Analyzing your Human Research Protection Program— A systematic approach to creating an effective structure

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HUMAN RESEARCH PROTECTION PROGRAM (HRPP)— The systematic and comprehensive approach by an organization to ensure human subject protection in all research. The implementation of any part of the program may be delegated to specific committees, individuals or entities by the organization.

The Institutional Review Board (IRB), established to protect the rights and welfare of the human subjects, does not function in isolation but rather is central to and a crucial element in an institutional/organizational system for protecting the human research participants. This system, commonly referred to as the Human Research Protection Program or HRPP, extends beyond the IRB to encompass the total effort to protect the human subjects of research.

In most institutions/organizations, the HRPP includes the investigators and their staff who actually conduct the research, the department/office/individual(s) who have responsibility for meeting the obligations imposed by the assurance, and the site(s) where the research is being done. Depending on the type of research being done, other groups/entities/committees/departments could also be considered part of the HRPP. Institutions and organizations should think in terms of such an overarching system rather than a single committee—of a comprehensive program, rather than an IRB.

At the same time, it is important to emphasize that the IRB is central to this system and plays a pivotal role in its functioning, as opposed to simply being one committee operating within it. If the IRB is not functioning properly, it can be said the HRPP is not functioning properly.

In such a system, communication plays an important role in the successful operation of any HRPP. Such communication may be written or oral; however, it is extremely important that the communication does occur. For this reason, it is a good idea to develop standard operating procedures (SOPs) that describe lines of communication and how the communication will be accomplished within the HRPP.

Analyzing the HRPP—It is greater than the sum of its parts.

- Identify the elements of the HRPP in your institution (institutional official, IRB, IRB administration, scientific or research oversight committees or advisory committees, research program administration, research safety office, compliance office, etc.) How is your institution structured?

- Identify the roles and responsibilities of each element.
  - How are the lines of authority and responsibility structured?
  - What are the most important responsibilities of each element?
  - Which offices develop policy and procedures; which offices manage certain daily operations?

The institution need not establish new committees or departments to carry out HRPP functions. Many of the functions may already be housed within existing structures, committees, and jobs.

- Examine how each element relates to the others. How does the work flow? For many people, a flow chart provides a picture of the relationships more clearly than text.
- Some institutions use decision trees. What decisions are made, and how are they coordinated?
- Are there written procedures for situations that span the HRPP? Are they current/adequate? What documentation is kept for the HRPP, and where is the information found?

  - For example: The procedures for ensuring prompt reporting to the IRB, the appropriate institutional officials, any department or agency head, and the Office of Human Research Protection (OHRP) of (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with federal regulations, or with the requirements or determinations of the IRB; and (c) any suspension or termination of IRB approval.

The following is a list of documents and information that should be maintained for an HRPP. The location of this information may vary depending on what office or person has responsibility. The information does not need to be in one location.

I. INSTITUTIONAL RECORDS

A. Regulatory and Ethical Reference Materials

1. Most current pertinent Federal regulations
2. Most current pertinent sections of the institutional policies
3. Statements of ethical principles: Belmont Report, Nuremberg Code, Declaration of Helsinki

B. Organizational Information

1. Written description of the HRPP, which may be a single document, or may be incorporated into several documents (e.g., Federalwide Assurance [FWA], institutional organizational charts, job descriptions, policies and procedures for the IRB and the institution, budget/time

allocation, formal IRB agreement, any Research Oversight Committee charter). The HRPP includes

a) A statement of principles concerning protection of human research subjects

b) Identification of the institutional official accountable for the HRPP

c) The organizational structure, process, roles and responsibilities for making policy to protect human research subjects

d) Roles and responsibilities of the Research Oversight Committee in protecting human subjects

e) One or more of the following arrangements for an IRB: (i) the institution has an FWA with an IRB (Human Subjects Subcommittee) reporting to the Research Oversight Committee and registers the IRB with the OHRP; (ii) the institution has a written arrangement with another VA IRB that is registered with OHRP and has an OHRP assurance; (iii) the institution has a written arrangement with an affiliated medical or dental school or university that has OHRP assurances and use of its registered IRB

2. Organizational Chart
3. Fully executed FWA and/or fully executed assurance issued by other Federal department if applicable
4. IRB Authorization Agreement (OHRP) or Memorandum of Understanding (MOU) for use of an external IRB of record, if applicable
5. Records of resource allocation for HRPP (e.g., budget records, institutional policy regarding budget, budget analysis forms, reports)

C. Training Records

1. Training manual/materials for human subject research
2. Records of completed training for the following:
   a) Investigators
   b) Key research office personnel
   c) IRB chair and members
   d) Others as required by local policy
   e) Others as required by the FWA

D. Written Procedures and Guidelines

1. IRB SOPs
2. Research Oversight Committee or Advisory Committee policy memoranda or SOP manual
3. Medical center or institutional policies
4. Policies and procedures regarding the use of investigational devices
5. "Free-standing" memos/directives issued by the institution
6. Pharmacy Service policies and procedures for handling investigational drugs
7. Any additional written guidelines, such as instructions, forms, or guidebook for investigators

E. Research Oversight Committee Membership (if one exists in the Institution)

1. Committee membership roster showing qualifications of members
2. Copies of correspondence related to members' appointments

F. Minutes of Research Oversight Committee Meetings (if applicable)

Note: Minutes show the following:

1. Presence of a quorum
2. Before final approval is granted, protocols involving human subjects are reviewed and discussed to determine that
    a) IRB recommendations are appropriate
    b) Level of human subject risk and benefit is appropriate
    c) Scientific merit is appropriate
3. Review and approval of IRB minutes
4. Review and approval of protocols that have been exempted from IRB review
5. IRB minutes are appended to the Research and Development (R&D)Committee minutes
6. If the institution relies on an external IRB, the evaluation, initially and at least annually, of the designated IRB's charter, policies, and procedures and whether the designated IRB is in compliance with current institutional, Federal, and other regulations and guidance (alternatively, this documentation may be in the form of a report, as in H.2. below, or correspondence)
7. Consideration of qualifications and experience of IRB chair prior to recommendation for appointment
8. Ongoing evaluation and oversight (alternatively, this documentation may be in the form of a report, as in H.2. below, or correspondence)
    a) Evaluation at least annually of the IRB membership and IRB performance (e.g., content and accuracy of approved informed consent documents, IRB analysis of risks and benefits)
    b) Consideration of Pharmacy Service and overall institutional compliance with policies and procedures regarding the use of investigational drugs
    c) Evaluation of compliance with policies and procedures regarding the use of investigational devices

G. List of Active Protocols

1. Current list of research projects (may be maintained electronically), including notation to identify
    a) The principal investigator (PI)
    b) If the research was exempted or approved by expedited review

c) If the research was judged to be high-risk
d) If the research includes vulnerable subjects
e) The date of the most recent IRB approval

H. Reports to Regulatory Agencies and Institutional Officials

1. Copies of all reports of serious adverse events, unanticipated problems posing risk to subjects or others, suspensions or terminations of protocols, and serious or continuing noncompliance made to appropriate regulatory agencies and institutional officials
2. Copies of reports made to institutional officials as a result of HRPP monitoring/auditing/oversight/QI. Reports include identified need for improvement, action taken to improve, and results of QI activities, including pre- and post-evaluation measurement
    a) Evaluations of IRB performance and membership
    b) Reports of monitoring/auditing of the conduct of approved protocols
    c) Reports of evaluations of Pharmacy Service compliance with policies and procedures regarding the use of investigational drugs
    d) Evaluations of institutional response to research-related questions, concerns and complaints
    e) Evaluation of compliance with policies and procedures regarding the use of investigational devices

I. Investigations and Site Visits

Copies of all reports and correspondence related to investigations and site visits:

1. From the internal quality assurance process
2. From internal investigations of non-compliance
3. From site visits by accrediting bodies, OHRP, Food and Drug Administration (FDA), (including inspections of both IRBs and investigators) or other regulatory or accrediting agency
4. From site visits performed by outside consultants retained by the institution, IRB, or some other part of the HRPP

J. Investigational Pharmacy or Pharmacy Service (if applicable)

1. Pharmacy Service policies and procedures for handling investigational drugs
2. Investigational drug logs (paper or electronic)
3. Copy of signed consent form 10-1086 for each subject
4. VA form 9012 and copy of protocol for each active protocol using investigational drugs
5. Evaluations of Pharmacy Service compliance with policies and procedures regarding the use of investigational drugs (e.g., quality assurance reports, consultant reports, minutes, documentation, review of performance)

K. Investigational Devices (if applicable)

1. Policies and procedures regarding the use of investigational devices
2. Evaluation of compliance with policies and procedures regarding the use of investigational devices

II. IRB-SPECIFIC RECORDS.

A. IRB Membership

1. IRB membership roster showing qualifications
2. Resumes, addresses, telephone numbers, and e-mail addresses of all members (on file, or ready office access)
3. Copies of correspondence related to members' appointments

B. Minutes of IRB Meetings

Items marked with * are those that ORHP strongly recommends be documented in the minutes. IRB meeting minutes include (if applicable to your research)

1. Date and time meeting starts and ends
2. Members present (any consultants/guests/others shown separately). Presence of alternate members includes identification of the member for whom the alternate is substituting. Attendance is recorded so the presence of a quorum can be determined at any point in the meeting
3. Approval of minutes of previous meeting
4. Summary and disposition of old business
5. Summary of discussion:
    a) Of controverted issues
    b) When the IRB approves the use of an investigational drug or device under a "Treatment or Emergency Investigational New Drug," "Humanitarian Device Exemption," "Single Patient Use" or "Parallel Track Mechanism," or other special use/expanded access as defined by FDA regulations
    c) For research proposals with elements warranting special attention (e.g., placebos, challenge studies, radiation exposure, deviations from standards of care). This may, alternatively, be documented elsewhere
    d) Significant/nonsignificant risk (SR/NSR) determination for investigational devices
6. Record of IRB decisions, including conditions for approval, required modifications, or reasons for disapproval
7. Documentation that the IRB considered protocol-specific information in sufficient detail to find that all required criteria for IRB approval of research were satisfied. May be documented in minutes, in reviewers' comments or checklists, or in IRB application documents.
    (a) Risks to subjects are minimized
    (b) Risks are reasonable in relation to anticipated benefits

(c) Selection of subjects is equitable
(d) Informed consent will be sought
(e) Informed consent will be appropriately documented
(f) Research plan makes adequate provision for monitoring data to ensure subject safety (when appropriate)
(g) Adequate provisions are made to protect privacy and maintain confidentiality (when appropriate)
(h) Additional safeguards are included in study to protect rights and welfare of any subjects likely to be vulnerable to coercion or undue influence (when applicable)

8. Documentation of required determinations, including protocol-specific information justifying each IRB finding. The National Committee for Quality Assurance and OHRP recommend that these findings be included in the IRB minutes, but they may, alternatively, be documented elsewhere.
   a) *Basis for approving a procedure that alters or waives the requirements for informed consent
   b) *Basis for approving a procedure that waives the requirement for obtaining a signed consent form
   c) *Basis for approving research involving prisoners
   d) *Basis for approving research involving children
   e) *Basis for approving research in which surrogate consent will be sought
9. *For approved protocols, assessment of risk and term of approval period
10. For suspended or terminated protocols
   a) Summary of reasons causing IRB to suspend or terminate the study
   b) Description of IRB actions to minimize harm to the research subjects
   c) Request to PI to provide the IRB with a list of research subjects for whom termination/suspension may cause harm (alternatively, may be documented by correspondence copied in the protocol file)
   d) Description of IRB actions such as an inquiry by a subcommittee
   e) Documentation that the suspension/termination will be appropriately reported to the institution, sponsor, and regulatory agencies
11. Record of voting (showing votes for and against, abstentions, and recusals for conflict of interest). Those abstaining or recusing themselves are named. When a member has recused him/herself, the minutes show that the member left the room for the deliberation and vote, and that a quorum was maintained
12. Record of reports to the IRB, including emergency use reports, decisions taken by expedited review, lists of exempted protocols, quality assurance/monitoring/auditing reports, and investigations
13. Record of decisions made about IRB policies or procedures

C. Protocol Files: Initial Review, Non-Exempt Research

1. Copy of the protocol, including
    a) Title of the study
    b) Purpose of the study (including the expected benefits obtained by doing the study)
    c) Sponsor of the study
    d) Results of previous related research
    e) Subject inclusion/exclusion criteria and number of subjects to be studied
    f) Justification for use of any special/vulnerable subject populations
    g) Study design (including as needed, a discussion of the appropriateness of research methods)
    h) Description of procedures to be performed
    i) Provisions for managing risks and adverse reactions
    j) The circumstances surrounding the consent procedure, including setting, subject autonomy concerns, language difficulties, and vulnerable populations
    k) The procedures for documentation of informed consent, including any procedures for obtaining assent from minors or surrogate consent for incompetent persons, using witnesses, translators, and document storage
    l) Compensation to subjects for their participation.
    m) Any compensation for injured research subjects
    n) Provisions for protection of subject's privacy and confidentiality
    o) Extra costs to subjects for their participation in the study
    p) The case report form (when one exists)
    q) Any materials used to recruit participants
    r) Questionnaires for subjects or for study personnel
    s) For devices labeled by the sponsor as NSR, an explanation of why the sponsor considers the device an NSR device
2. Investigator's brochure (when one exists)
3. Copy of the approved consent form
4. Any applicable grant application
5. Copy of the approval letter to the PI
6. Copy of any other correspondence used to communicate changes required before approval
7. In the minutes, record of discussion and decision
8. For expedited review, documentation of the criteria by which the project qualified for expedition
9. Completed IRB reviewers' checklists or review forms, if used

D. Protocol Files: Initial Review, Exempt Research

1. Copy of request for exemption (includes a protocol or adequate summary of project to determine exempt status)

2. Documentation of criteria for exemption
3. Copy of approval letter to PI or other documentation of review and approval
4. Completed IRB reviewers' checklists or review forms, if used

E. Protocol Files: Ongoing Projects

1. Revisions/amendments
   a) Copy of request for approval of the revision
   b) Copy of details of the revision (e.g., a highlighted copy of the protocol showing the changes or a cover memo/letter with a list of changes in sufficient detail to understand what the changes were and the rationale for the change)and any updated investigator's brochure
   c) Copy of the new consent form or advertisement, if any
   d) Copy of the approval letter to the PI
   e) Copy of any other correspondence used to communicate changes required before approval
   f) In the minutes: Record of discussion and decision
   g) Completed IRB reviewers' checklists or review forms, if used

2. Continuing review
   a) Copies of notices to PI of progress report due
   b) Where applicable, copy of notice to PI of lapsed approval, with instructions to cease research activity
   c) Copies of progress reports
   d) Copy of the current consent form or advertisement, if any
   e) Copies of approval letters to PI
   f) Copies of any other correspondence used to communicate changes required before approval
   g) In the minutes: Record of discussion and decision
   h) Completed IRB reviewers' checklists or review forms, if used

3. Adverse event reports (Note: This reflects one way of organizing adverse event reporting. Other approaches may also be acceptable)
   a) For on-site events, a copy of the report sent to the sponsor or a report from the PI describing the event, including an estimation of its seriousness, the likelihood that it was related to the experimental intervention, and any plans for changing the clinical management of patients in the study based on this event
   b) For off-site events in multi-site studies, a summary report of adverse events by the trial's Data Safety and Monitoring Board (DSMB) or Data Monitoring Committee
   c) For off-site events for trials that do not have a DSMB, a report as described in (a) above
   d) Revised consent form, protocol, or investigator's brochure if applicable

e) Documentation of the decision whether to bring the report to the full committee
f) For events that are both serious and unexpected, record of the committee discussion and decision in the IRB minutes
g) Copy of letter to PI if the IRB will require changes based on the adverse event
h) Statements of significant new findings provided to subjects
i) Copies of IRB reports to sponsors, institutional officials, and regulatory agencies, if applicable
j) Completed IRB reviewers' checklists or review forms, if used

4. End of study
Copy of final progress report or termination report

F. Expedited Review Reports

Note: Reports are usually made in the minutes, but other approaches may also be acceptable)

1. Report to IRB documenting and justifying research proposals reviewed and approved using an expedited review procedure. The appropriate category of expeditable research that applies should be identified.
2. Report to IRB documenting minor changes to research proposals reviewed and approved using an expedited review procedure

G. Emergency Use Reports

1. Report to IRB documenting and justifying emergency use and/or emergency use consent exception of an investigational drug or device
2. In the minutes: Record of report of the emergency use

H. Record Access

1. Access logs for IRB files recording access by persons other than IRB and research office staff

III. INVESTIGATOR FILES

A. Protocol File

1. Copy of report of Subcommittee on Human Studies VA form 10-1223
2. Current curriculum vitae for all involved investigators
3. Current Food and Drug Administration (FDA) form 1572 for all involved investigators, if applicable
4. Copy of Investigational Drug Information Record VA form 10-9012, if applicable
5. Copy of Investigational New Drug Application FDA form 1571 if the PI is a sponsor-investigator
6. Current clinical laboratory certification (lab certifications are good only for specified periods)
7. Current protocol and operations manuals
8. All protocol changes, including applicable correspondence from the sponsor

9. Current investigator brochure, if applicable
10. Copy of current IRB approved informed consent form, VA form 10-1086
11. All written communication with IRB, including
    a) Requests to approve amendments
    b) All progress reports
    c) All adverse event reports
    d) All DSMB reports, if applicable
    e) Certifications of any applicable training (e.g., in human research protection) for all research personnel involved with the study
    f) Reports of problems or complaints, etc.
    g) Correspondence from the IRB and R&D committees
12. Copies of all executed consent documents
13. Any other correspondence regarding human research protections (e.g., with sponsor, other investigators, federal regulatory agencies)
14. Copies of any reports from monitor site visits, inspections or internal quality assurance audits
15. Copies of any reports resulting from investigations of the study

IV. PATIENT RECORDS

A. Medical Chart/Source Documents
1. Medically significant events related to the research are noted in subject's official medical record:
   a) Enrollment
   b) Informed consent documentation
   c) Study drugs involved
   d) Serious adverse events
   e) Study complications
2. Clinical warning on medical chart or electronic flag placed in Computerized Patient Record System records of study patients
3. Original executed consent document

Self-assessment will help you to identify strengths and weaknesses and find corrective measures. Select certain processes for review. Break the process into each event or step. Where is the risk in the processes? What is working, what is not?

A number of tools can be used to do self assessment.

- See OHRP Common Findings and Guidance and published determination letters for where things go wrong. Review your institution’s processes in comparison

- Self-assessment checklists—(which ones to recommend)

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