Purpose and Scope

This Standard Operating Procedure (SOP) describes the process to conduct quality improvement of the human research protection program.

These procedures are applied to all Human Studies Program staff, UH IRB members, and UH Investigators and key research personnel (e.g., sub-investigators, study coordinators, research assistants, etc.). Human Studies Program staff ensures completion of these procedures.

Definitions

Institution refers to any public or private entity or agency (including federal, state, and other agencies).

Clinical Drug Trials

- Phase 1 trials refer to testing within a small group of people (20–80) to evaluate safety, determine safe dosage ranges, and begin to identify side effects.

- Phase 2 trials refer to testing with a larger group of people (100–300) to see if it is effective and to further evaluate its safety.

- Phase 3 trials refer to testing with large groups of people (1,000–3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow it to be used safely.

On-Site Visits

- Routine Review refers to a comprehensive on-site review conducted on a scheduled basis.

- For-Cause refers to a comprehensive or targeted on-site review to provide an assessment of study compliance.

- Investigator-Requested refers to an on-site review based on self-reported actual or perceived deficiencies in which there is a potential risk to human participants.

Site Visit Review Ratings

- Acceptable refers to a site visit that result in a finding of no deficiencies or lesser deficiencies that do not appear to involve risk to human participants.
• **Acceptable with Conditions** refers to a site visit that result in findings of multiple lesser deficiencies that presents a potential risk to human participants that needs further consideration.

• **Unacceptable** refers to a site visit that result in findings of one or more major deficiencies that impacts human participant safety and welfare.

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**Procedures**

**External Compliance Monitoring of Research Conduct**

To meet the objective for improving compliance of investigators with their responsibilities, the following procedures will take place:

**Selection Criteria**

1. **Routine Site Visit.** Studies are randomly selected by the QIP Monitor, but the QIP will pay greater attention to biomedical and social and behavioral science studies below.
   
   a. Investigator-Initiated Phase I, II, and III studies;

   b. Risk level is more than minimal per federal definitions;

   c. Studies involving vulnerable populations as defined by federal regulations (e.g., children, pregnant women and neonates, and prisoners);

   d. Studies not otherwise reviewed by external regulatory entities.

2. **For-Cause.** The IRB can identify a study and request a comprehensive or targeted on-site visit to assess compliance. The IRB can specify whether the review focuses on one aspect of the research (i.e., the consent process) or a broad review of the study conduct.

3. **Investigator-Requested.** An Investigator may request a comprehensive or targeted QIP review. These reviews are conducted within limitations of available resources.

4. **Observation of the Informed Consent Process.** Investigators can request an overview of the consent process at any time before or during initiation of a study.

   Unless otherwise noted, the procedures in the Notice of Audit, Visit Review Preparation, and Site Visit, described below, will apply to Routine, For-Cause, and Investigator-Requested site visits.

**Notice of Audit**

Except in cases where the safety of subjects is a concern or where the IRB specifically requests an unannounced site visit, the HSP will provide written or email notification of a monitoring visit. Depending on the nature of the research study, an IRB member who has experience in the study topic may participate in the site visit.
The Compliance Specialist will contact the Investigator to arrange a site visit. For Routine and Investigator-Requested Site Visits, the Compliance Specialist will contact the Investigator to schedule the visit at a mutually convenient date and time. In the case of a For-Cause Site Visit, the Compliance Specialist or a designee appointed by the IRB, will provide the Investigator with at least twenty-four (24) hours notice by telephone and email of the site visit.

Visit Review Preparation

Prior to the Site Visit: The Compliance Specialist will notify Investigator by letter or email that the Investigator’s study has been selected for review. Before the site visit, Investigators will collect and make all documentation related to the study in the IRB file available for the research conduct assessment (see Appendix A).

Site Visit Checklist. Investigators will prepare for the site visit by reviewing the checklist of questions (see Appendix B). Please note that not all items on the checklist apply to all research studies. Investigators must make available private space for the Compliance Specialist’s use to review study files and other documentation.

Regulatory Requirements. Compliance with regulatory requirements is a significant component of QIP. To evaluate compliance, the Compliance Specialist, through observation, interviews, and record review, may focus on various aspects of the regulatory requirements involved in the study (see Appendix C).

Site Visit Process

The Site Visit will follow the process described below:

1. The Compliance Specialist will meet with the Investigator to briefly discuss the study.
2. The Investigator will provide the Compliance Specialist with the study files for review.
3. The Compliance Specialist may interview the Investigator who is familiar with the study, or any research personnel knowledgeable about specific aspects of the study.
4. Throughout the site visit at and at the conclusion, the Compliance Specialist may provide recommendations and educational support to the Investigator and their research personnel based upon the Site Visit findings.
5. After the Site Visit, the Compliance Specialist will meet with the Investigator and provide a brief summary of findings.

Post Visit

Summary Report of Findings.

1. The Compliance Specialist will draft a Summary Report and submit to the Investigator for review. The Summary Report will provide a detailed summary of the review identifying areas of improvement and recommendations for improvement.
2. The Compliance Specialist and Investigator will sign the Summary Report. The Compliance Specialist will provide a signed Summary Report to the HSP Director, the Investigator, and the IRB Chair.

3. When the Summary Report contains findings of non-compliance, the Investigator will respond with a plan of corrective action for each finding. The Investigator will submit the corrective action plan to the IRB within two (2) weeks of the date of the Summary Report.

4. **In most cases, serious violations that present the risk of injury to study participants should have been immediately reported to the IRB by the Principal Investigator.** However, if an audit demonstrated that a serious violation involving risk of injury to participants has not been reported, it will be reported immediately to the IRB Chair, HSP Director, and to the Assistant Vice Chancellor of Research Compliance (AVCRC), or designee.

5. The Summary Report, including the Investigator’s responses, will be reviewed at the next convened IRB meeting. The IRB may take the following actions with respect to the Summary Report:
   a. **Acceptable** referring to a site visit that result in a finding of no deficiencies or lesser deficiencies that do not appear to involve risk to potential subjects.
   b. **Acceptable with Conditions** referring to a site visit that result in findings of multiple lessor deficiencies that presents a potential risk to potential subjects that needs further consideration.
   c. **Unacceptable** referring to a site visit that result in findings of one or more major deficiencies that impacts human subjects safety and welfare.

6. The IRB will issue a letter to the Investigator after the IRB has made a decision on the Summary Report. Where the IRB decision is Acceptable with Conditions or Unacceptable, the IRB may require additional monitoring and education as required.

**Monitoring of Informed Consent/Assent Process**

During an audit of consent, the Compliance Specialist will review:

1. The timing of recruitment and screening in relation to informed consent.
2. The appropriateness of the person obtaining consent.
3. The consent process to meet the needs of vulnerable populations.
4. Steps to aid participants with barriers to understanding or lack of capacity to consent (language, reading level, etc.).
5. Steps to see if the participant understands the research purpose risks, benefits, voluntary participation, withdrawal, confidentiality, costs/compensation, and contacts for questions or injuries.
Review Rating.

Investigator-requested site visits focused on the informed consent process may include observation, interview, and record review. The monitor will provide feedback during and provide a brief summary of the findings at the conclusion of the visit.

Internal Compliance Monitoring of IRB Operations

To meet the objectives for improving compliance of IRB meeting minutes with regulatory compliance and increase efficiency of recording and finalizing minutes, the following procedures will take place:

1. The HSP Director and/or Compliance Specialist will conduct administrative reviews of at least one set of IRB meeting minutes every other month on a rotating basis so that each IRB has at least two (2) sets of minutes reviewed per year. Minutes are assessed for completeness and adherence to the requirements outlined under 45 C.F.R. 46.115(2). These administrative reviews of the minutes will also involve verification that the IRB membership listed on the minutes for a given IRB meeting is accurate according to the master list maintained by the IRB administration as well as the roster provided to OHRP.

2. Feedback will be provided to the staff members associated with the generation of minutes, and findings will be reported to the Assistant Vice Chancellor of Research Compliance and to the Institutional Official.

3. Corrective actions such as re-training of the staff will occur both individually and at the monthly meetings of the research compliance administrators and the IRB administration.

4. The Director or designee will be available for every convened meeting of the IRBs to answer regulatory questions for the members and to advise on policy issues.

5. In addition to the HSP staff member assigned to record meeting minutes during a convened IRB meeting, a second staff person will be in attendance to record presence and absence of members; to assure that a quorum is met and maintained; and to count and record votes. This additional staff support will help ensure the accuracy of the assessment of IRB chairs and members will be conducted annually. The Director will meet record of the IRB’s activities that will be reflected in the minutes from each meeting.

6. Assessment of IRB chairs and members will be conducted annually. The Director will meet with each IRB Chair to assess the constitution of the committee as well as members performance and need for additional training.
**Materials**

- WKSH 322 Consent Observation Checklist
- WKSH 350: Study Documentation Checklist
- WKSH 351: Site Visit Checklist
- WKSH 352: Regulatory Requirements Checklist
- WKSH 353: Post-Approval Monitoring Site Visit Checklist and Report (Biomedical, Clinical Studies)
- WKSH 354: Post-Approval Monitoring Checklist (Social & Behavioral Sciences)
- WKSH 355: IRB Meeting Minutes Quality Assessment
- WKSH 357: Quorum and Expertise
- WKSH 358: Protocol Assessment – Internal Review

**References**

- The Organization conducts audits or surveys or uses other methods to assess compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The Organization makes improvements to increase compliance, when necessary (**AAHRPP Element I.5.A.**).  

- The Organization conducts audits or surveys or uses other methods to assess the quality, efficiency, and effectiveness of the Human Research Protection Program. The Organization identifies strengths and weaknesses of the Human Research Protection Program and makes improvements, when necessary, to increase the quality, efficiency, and effectiveness of the program (**AAHRPP Element I.5.B.**).

**Appendix A – Study Documentation Checklist**

The study documentation may include the following:

1. Grant Application, IRB approved protocol or proposal.

2. IRB submissions and IRB acknowledgment and correspondence, including: (a) modifications, (b) protocol violations, (c) unanticipated problems, and (d) continuing review and status reports.

3. IRB approved Informed Consent documentations.

4. Study instruments.

5. Recruitment materials.

6. Training documentation.

7. Other relevant research management tools used by Investigator, including (a) delegation logs, (b) screening/enrollment log, (c) accountability logs, and (d) subject visit schedule logs.

8. Subsequent publications resulting from IRB approved protocols.
Appendix B – Site Visit Checklist

Questions to assist Investigators and research study team in preparation for the site visit:

1. Does the Investigator have available the most recently approved protocol, consent form, and study documents?

2. How many participants are currently enrolled in the study? What is the IRB approved target enrollment number?

3. Are all key personnel listed on the Delegation Log? Are personnel conducting procedures according to their role in the study?

4. Have any participants withdrawn/dropped from the study? If so, why?

5. Have any adverse events occurred? Were any of these events reported to the IRB?

6. Have participants provided their consent based on the most recent IRB approved stamped version? Have all the consent forms been signed and dated by both the participants and the person designated to obtain consent?

7. Have all study measures and procedures been approved by the IRB before implementation?

8. Are all study records stored as indicated in the protocol?

9. Do all advertisements and methods of recruitment being used have IRB approval?

10. Are study documents maintained as outlined in the protocol?

11. Are participant identification numbers generated as described in the protocol?

12. Have all enrolled participants met eligibility criteria? Is there documentation of eligibility?

13. Has there been any protocol deviation? Have these deviations been reported to the IRB?

14. Have there been any unanticipated problems with protocol implementation? Have these problems been reported to the IRB?

15. Has participant compensation for the study been documented?

16. Have there been any participant complaints?

17. Are raw data files organized, complete, and legible?
Appendix C – Regulatory Requirements Checklist

The following areas, as they pertain to regulatory requirements, are subject to review:

1. Roles and responsibilities of Investigators and key personnel.

2. Any research management documentation, e.g., delegation logs, accountability logs, screening and enrollment logs.

3. IRB Documentation, i.e., submission forms, approval letters, IRB correspondence, etc.

4. Consent/Assent Forms.

5. Participant Research Records. A random sample to determine if:
   a. The participants met the inclusion/exclusion criteria for the study.
   b. Study-related procedures are performed according to the protocol.
   c. Study-related procedures are scheduled and performed per the study time line.
   d. Data are recorded in a manner as described in the IRB-approved protocol and consent Form.
   e. Unanticipated problems/ adverse events have been reported according to institutional policy. Protocol deviations and violations have been reported to the IRB, as appropriate.
   f. Compensation provided to participants as described in the protocol.
   g. Participant ID numbers are assigned according to the protocol.

6. Facilities.
   a. Research data stored securely as described in the IRB approved protocol.
   b. Materials containing Participant’s PII information stored securely and separately from research data as described in the IRB approved protocol, e.g., signed consent forms.
   c. Location/setting where research is being conducted is as described in the IRB approved protocol.