled participants IRB may decide notification/follow-up, etc. |
| Suspensions & Terminations: | **Suspension** = temporary withdrawal of IRB approval  
**Termination** = permanent withdrawal of IRB approval |
| Internal/External Reportable Events | **Determinations of serious/continuing noncompliance and UPs are** reported to Institutional Official (IO); staff facilitate external reporting.  
• For HHS supported or conducted research, the IRB reports to OHRP.  
• For research subject to FDA regulations (any activity that involves an approved or unapproved drug or medical device), the IRB reports to the FDA.  
• For HHS supported or conducted research and research subject to the FDA, the IRB reports to OHRP AND FDA. |

### 10. RESEARCH CONFLICT OF INTEREST (COI)

| What is the process for ascertaining researcher Financial COI? | • OPACS system is used for annual reporting, and for reporting for each protocol.  
• Investigators must log on to their OPACS dashboard prior to engaging in research related to any PHS-funded grant.  
• Resource: Research Policy Handbook: Chapter 4 – Conflicts of Commitment and Interest  
• **Significant Financial Interests** (SFI) disclosures threshold:  
  o Public Health Service (PHS) = over $5,000  
  o National Science Foundation (NSF) = over $10,000 |
| IRB review of COI | • For any confirmed conflict, the IRB reviews the COI Transactional Assessment Report (TAR) for any management plan and consent form language  
• The IRB is the final reviewer/approver of any COI consent language, and management plan if applicable. |

### 11. IRB MEMBERS

| Member Feedback and Evaluations | IRB Members receive annual evaluation & feedback from the IRB Chair |
| IRB member selection | • Unaffiliated (public) members *represent the general perspective of participants*  
• IRB members have varying backgrounds to promote complete and adequate review of research activities commonly conducted by Stanford.  
• IRB members should be equitably selected and are sufficiently qualified through their experience and expertise (professional competence)  
• Our members should be diverse in their race, gender, cultural backgrounds, and sensitivity to community attitudes.  
• The IRB should provide an inclusive environment that allows for minority voices and opinions |
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**IRB Member COI**
- Disclose to IRB staff and Chair; ensure IRB members recuse themselves from review & discussion/vote.
- Notification of COI prior to meeting would enable protocol to be transferred to another IRB.

**Undue influence**
- **Undue influence** – IRB preserves the anonymity of members reviewing protocols; reports of undue influence go to IRB Chair/member/VP & DoR – treated like possible noncompliance reports
- **HRPP Policy Manual Ch 6.1** “neither the Vice Provost and Dean of Research, the Provost, nor any other Stanford official or committee may approve a protocol that has not been approved by the decision of one of the Panels, nor apply undue pressure on the Panel to reverse a decision.”

**Who approves human subjects research?**
- Research is approved by the IRB. Depending on the characteristics of the research, other reviews might also be needed (e.g., Radiation Safety, VA Research and Development Committee, Conflict of Interest Committee, etc.)

### 12. EDUCATION AND RESOURCES

<table>
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<tr>
<th>Training/ education for IRB Members and researchers?</th>
<th><strong>CITI online human research training</strong> is required for IRB staff, IRB members and researchers every 3 years</th>
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<tbody>
<tr>
<td></td>
<td>New IRB members orientation and training session with the IRB manager and Chair</td>
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<td>Education session at each IRB meeting</td>
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<td></td>
<td>IRB Presentations: targeted outreach to Departments and meet with IRB staff</td>
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<td>IRB Education– available by email/phone, as are all IRB Staff</td>
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<td></td>
<td><strong>Human Subjects Research website</strong>, with links to the Stanford <strong>HRPP Policy Manual</strong>, instructional information, FAQs, educational material, templates, and guidances</td>
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<td></td>
<td>eProtocol system includes instructional text, links to policies and guidances, live chat, &amp; explanation in the application</td>
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<td>eProtocol training and process videos</td>
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<tr>
<th>Other education/training</th>
<th><strong>RPH</strong>: <strong>Research Policy Handbook</strong></th>
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<td>The Office of the Vice Provost and <strong>Dean of Research website</strong></td>
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<td><strong>Spectrum</strong> (non-cancer studies) provides education, training and mentoring to clinical research coordinators and staff, including GCP training</td>
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<td>Stanford Cancer Institute (cancer studies) – provides oversight to all research studies at SCI</td>
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<td></td>
<td>PRIMR Meetings; Webinars; Other Conferences; Research Office, SOM</td>
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### 13. CHAIR RESPONSIBILITIES

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<th>What are the Chair’s IRB membership duties?</th>
<th><strong>Diverse IRB member selection and recruitment</strong></th>
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<td></td>
<td><strong>Provide leadership and mentorship</strong></td>
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<td><strong>Current knowledge of regulations and policies</strong></td>
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<td></td>
<td><strong>Evaluation (annual):</strong></td>
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<td>o <strong>IRB Members</strong> – by IRB Manager &amp; Chair (meeting attendance, educational session attendance, satisfactory service on IRB) <strong>Note that evaluation of Chair</strong> is by RCO Director and IO</td>
</tr>
</tbody>
</table>
### Human Research Protection Program (HRPP) Information Guide

<table>
<thead>
<tr>
<th>What are some review duties outside of the convened meeting?</th>
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<tbody>
<tr>
<td>- Review outside of meetings (e.g., compassionate use, emergency use, etc.)</td>
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<tr>
<td>- Expedited reviews</td>
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<tr>
<td>- UPs, noncompliance pre-review</td>
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<tr>
<td>- Subcommittee investigations (e.g., potential UP and noncompliance cases, etc.)</td>
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<tr>
<td>- IRB manager consults with Chair as needed for protocol reviewer assignments</td>
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<tr>
<td>- Requesting consultants for expertise</td>
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<table>
<thead>
<tr>
<th>What is the Chair responsible for at the convened meeting?</th>
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<tr>
<td>- Address any IRB reviewers’ concerns in preparing for the meeting</td>
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<tr>
<td>- Ensure quorum with IRB manager, including a nonscientist</td>
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<tr>
<td>- Encourage participation from all members</td>
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<tr>
<td>- Allow ample time for discussion of each agenda item</td>
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<tr>
<td>- Aware when member has a COI/recusal</td>
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<tr>
<td>- Discuss and resolve controverted issues</td>
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<tr>
<td>- Ensure that all required changes to protocol are documented</td>
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<tr>
<td>- Call for vote, ensure all IRB regulatory determinations are addressed:</td>
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<tr>
<td>- waivers</td>
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<tr>
<td>- Criteria for approval</td>
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<tr>
<td>- Consent elements</td>
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<tr>
<td>- Children’s findings and special populations</td>
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<tr>
<td>- ethical principles and Stanford HRPP policy</td>
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</tbody>
</table>

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<tr>
<th>What are some other Chair duties?</th>
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<tbody>
<tr>
<td>- Chairs’ meetings</td>
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<tr>
<td>- Policy development</td>
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<tr>
<td>- Review resources for the IRB (metrics; CQI reviews; etc.)</td>
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<tr>
<td>- Request post approval monitoring</td>
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### 14. THE HRPP AT STANFORD; IRB AUTHORITY; INSTITUTIONAL OFFICIAL’S ROLE IN THE HRPP

<table>
<thead>
<tr>
<th>Institutional Official</th>
<th>Institutional Official for HRPP is Kathryn Moler, Ph.D., Vice Provost and Dean of Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the line of authority?</td>
<td><strong>Line of Authority: delegated from President ➔ VP &amp; DoR</strong></td>
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<td></td>
<td>- The President of Stanford University delegates the primary responsibility to the Vice Provost and Dean of Research to establish, maintain, and oversee the HRPP.</td>
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<td></td>
<td>- The HRPP is approved by the IO. The written plan for the HRPP is comprised of policies, guidance, and supporting documents governing human subject research and the protection of participants.</td>
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</table>
## Human Research Protection Program (HRPP) Information Guide

| How does the IRB get its authority? | **IRB Authority:** The Vice Provost and Dean of Research appoints the Chairs and the members of the IRBs and assigns their authority and responsibility.  
- The *Charges to the Administrative Panels* emphasize that the IRBs are functionally independent and have ready access to the highest officials, if needed, to ensure protection for human research participants. |
| Charge to IRB | See *Charges to the Administrative Panels* which emphasize that the IRBs are functionally independent and have ready access to the highest officials, if needed, to ensure protection for human research participants. |
| IRB approval of research | **Research is approved by the IRB.** Depending on the characteristics of the research, *other approvals might also be needed* (e.g., Contracts, Biosafety, Radiation Safety). |
| Protocol not approved by IRB | NO person or body can approve a non-exempt or Limited IRB Review protocol that has not been approved by the IRB. |
| Describe the role of IO of the HRPP at Stanford | **IO role:** As Stanford University’s Institutional Official, the Vice Provost and Dean of Research signs the Federalwide Assurance of Compliance (FWA) on behalf of the institution and is ultimately responsible for:  
- Creating, establishing, and maintaining the policies and procedures for the HRPP and related research policies and procedures on behalf of Stanford University  
- Overseeing the protection of human participants, regulatory compliance, and the implementation of the HRPP for Stanford  
- Ensuring that **open channels of communication are maintained between the components of the HRPP**  
- Overseeing research investigators and staff, and research management  
- **Ensuring the independence of the IRB, including the authority to act without undue influence**  
- Requiring periodic reviews of the HRPP  
- Ensuring that the HRPP is functional, adequately staffed and funded, involving:  
  1. **Annual review of the resources allocated to the HRPP**  
  2. Participation in the annual budget preparation for the HRPP and incorporation of the HRPP budget into the budget of Stanford University.  

In addition:  
**IRB determinations of UPs, serious or continuing noncompliance:** Decisions to suspend or terminate research, and any other ‘reportable decisions’ are reported to the DoR, and further reported externally (to federal agencies, sponsors, etc.) as appropriate. |

### 15. INDEPENDENCE OF IRBs & UNDUE INFLUENCE

| Who approves human subjects research? | Research is approved by the IRB. Depending on the characteristics of the research, other reviews might also be needed (e.g., Radiation Safety, VA Research and Development Committee, Conflict of Interest Committee, etc.) |
| How is undue influence avoided? | - **Undue influence** – We preserve the anonymity of members reviewing protocols; reports of undue influence go to IRB Chair/member/VP & DoR and treated like possible noncompliance reports. |
### 16. ENSURING ADEQUATE RESOURCES FOR THE IRBs, AND HRPP AS A WHOLE

How are resources allocated and adjusted to meet the needs of the HRPP?

- The RCO receives its annual budget through the Office of the Vice Provost and Dean of Research.
  - The annual budget is established by:
    1. RCO Director, RCO Deputy Director and budget officers in the Office of the Vice Provost and Dean of Research.
    2. Resource needs are discussed to prepare income and expense forecasts for the following year.
    3. Forecasts are converted into a budget ultimately reviewed and approved by the Provost. This budget is then integrated by the University Budget Office into the University’s consolidated budget forecast presented to the Board of Trustees for approval. It takes effect on September 1 of each year.

### 17. ROLE OF PROTOCOL DIRECTOR VS. OTHER RESEARCH PERSONNEL

What are the Protocol Director’s responsibilities?

- PDs are ultimately responsible for the safety and welfare of participants. When conducting research with human participants, the PD agrees to, as part of the Protocol Application (Obligations section):
  - Design studies that are scientifically sound and that will yield valid results and conduct the study according to the protocol approved by the IRB
  - Conduct study as written in approved protocol
  - Be appropriately qualified to conduct the research and trained in Human Research Protection ethical principles, regulations, and policies and procedures, and ensure all research personnel are adequately trained and supervised
  - Disclose to the appropriate departments any potential conflicts of interest
  - Report promptly any new information, potentially serious or continuing noncompliance, or unanticipated problems involving risks to subjects or others
  - Obtain prior approval of the IRB before initiating any changes to the approved protocol except where necessary to eliminate apparent immediate hazards to participants
  - Ensure that the rights of participants are protected, including privacy and confidentiality of data
  - Do not attempt to re-identify de-identified materials obtained for research purposes

As PD, how do I ensure sufficient resources to conduct research?

- Access to a sufficient number of qualified staff with regard to specific research needs
- Secure appropriate facilities
- PD and staff have sufficient availability and time to conduct the research
- Team has access to target population
- Access to medical or psychological resources for participants are available as applicable
**What is the role of other research personnel?**

Research co-investigators and staff, although not having the same overall responsibility for the study and oversight as the PD, are expected to understand the research protocol and their role (e.g., consenting participants), to be adequately trained, and to follow all relevant policies and procedures.

**18. STUDY DESIGN**

What are the HRPP considerations that constitute good study design?

A research study should be designed to **minimize risks to participants**: the IRB must be able to determine that the potential benefits to the participants from the research justify the potential risks:

1. **Risks to subjects are minimized:**
   - By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
   - whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

2. **Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result.**
   - If risks outweigh potential benefit to participants, the Protocol Director (PD) should be prepared to justify why the procedure is necessary to achieve the research objectives, or why enrollment should not be limited to those already scheduled for the procedure for non-research purposes.
   - **Risks**: Risks may affect physical, psychological, social, legal, or economic well-being, including loss of privacy or breach of confidentiality.

What will the IRB look for in the protocol?

- Risks are minimized and research design is sound
- Risks are reasonable compared to benefits
- Equitable selection of subjects
- Informed consent obtained or waived
- Documentation of consent obtained or waived
- Data and safety monitoring plan for greater than minimal risk
- Protect subject privacy and data/specimen confidentiality
- Additional safeguards for vulnerable subjects

**19. PARTICIPANT RECRUITMENT, QUESTIONS, COMPLAINTS**

What must I consider about participant selection and recruitment?

The PD must consider the following elements

- **Equitable Selection:**
  - Purposes of the research
  - Research environment
  - Recruitment methods and materials to facilitate enrollment of a diverse population
  - Timing of the consent process
  - Inclusion/exclusion criteria
**Human Research Protection Program (HRPP) Information Guide**

- Whether participants may be susceptible to coercion or undue influence
- Whether population that stands no chance of benefiting is being selected to assume the risk
- Investigators must provide a rationale for involvement of vulnerable subjects, such as children, prisoners, economically and educationally disadvantaged, persons with impaired decision-making, and those experiencing homelessness. IRB assesses the additional safeguards proposed by the PD to minimize the possible risks.

- **Recruitment material to submit for IRB review:**
  - Audio and video advertisements: The IRB may review and approve the wording prior to taping in order to preclude re-taping due to inappropriate wording, with expedited review of final broadcast-ready tape.
  - Website, social media and printed/electronic advertisements: The IRB will review the final copy
  - Phone/internet scripts and eligibility screening: Sample scripts on Human Subjects Research website
  - Internet and web postings: No IRB review necessary if it only lists basic information

- **Payment:**
  - PDs must disclose any proposed payments to participants in the protocol application form and consent form, including the method, type, and timing of the payments
  - May not be of such an amount as to result in coercion or undue influence
  - If a study has multiple paid visits, payment should be prorated throughout the duration

<table>
<thead>
<tr>
<th>How are participant questions or complaints handled?</th>
<th>The PD is expected to investigate and respond promptly to all complaints. Complaints may come from participants, family members, other study team members, or from those who donated specimens.</th>
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<td>A complaint that is unresolved by the research team, or that indicates increased or unexpected risks, must be promptly reported to the IRB</td>
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</table>

**20. RESEARCH WITH EXTERNAL COLLABORATORS/MULTIPLE SITES**

**What is expected of me if I am relying on another IRB for my research?**

The Protocol Director (PD) is required to submit a sIRB eProtocol (eP) application to request reliance on a sIRB. The study team must follow the IRB approved protocol, see here for additional Relying PI responsibilities or in the sIRB application process. The following is required in the sIRB eProtocol application:

- Study Protocol
- Consent form (Any template can be used as long as Stanford required elements are included)
- IRB Reliance document (check with the sIRB which agreement they would like to use)
- Additional documents that may be required (if available)
- Federal Grant (when Stanford is the prime awardee)
- Initial IRB approval letter for overall study
- IRB approval letter specifically approving Stanford site & Stanford consent form(s) (if applicable)
- Local Context document (when requested by sIRB)
- Medical: Investigator Brochure or FDA documentation and Research Protocol
# Human Research Protection Program (HRPP) Information Guide

| What should I do if my federal sponsor wants me to use a single IRB for collaborative research? | When Stanford is the Prime Awardee or the lead site for a federally supported project that is multi-site study or cooperative research requiring a single IRB, researchers will need to consider the following reviewing IRBs to include in their proposal submitted to the Federal Department or Agency (e.g., NIH, NSF, DoD, VA, ED, DOE) for the use of an sIRB:  
  - Commercial IRB, e.g., Advarra IRB, WIRB  
  - Trial Innovation Network Central IRB  
  - Another academic IRB (i.e., one of the other participating institutions)  
  - Questions about the reviewing IRB process, please contact IRB Reliance Manager at singleirb@stanford.edu |
|---|---|
| When Stanford is serving as the coordinating institution, what additional responsibilities do I have as the PD? | • PD must describe the plans for communicating information relevant to the protection of participants among the participating sites and institutions  
  • PD is responsible for receiving data and reports from the outside sites in a timely manner and distributing them to the Stanford University IRB as required  
  • PD must report any material changes in the protocol that take place at any of the participating research sites  
  • PD must ensure that all participating sites have obtained IRB approval prior to initiation of the research at that site  
  • There must be documentation of regular communication (e.g., teleconferences) with the participating sites to update and inform all participating sites about progress of the study. |

## 21. DATA AND SAFETY MONITORING

| When is a data and safety monitoring plan required? | A Data and Safety Monitoring Plan (DSMP) is required for:  
  • More than minimal risk studies, for example: - Phase III clinical trials  
    o New, unfamiliar interventions not otherwise categorized as phase III clinical trials  
    o Multi-site research where Stanford is the coordinating site  
    o Research that is blinded, multi-site, enrolls vulnerable populations, or employs high-risk interventions  
  • NIH sponsored Phase I, II, and III clinical trials, and multi-site clinical trials involving interventions that entail potential risk to the participants  
  • Studies with an NIH or FDA requirement for a plan  
  • Other studies when required by the IRB |
|---|---|
| When must I have a data and safety monitoring plan for my protocol and what is involved? | Data and Safety Monitoring Plan (DSMP) provisions should be tailored to the nature, size, complexity, and risks of the individual study and should be described in the protocol application.  
  • The DSM Plan might need to include a Data Monitoring Committee (DMC) or Data and Safety Monitoring Board (DSMB)  
  • New Protocols: When applicable, the study design should include procedures to monitor data to ensure the safety and well-being of participants.  
  • Continuing Review eProtocol application: Include all monitoring entity reports, and reports from multi-center trials.  
    o The report should include information reviewed, date of the review, & monitoring entity’s assessment of information. |
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<th><strong>Human Research Protection Program (HRPP) Information Guide</strong></th>
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<td>o Even when a DMC or DSMB has not identified any problems and simply recommends continuation of the research study as designed, the IRB should be informed of this recommendation.</td>
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<tr>
<td><strong>What is expanded access?</strong></td>
<td>• Also referred to as “compassionate use”, expanded access allows use of investigational new drugs and approved drugs where availability is limited by a risk evaluation and mitigation strategy (REMS) when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition. The aim is to facilitate the availability of such drugs to patients with serious diseases or conditions when there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the patient's disease or condition. [21 CFR 312.300 (Subpart I)]</td>
</tr>
<tr>
<td></td>
<td>• See <a href="#">GUI-19m Expanded Access to Investigational Drugs and Devices</a> for more information</td>
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