Overview of the Accreditation Process and Standards

What is New in the AAHRPP Process?

- Draft Site Visit Reports are being sent to sites when they are ready, but no longer than 30 days.
- Evaluation Instrument changes
  - DoD Instruction 3216.02
  - DHHS Conflict of Interest Regulations
- Application forms
  - Added three questions on COI

Human Research Protection Program (HRPP)
Accreditation Standards

- Human Research Protection Program:
  - Domain 1: Organization.
  - Domain 2: IRB or EC.
  - Domain 3: Researchers and Research Staff.

Other Regulations and Guidance Added to the Revised Evaluation Instrument

- Veteran's Affairs Administration
- Department of Defense
- Department of Education
- Department of Justice
- Department of Energy
- Environmental Protection Agency
- ICH-GCP (E6)

For Countries other the US

- You will accredited to the AAHRPP Standards plus all applicable laws, regulations and guidance from your country.
TOOLS

Instructions

Guidance
Templates

Templates for:
- IRB Roster
- Key Personnel
- Active Protocols

Use of the Evaluation Instrument for Accreditation

- The Evaluation Instrument tells you what is needed to meet a particular element.
- Accreditation directors and site visitors use the Evaluation Instrument to guide them when reviewing applications and sites.
- Addressing all the relevant written materials and common materials in your application will help ensure you met that element.
Element(s) Tip Sheet is related to

Recommended content to include in your polices and procedures

PROCESS

The Accreditation Process

Self Assessment

Submit Application

Element by Element Feedback

Submit Revised and Additional Materials

Evaluate Written Materials

Feedback as Needed

Site Visit - Evaluation of Practices

Draft Site Visit Report

Response Evaluation

Prepare Response

Council on Accreditation

Accreditation Decision
TIMELINE

THE SELF-ASSESSMENT PROCESS
Conducting a Self-Assessment: Getting Ready

- Download the *Evaluation Instrument for Accreditation*.
- Download the *Instructions to Apply for Accreditation*.
- Gather all written policies and procedures, and organize them by topic.
- Use the Tip Sheets.

Make sure that your SOPs meet the requirements in the Evaluation Instrument

In the Step 1 Application list your policies that address each individual Element

Tips on Conducting Your Self-Assessment

- The time it will take to complete the self-assessment and submit an application is dependent on:
  - The current status of your program and SOPs.
  - The personnel resources dedicated to the effort.
- Most clients have said it takes 12-18 months from start to submission.
Use a Task Force or Working Group Approach

- Assemble core team – meet regularly
  - Institutional administration.
  - IRB administration.
  - Legal counsel.
  - Sponsored programs.
  - Education coordinator.
  - Documents specialist.
- Delegate responsibilities and tasks
- Use other committees
  - Specific purpose (e.g. conflict of interest).
  - Get input and buy-in.

Conducting the Self-Assessment

- Identify who is the leader for the application.
- Identify who will work on the application.
- Divide tasks.
- There are 62 elements or standards to be addressed.
- Plan out the work to complete at your target date.
- A journey of 1000 miles begins with a single step.
  - Lao-tzu
- Get started!
- Keep working.
- Work toward your target date.

Organizing the Work

<table>
<thead>
<tr>
<th>Element</th>
<th>Laws</th>
<th>SOP(s)</th>
<th>GAPS</th>
<th>RESPONSIBLE PARTIES</th>
<th>SOP Due Date</th>
<th>Forms to create</th>
<th>Other Resources</th>
<th>Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Element</td>
<td>I.1.A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Element</td>
<td>I.1.B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Build in time to:

- Gather information and input.
- Develop new policies and procedures.
- Educate IRB members and researchers and research staff.
- Compliance issues.
- Culture shift.
- Prepare the application.
- Conduct an internal or external review of your application.
  - Include legal counsel.

THE STEP 1 PROCESS

Step 1 Application

- Application is submitted to AAHRPP
  - Instructions to complete an application are on the AAHRPP website.
  - Application form, overview, and SOPs.
  - Must be in English.
- Staff review the application within 60 days and provide feedback
- Site responses with changes to AAHRPP
Instructions and Form

- Read the “Instructions to Apply for Initial Accreditation and Reaccreditation.”
- Complete the “Step 1 Application Form for Accreditation.”
**Construct an Element-by-Element Index to the Supporting Documents**

- List the supporting documents for each element.
- Reference the document number.
- Provide a brief explanation, if needed.
- Make it easy for site visitors to find the information.
- Use page numbers, paragraph numbers, line numbers, item numbers, chapter titles, and section headings to pinpoint the supporting information.
- This becomes Section C of your application.

**Step 1 Application – Section C.**
Copy Documents

- Make a copy of each document authored by your organization and cited in the Element-by-Element index.
- If cited for more than one element, include only one copy.
- Assign a reference number to each document.
- This becomes Section D of your application.

Within 60 days You Will Receive the Step 1 Report

- Read through the entire report.
- Develop a plan to respond to each Element—Pick the ones to finish first.
- Develop a timeframe to respond to all Elements.—Usually 60 days.
- Contact your assigned accreditation director for any clarifications.

Step 1 Review of Application Materials
After you Receive the Step 1 Review of Materials:

- Address each area of concern.
- Send revised policy and procedure or revised forms in an email
  - One element per email
  - Type element being addressed in subject line (e.g. II.2.A.).
- The Step 1 report is very prescriptive (e.g. to policy 25, add...)
- This is an interactive process – talk and ask questions. While most work can be done by email, sometimes a phone call is in order

Element-by-Element Response

STEP 2
SITE VISIT
The Accreditation Process

- Self Assessment
- Submit Application
- Evaluation of Written Materials
- Submit Revised and Additional Materials
- Site Visit - Evaluation of Practices
- Draft Site Visit Report
- Response Evaluation
- Prepare Response
- Counsel on Accreditation
- Accreditation Decision

Step 2 Application

- Application is submitted to AAHRPP
  - Instructions to complete an application are on the AAHRPP website
  - Application form, overview, SOPs, IRB minutes, IRB rosters, key personnel, and active protocols
  - Must be in English
- Site visit is scheduled within 90 days

Site Visit Agenda

- Agenda set up in advance
- Organization works with program assistant and accreditation director to finalize agenda.
- Team has flexibility to change agenda
Privacy and Confidentiality

- No contact with visitors before or after site visit.
- Direct all inquiries to AAHRPP staff
  - An accreditation director will be assigned
Site Visit Outline

- Introductory meeting.
- Records review.
- Front-line interviews.
  - IRB chairs, members, staff.
  - Researchers and research staff.
- Management interviews.
- Senior management interviews.
- Closeout session.

Introductory Meeting:

- Typically includes:
  - Site visit team.
  - Lead contact from your organization.
  - Organizational official.
  - Other staff members that you’d like to invite.
- Team leader will introduce site team members and will describe the accreditation process.
- You can introduce people from your organization and present a short overview of your program.
- This is also an ideal time for representatives of your organization to ask questions.

Records Review

- Protocol files
- IRB records
- Contracts
- Training records
- Site agreements
- Site records
- Study logs
- Non-compliance
- Conflict of interest
- Scientific review
Records Review

- Representative sample.
- Chosen in advance.
- Requested shortly before site visit.
- Site visitors may ask for additional records on-site.
- Focuses on key areas.

Closeout Session

- Organization decides who attends.
- Site visitors describe their observations.
- Chance to:
  - Provide additional information.
  - Clarify issues.
  - Correct errors.
- Site visitors offer general advice.

After the Site Visit You Will Receive a Draft Site Visit Report in No Later Than 30 Days.

- Read through the entire report.
- There will be “Observations” and “Areas of Concern.”
Draft Site Visit Report

Writing a Response

- Develop a plan to address the “Areas of Concern.”
  - Correct errors in fact.
  - Change practice to match policies.
  - Change policies to match practice.

- Make corrective actions:
  - Indicate the changes you made.
  - Indicate education for key people involved.
  - Monitor to ensure implementation of the changes.

- You may communicate with AAHRPP for information and advice during the 30 days – email or phone.

Response to the Draft Site Visit Report

- Evaluated by site visit team.
- Response and evaluation go to Council on Accreditation for decision on accreditation.
Response - Final Site Visit Report

The Accreditation Process

Council Determinations

- New applicants
  - Full Accreditation
  - Qualified Accreditation
  - Accreditation - Pending
  - Accreditation Withheld

- Renewing applicants
  - Full Accreditation
  - Accreditation - Pending
  - Probation
  - Accreditation Revoked
Accreditation Status

- New applicants
  - Valid for three years
- Renewing applicants
  - Valid for five years

Accountability While Accredited

- Annual reports
  - Notify AAHRPP of sentinel changes.
- Status reports
  - Used to document practice, including education and monitoring.
- Limited site visits
  - Used to verify practice.
- Mandatory site visits
  - Used to investigate wrongdoing.

The Accreditation Process

[Diagram showing the accreditation process]
Element I.1.A. The Organization has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program.

- Research is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge, or an equivalent definition.
  - The Organization should define "a systematic investigation."
  - The Organization should define "generalizable knowledge."

Element I.1.E. The Organization has an education program that contributes to the improvement of the qualifications and expertise of individuals responsible for protecting the rights and welfare of research participants.

- The Organization maintains a list of educational activities.
- Policies and procedures include initial training requirements, including timeframes, for Researchers and Research Staff; IRB staff, IRB chairs, and members; and others.
- Policies and procedures describe continuing education requirements and timeframes.
- Policies and procedures describe what actions the IRB or the Organization takes if training requirements are not fulfilled.
Standard I.2: The Organization ensures that the Human Research Protection Program has resources sufficient to protect the rights and welfare of research participants for the research activities that the Organization conducts or oversees.

- The Organization has allocated the financial and personnel resources necessary to carry out the policies and procedures of the HRPP.
- The Organization periodically reviews the resources allocated to the HRPP and adjusts resources as needed.
- The Organization periodically evaluates whether the number of IRBs is appropriate to the volume and types of research reviewed, and makes adjustments so that reviews are accomplished in a thorough and timely manner.

Standard I.3: The Organization’s transnational research activities are consistent with the ethical principles set forth in its Human Research Protection Program and meet equivalent levels of participant protection as research conducted in the Organization’s principal location while complying with local laws and taking into account cultural context.

- The Organization has policies and procedures for reviewing transnational research including:
  - Ensuring appropriate expertise and knowledge of the country(ies) either through IRB membership of consultants.
  - Confirming the qualifications of the researchers and research staff for conducting research in that country(ies).
  - Initial review, continuing review, and review of modifications
  - Knowledge of local laws
  - Post-approval monitoring
  - Handling of complaints, non-compliance and unanticipated problems involving risk to participants or others.
  - Consent process and other language issues.

Element I.4.C. The Organization promotes the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results.

- The Organization supports mechanisms that allow Researchers to involve community members in the research process, when appropriate.
- Policies and procedures describe the additional considerations for reviewing community-based research.
- When appropriate, the Organization promotes the involvement of community members in the design and implementation of research.
- When appropriate, Researchers involve community members in the design, conduct, and analysis of data.
- When appropriate, Researchers inform community members about the results of the research study and utilize community members to help disseminate results.
Standard I-4: The Organization responds to the concerns of research participants.

- Element I.4.A. The Organization has and follows written policies and procedures that establish a safe, confidential, and reliable channel for current, prospective, or past research participants or their designated representatives that permits them to discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol or plan.

- Element I.4.B. The Organization conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement.
  - Website
  - Brochure about research

Standard I-5: The Organization measures and improves, when necessary, compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The Organization also measures and improves, when necessary, the quality, effectiveness, and efficiency of the Human Research Protection Program.

- Element I.5.A. 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.

- Element I.5.B. 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.

For both I.5.A and I.5.B, policies and procedures state:
- The plan states the goal… **At least one goal**
- The plan defines measures… **At least one measure**
- The plan describes the methods to assess …and make improvements.
Collect Metrics for Your Program

- To know your program.
- To assess your program.
- For quality improvement.
- To compare your program.

Element I.5.D. The Organization has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. The Organization works with the Institutional Review Board or Ethics Committee, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate.

- Definitions:
  - Non-compliance
  - Serious Non-Compliance
  - Continuing Non-Compliance

Element I.5.D. Non-Compliance

- Reporting or Finding Non-Compliance
  - Reports
  - Audits
  - Complaints
  - Protocol Deviations
  - Unanticipated problems involving risks to participants or others
- Process to investigate non-compliance
- Review by the IRB
  - Manage non-compliance
    - Possible actions
  - Determination if serious or continuing
- Reporting
Element I.6.A. The Organization has and follows written policies and procedures to identify, manage, and minimize or eliminate financial conflicts of interest of the Organization that could influence the conduct of the research or the integrity of the Human Research Protection Program.

- Policies and procedures provide a definition of organizational financial conflict of interest that includes: licensing, investments, gifts, other financial interests
- Policies and procedures describe the process to identify or disclose financial conflicts of interest of the organization:
  - A policy addressing financial conflict of interest pertaining to technology transfer and patents is not required if this matter is addressed in other policies and procedures.
  - A separate policy addressing the identification and management of financial conflicts of interest of senior administrative officials is not required, if this is covered in the Organization’s financial conflict of interest policy for individuals.
- Policies and procedures describe the process that the Organization uses to evaluate organizational financial conflict of interest.
- Policies and procedures describe:
  - The process the committee or individual who evaluates and manages financial interests of the Organization uses to inform the IRB of the evaluation, including any management plan.

Element I.6.B. The Organization has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and Research Staff that could influence the conduct of the research or the integrity of the Human Research Protection Program. The Organization works with the Institutional Review Board or Ethics Committee in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate.

- Define what financial interests must be disclosed.
- Process of disclosure for researchers and research staff.
- Process for management.
- IRB considers management plan in its review.

Standard I-8: The Organization works with public, industry, and private Sponsors to apply the requirements of the Human Research Protection Program to all participants.

- Element I.8.B. In studies where Sponsors conduct research site monitoring visits or conduct monitoring activities remotely, the Organization has a written agreement with the Sponsor that the Sponsor promptly reports to the Organization findings that could affect the safety of participants or influence the conduct of the study.
- Element I.8.C. When the Sponsor has the responsibility to conduct data and safety monitoring, the Organization has a written agreement with the Sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to the Organization.
- Element I.8.E. When participant safety could be directly affected by study results after the study has ended, the Organization has a written agreement with the Sponsor that the Researcher or Organization will be notified of the results in order to consider informing participants.
Domain II: IRB or EC

- Standard II-1: The structure and composition of the IRB are appropriate to the amount and nature of the research reviewed and in accordance with requirements of applicable laws, regulations, codes, and guidance.
- Standard II-2: The IRB evaluates each research protocol or plan to ensure the protection of participants.
- Standard II-3: The IRB approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance.
- Standard II-4: The IRB provides additional protections for individuals who are vulnerable to coercion or undue influence and participate in research.
- Standard II-5: The IRB maintains documentation of its activities.

Element II.1.B. The IRB or EC has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB or EC are periodically reviewed and adjusted as appropriate.

- Policies and procedures describe the appointment of:
  - IRB members.
  - IRB chairs and vice-chairs when appropriate.
  - Alternate members.
- Policies and procedures describe the function of alternate members.
- Policies and procedures describe the periodic assessment and feedback provided to:
  - IRB members.
  - IRB chairs, and vice-chairs when appropriate.
  - IRB staff.

Evaluation of IRB Chairs and Members

- This requirement is making a difference in the quality, efficiency, and effectiveness of IRBs.
- Areas of need are being identified and addressed.
  - Membership.
  - Education.
- Less productive members are being remediated or replaced with higher performing members.
Element II.2.C. The IRB or EC has and follows written policies and procedures for conducting meetings by the convened IRB or EC.

- Scheduling of meetings
  - Timing of distribution of documents
  - Limits of items on the agenda, if any.
- Conducting convened meetings
  - Quorum
  - Non-scientist must be present
  - Unaffiliated members should be present most of the time.
  - Member representing the perspective of participants should be present most of the time.
  - Other required expertise.
- Use of technology at meeting.
- Voting
- Role of chair and vice-chair

Element II.2.D. The IRB or EC has and follows written policies and procedures to conduct reviews by the convened IRB or EC.

Element II.2.D.1. – Initial review
Element II.2.D.2. – Continuing review
Element II.2.D.3. – Review of proposed modifications to previously approved research

Element II.2.E. The IRB or EC has and follows written policies and procedures to conduct reviews by an expedited procedure, if such procedure is used.

Element II.2.E.1. – Initial review
Element II.2.E.2. – Continuing review
Element II.2.E.3. – Review of proposed modifications to previously approved research

Element II.2.G. The IRB or EC has and follows written policies and procedures for suspending or terminating IRB or EC approval of research, if warranted, and for reporting these actions, when appropriate.

- The IRB has the authority to suspend or terminate its approval of the research.
- Designate the individuals who have the authority to suspend or terminate research on an urgent basis.
  - IRB: for example IRB director, IRB chair
  - Outside of the IRB: for example, vice president for research, organizational official
- When suspending or terminating research, the IRB makes determinations about the participants in the study.
- Internal reporting
- External reporting
Standard II-3: The IRB or EC approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance

- Risk and benefits
- Data and safety monitoring
- Equitable selection of participants
  - Recruitment and advertisements
- Privacy of participants
- Confidentiality of data
- Consent process
- Waivers of consent process or documentation.

Element II.3.F. The IRB or EC has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process.

- Review of the consent process.
  - Who conducts consent?
  - Waiting period to decide
  - Language used
  - Steps to minimize coercion or undue influence.
- Consent document
  - Elements of disclosure

Element II.2.F. The IRB or EC has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate.

- Definitions and reporting requirements:
  - Adverse events.
  - Protocol deviations.
  - Unanticipated problems involving risks to participants or others.
- Process to review and manage those with no more than minimal risk.
- Review and management by the IRB.
- Reporting.
Element II.4.A. The IRB or EC has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance.

- Determinations and documenting additional protections for vulnerable participants:
  - Pregnant women.
  - Children.
  - Prisoners.
  - People with diminished capacity.
  - Other vulnerable participants.

Domain III: Researcher and Research Staff

Standard III-1: In addition to following applicable laws and regulations, Researchers and Research Staff adhere to ethical principles and standards appropriate for their discipline. In designing and conducting research studies, Researchers and Research Staff have the protection of the rights and welfare of research participants as a primary concern.

Standard III-2: Researchers and Research Staff meet requirements for conducting research with participants and comply with all applicable laws, regulations, codes, and guidance; the Organization’s policies and procedures for protecting research participants; and the IRB’s or EC’s determinations.

Questions
Developing an Integrated and Communicative HRPP

Integrate [in-ti-greyt]  in-te-grate
verb (used with object)
1. to bring together or incorporate (parts) into a whole.
2. to make up, combine, or complete to produce a whole or a larger unit, as parts do.
3. to unite or combine.

Outline:
- The HRPP concept
- The AAHRPP Standard
- Identification of the HRPP components
- Assessment of Component function
- Coordination of HRPP
- Communication about and to HRPP
- Evaluation of the HRPP
- Discussion
The Concept

- DHHS commissioned the Institute of Medicine to empanel a committee to evaluate human research protections. (2001)
- “Preserving Public Trust: Accreditation and Human Research Participant Protection Programs” [HRPPPs]

IOM Committee:

“the committee envisions a broader human research participant protection system than just the IRB, with multiple functional elements that in total are referred to as human research participant protection programs, or HRPPPs”

They Advocated for:

“Comprehensive review of protocols (including scientific, financial conflict of interest, and ethical reviews); ethically sound participant-investigator interactions; on-going and risk-appropriate safety monitoring; and quality improvement and compliance activities. “
To be Effective:

“…HRPPs should operate within environments that emphasize accountability for the provision of participant protection, assure adequate resources for robust protection activities, provide ethics education programs to those conducting and those overseeing research with humans, and seek open communication and interaction with all stakeholders in the research enterprise.”

AAHRPP Standard I-1:

The Organization has a systematic and comprehensive Human Research Protection Program that affords protections for all research participants. Individuals within the Organization are knowledgeable about and follow the policies and procedures of the Human Research Protection Program.

Evaluation Instrument for Accreditation:
Commentary on Domain I

This Domain describes the structural characteristics of the entity that assumes responsibility for the Human Research Protection Program (HRPP) and applies for accreditation. The organizational structure is the means by which the Organization meets the range of responsibilities of the HRPP.
The Organization applies its HRPP to all research regardless of funding source, type of research, or place of conduct of the research. The Organization exercises these responsibilities through relationships with Researchers and Research Staff, IRBs or ECs, Sponsors, participants, and the community.

An Organization has the responsibility not only to protect the rights and welfare of human research participants but also to involve research participants in the research enterprise. The involvement of research participants at every stage of the research enterprise helps everyone to achieve the ethical principle of respect for persons. In addition to enhancing the appropriate safeguards and protecting the rights and welfare of research participants, involving research participants in the research process can improve recruitment and retention of participants and also improve the overall quality of research.

The conduct of research is highly dependent upon the partnership between Organizations and Sponsors. A Sponsor is the company, institution, individual donor, or government agency responsible for the initiation, management, or financing of a research study. Sponsors may enter into agreements with intermediaries that act as agents, such as clinical research organizations or coordinating centers. In sponsored research, both the Sponsor and the Organization have obligations to protect human research participants. In this Domain, the focus is on the obligations of the Organization. In seeking accreditation, the Organization must address human research protection requirements with all Sponsors and apply its HRPP to all sponsored research.
Flexibility

- AAHRPP is flexible about the structure and components of your HRPP.
- Each HRPP looks different.
- There are many right ways to design an HRPP—find what works for your organization.

Identification of the Components

- During the self assessment for step one of the application:
  - How, where, and by whom, do the standards get implemented?
- Think broadly—whole organization

Identification of the Components

- During the preparation for re-accreditation, identify changes in the program components
  - What has changed in the how, where, by whom
    - New initiatives?
    - New standards?
    - New personnel—reorganization of activities?
Think Big and Broadly (Outside the IRB)

- Where are contracts managed?
- Who conducts education and training?
- Where is scientific review performed?
- How is monitoring implemented?
- How are legal questions addressed?
- How is communication (outreach) handled in your organization—media relations—community partnerships—research outreach center—extension service?

Not the IRB

- It is not the IRB’s job to implement every standard—some standards and elements are outside of the IRB’s expertise or charge.

Assessment of Functions

- Meet with all components and assess functions based on the Evaluation Instrument.
Coordination of Components

- Assess how the component parts interact to accomplish the requirements in the standards.
- Make changes or improvements based on the assessment.
- Hold components accountable for their role in the HRPP.

Connections and Communication

- Researchers and research staff are part of the HRPP.
- They should know this!
- Communicate often and succinctly with the component parts of the HRPP.
- Recognize and reward participation.

Evaluation

- The entire HRPP should be evaluated on a periodic basis.
  - Determine what/who should be evaluated.
  - By whom?
  - How will you have evaluation documented?
  - Who should review results of evaluation?
  - Who should determine action required following the review?
An Effective Program is

- Integrated—parts working together
- Continuously looking for ways to improve

Leadership

- Critical to the success of an HRPP is leadership—at all levels and in all component parts of the HRPP.

Recognizable

- Members of the organization should know what parts of the process comprise the HRPP and they should know how the parts work together.
Questions to Ask Yourself:

Do we have a Program?
Are all components in functioning?
Is the program strong and reliable?
Is the program recognizable inside the institution?
Can we describe the program to outsiders?

Focus on outcomes and processes

Ongoing Process of Evolution

- Programs change, grow, expand
- Mission may change
- Program should expand or change accordingly

IOM Model

"The components in the large box are all parts of an HRPPP. Arrows represent information flow pathways, not organizational responsibilities. All units within an HRPPP should have formalized communication procedures."
Every Program is Different

- How does it work at your institution?
“A Rose by Any Other Name….”

Other commonly used terms for “contingent approval:”

- Approved with Stipulations
- Conditional Approval
- Approved Pending Modifications
- Accepted Pending Modifications
- Others???

Possible IRB Actions

<table>
<thead>
<tr>
<th>IRB Action</th>
<th>Full Committee</th>
<th>Expedited</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval</td>
<td>• Approval criteria met.</td>
<td>• Acceptable as is; no changes required.</td>
</tr>
<tr>
<td>Contingent Approval</td>
<td>• Approval criteria met.</td>
<td>• Specific, non-substantive changes required.</td>
</tr>
<tr>
<td>Deferred</td>
<td>• Approval criteria not met.</td>
<td>• Substantial modifications and/or additional information required to make determination.</td>
</tr>
<tr>
<td>Disapproval</td>
<td>• Approval criteria not met (nor likely to be met).</td>
<td></td>
</tr>
</tbody>
</table>
### Federal Criteria for Approval

1. Risk to subjects are minimized
2. Risks to subjects are reasonable in relation to anticipated benefits and the importance of the knowledge that may reasonably be expected to result
3. Selection of subjects is equitable
4. Informed consent will be sought or waived in accordance with 45CFR46.115 (and/or other applicable regulations)
5. Informed consent will be documented in accordance with 45CFR46.117 (and/or other applicable regulations)
6. Provisions for monitoring collected data are adequate...
7. Provisions to protect for privacy of subjects are adequate...
8. Provisions to protect confidentiality of data are adequate...
9. Vulnerable populations are adequately protected by additional safeguards.
10. If multi-site research, management of information... is adequate
11. New information that might affect subject willingness to continue participation will be provided.

### Other Criteria for IRB Approval

- State Laws
- Institutional Requirements
- Veterans Affairs Health Care Centers
- Funding Agencies
- Country Requirements

### Regulatory Criteria for IRB Approval Met*

- **Approved**: Acceptable as is. *No changes required.*
- **Contingent Approval**: *Minor specific changes are required.* Member comments must be *directive* requesting simple concurrences or specific, non-substantive changes.

*As determined by the IRB Chair or designee*
What is a contingent approval?

- A specific determination made by
  - The majority of voting members at a convened meeting of the full IRB or
  - An IRB Chair or designee conducting IRB review under expedited procedures

- The overall IRB determination must be that the study meets the regulatory requirements for approval (i.e., 45CFR46.111; 21CFR56.111, and others as required—DOD, DOE, EPA...) but...minor specific changes or additions are required.

After the determination of “contingent approval” what happens next?

- The PI must modify the IRB submission (protocol, consent form, recruitment materials, other attachments) in a way directed the IRB.
- The IRB Chair or designee must review the written response to determine if the response meets the requirements of the contingencies (stipulations, conditions).

What Should Be Included in Contingent Approval Correspondence?

- Request for a specific change or addition
- Brief rationale for change, as appropriate.
Regulatory Criteria for IRB Approval

Not Met*

- DEFERRED (also called TABLED**) FOR RE-REVIEW: Substantial modifications and/or additional information (e.g., details, clarifications, justifications) are required that are directly relevant to the Criteria for IRB approval.

- DISAPPROVED: Only the full Board may disapprove a study.

*As determined by the IRB.
**Tabled is sometimes used for cases in which criteria for a full board review are not met (i.e., loss of quorum, expert).

IRB Review of PI Response to Contingent vs. Deferred Comments

- CONTINGENT APPROVALS: IRB Chair or designee will verify that the appropriate additions/corrections were made and will
  - approve the study
  - impose additional contingencies or
  - return it to full committee.

- DEFERRALS: Require that the study with the additional information or modifications be reviewed by the convened meeting of the Full Board.

Examples of Contingencies

Example 1: As Calcipotriene can cause elevations of serum calcium, revise item 5.0 below to exclude subjects with hypercalcemia.

Example 2: The members noted that there was an inconsistency between the protocol and the consent form about dosing level. Please confirm their understanding that the Vasopressin inhaler will deliver 0.1 ml per actuation rather than 1.0 ml and correct the consent form in the description of procedures regarding the Vasopressin administration.
Examples continued…

Example 3: Due to the complexity of the biomedical procedures and the high level of potential risk of the study, the conduct of the consent process should be limited to the physician study investigators. Revise item 5.0 below to reflect this requirement.

Example 4: Please delete all references to children in your submission as clearly you will not be including participants below the age of 18 in this study.

Examples continued…

Example 5: The Response Form to be completed by potential subjects as part of the recruitment process asks them to complete the form “whether or not you are interested in participating in the study.” The form also contains fields for the potential subject to provide his or her name, address, cell phone number and email.

Please delete this requirement for those who do not wish to participate as you have provided no justification for maintaining this private information nor do you describe how you will protect the confidentiality of this data.

Example 5 continued…

If, however, you wish to retain this aspect of the study, provide a justification for doing so in your response. Also, explain in the form how this information will be used, how the confidentiality of the data will be protected, and make completion of this section optional for those who decide not to participate. The convened board of the Full IRB will review this additional information.

Note: Response maybe returned to Chair if study was initially submitted as minimal risk and meets the criteria for expedited approval.
Example continued…

Example 6: Please update item 7.0 below to (1) confirm our understanding that Phase 1 of the study has been completed and (2) that Phase 2 of the study has not yet started. Also provide your assurance that you will submit an amendment to the IRB before beginning recruitment for Phase 2.

Example 7: Before an IRB approval can be issued, the PI assurance must be completed. Please click the “PI Assurance” button…

Example continued…

Example 8: In the debriefing script, please provide the subjects with the option to withdraw their data from the research. Since subjects who consent to participate in the research will not be provided with complete information about the study prior to their participation, they should have the opportunity to withdraw their data after being informed of the information withheld from them.

Example continued…

Example 9: Please add the required IRB contact information to the Consent document below the contact information for the research team:

UCLA Office of the Human Research Protection Program (OHRPP): If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, please call the OHRPP at (310) 825-7122 or write to….
Phrases and Wording That Represent Deferrals Rather than Contingencies

- **Clarify**…the dosing…
- **Explain** whether you have considered the risk of …
- **Provide additional information about**… the methods that will be used to minimize risks to…the fetus in this study.
- **Describe**…the population…
- **Prepare a consent form for the**…control group…
- **The scientific design of this study**…

Note: Response maybe returned to Chair if study was initially submitted as minimal risk and meets the criteria for expedited approval.

Examples of Deferrals

**Example 1:** Revise sections X, Y and Z to consistently and accurately describe the intended subject population as well as the procedures to be performed by the investigator at this site. The members were unable to make an assessment of the risks and benefits of the study without this information.

**Example 2:** After considerable discussion, the members determined that the data safety monitoring plan is inadequate as presented. Your protocol does not describe stopping rules nor does it discuss who will be monitoring the safety of the participants. They asked that the study establish a formal data safety monitoring board. Please provide the details of how this will operate in your response. See guidance QRS on our website for additional information on this topic.
Helpful Tips

- Post or include directions to PI about how to respond to contingencies.
- Ask PI to use highlighted or tracked changes to identify specific revisions.
- Advise PI to call with any questions.
- SOPs should describe how responses to contingencies will be handled if PI does not respond as directed.
- Track commonly requested contingencies and make sure these are described in guidance or training for investigators.

Questions? Comments? Ideas?
Waiver or Alteration of Consent

- Waiver of or alteration in the consent process
  - IRB has authority under 45 CFR 46.116(c and d)
- Waiver of Requirement for Documentation of Informed Consent
  - IRB has authority under 45 CFR 46.117
- Waiver of consent for FDA-regulated studies
  - Covered under 21 CFR 50.23 and 50.24

Additional Requirements

- Children/Parents (Subpart D)
  - Assent of children and permission of parents generally required
    - 45 CFR 46.408(a)
    - Direct benefit exception for assent
  - Requirement for permission can be waived
    - Authorized under 45 CFR 46.408(c)
    - Not a reasonable requirement (e.g., abuse or neglect)
    - Appropriate mechanism substituted
Additional Requirements

- Department of Defense
  - Need approval of Secretary of Defense for "experimental subjects"
- Department of Education
  - Generally follows 45 CFR 46.116 and 46.408
  - May have FERPA and PPRA requirements
- Department of Justice
  - Consent required with DoJ-specific elements
- EPA
  - Generally follows 45 CFR 46.116 and 46.408

HRPP Requirements for Waiver Consideration

- Written policies and procedures
- Education
- Documentation

Written Policies and Procedures

- Conform to the regulations
- What if I "uncheck the boxes" on the FWA?
  - Equivalent protections or follow regulations
  - Can waive or alter some of the elements
    - Alternative procedures
    - Research-related injury
Education

- Investigators
  - Should be aware of their ability to request waivers or alterations of the consent process and waivers of the requirement to document consent
- IRB staff
  - Need to be able to advise investigators
- IRB chair and members
  - Critical
  - Need full understanding of requirements

Documentation

- IRB determinations must be fully documented
  - Waiver meets the regulatory requirements
  - Protocol specific information
- How should determinations be documented
  - Reviewer/IRB checklists
  - Minutes

Working with Investigators on Waivers

- Should I recommend requesting a waiver or alteration to the consent process
- Should I recommend requesting a waiver to document consent
- More applicable to social and behavioral science research
- May have to “convince” investigators that it is appropriate
  - Educate
  - Explain
  - They may still insist on a consent document
Outcome of an Appropriate Process

- Meets federal regulatory requirements
- Meets AAHRPP standards

Questions or comments
Making and Documenting Protocol Specific Determinations

Introduction

- Overview
- Goals and Objectives
- Applicable Standards
- Making Determinations
- Documenting Determinations
- Observations of a Site Visitor

Domain II: Institutional Review Board or Ethics Committee

Standard II-3: The IRB or EC approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance.

Standard II-5: The IRB or EC maintains documentation of its activities
Element II.5.B.

- The IRB or EC documents discussions and decisions on research studies and activities in accordance with legal and regulatory requirements, Sponsor requirements, if any, and organizational policies and procedures.

Documenting Determinations of the Convened Board

- Meeting minutes are the primary means of communicating the rationale for the IRB determinations. The IRB has a responsibility to communicate through meeting minutes that it considered each requirement in making each protocol determination.
- If the minutes don't document a thoughtful consideration the protocol application and the requirements it is as if it did not happen.

Good minutes should enable a reader who was not present at the meeting to determine exactly how, and with what justification, the IRB arrived at its decisions.
When Making IRB Determinations Using an Exempt/Expedited Review Process

- Not-Human subjects Research
- Exempt Research
- Expedited
  - Studies
  - Amendments/Modification
  - Continuing Reviews
  - Required Contingencies

How does the IRB Document Determinations?

How does the IRB document that all required approval criteria have been met and appropriate regulatory determinations have been made?

- IRB files – must show review process
- Reviewer checklists or notes – reviewer must cite specific category and document any waivers
- Correspondence with investigator (contingencies)
- Approval letters which cite specific Expedited or Exempt categories and any waivers

Criteria for Approval

45 CFR 46.111 & 21CFR 56.111
The IRB must satisfy all the regulatory review requirements. The Minutes Should Document any Specific Determinations made by the IRB or any Controverted Issues Related to the Criteria for Approval of Research:

- Risks to subjects are minimized (Element II.3.A.)
- Risks to subjects are reasonable in relation to anticipated benefits (Element II.3.A.)
- Selection of subjects is equitable (Element II.3.C. and Element II.3.C.1.)
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative (Element II.3.F., Element II.3.G., Element II.4.B., Element II.4.C.)
- Informed consent will be appropriately documented (Element III.1.F.)

Minutes Should Reflect IRB Determinations that:

- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects (Element II.3.B.)
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data (Element II.3.D. and Element II.3.E.)
- Determinations on vulnerable subjects (Element II.4.A.)

<table>
<thead>
<tr>
<th>Determination</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant risk and non-significant risk device determinations</td>
<td>21 CFR 812.2(b), 21 CFR 812.150(b)(9)</td>
</tr>
<tr>
<td>Approval of waiver or alteration of informed consent</td>
<td>45 CFR 46.116(c), 45 CFR 46.116(d)</td>
</tr>
<tr>
<td>Waiver of informed consent documentation</td>
<td>45 CFR 46.117(c) and 21 CFR 50.6(a)(1)(1)</td>
</tr>
<tr>
<td>Waiver of HIPAA Authorization</td>
<td>45 CFR 164.512(a)(1)</td>
</tr>
<tr>
<td>Waiver of HIPAA Authorization for recruitment on screening</td>
<td>45 CFR 164.512(a)(2)(ii)</td>
</tr>
</tbody>
</table>

Vulnerable Population - children:

Vulnerable Population - pregnant women, fetuses, neonates and fathers:
- 45 CFR 46.204, 45 CFR 46.205, 45 CFR 46.206, and 45 CFR 46.207

Vulnerable Population - prisoners:
- 45 CFR 46.200, 45 CFR 46.201, 45 CFR 46.202, and 45 CFR 46.207
VA Determinations VA Handbook
1200.05

Adults unable to consent in VA research
Waiver of requirement to maintain a master list of all subjects
If recruitment of non-Veterans is justified and appropriate
If medical record has to be flagged to protect the participant’s safety by indicating participation in the study and the source of more information on the study
The approval of research contingent on specific minor conditions by the chair, or designee, in the minutes of the first IRB meeting that took place after the date of the approval.
The determination of the level of risk
Attendance of members or alternate members who participated through videoconference or teleconference, and documentation that those members received all pertinent material before the meeting and are able to actively and equally participate in all discussions.

What are AAHRPP Site Visitors looking for in their Minutes Review?

- Actions taken by the IRB or EC in making required determinations
- Separate deliberations for each action
- Votes for each protocol as numbers for, against, or abstaining
- Attendance at the meeting (who is present for each vote)
- When an alternate member replaced a primary member
- The basis for requiring changes in research
- The basis for disapproving research
- The determination of the risk level with study-specific justification for the determination
- A written summary of the discussion of controverted issues and their resolution
- Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document
- For initial and continuing review, the approved period (if not 12 months—why)
- The names of IRB or EC members who left the meeting because of a conflicting interest along with the fact that a conflicting interest is the reason for the absence. (Documenting that the member is absent is not enough. Minutes should indicate that the member is absent because of a conflicting interest.)

Additional VA Considerations:

- The IRB provided the minutes for review of VA protocols to the Research and Development Committee.
- The IRB wrote minutes and made them available for review within three weeks of the meeting date.
- Once approved by the IRB members, IRB meeting minutes are not altered.
Making Determinations of Non-Compliance

- Non-compliance for matters that are reviewed at the convened IRB, the meeting minutes must capture that the matter was reviewed, whether or not the noncompliance presented serious and continuing noncompliance, the reasoning, and any controverted points or corrective actions.

Approving International Research

- STANDARD I-3: The Organization’s transnational research activities are consistent with the ethical principles set forth in its Human Research Protection Program and meet equivalent levels of participant protection as research conducted in the Organization’s principal location while complying with local laws and taking into account cultural context.

Element II.2.F. Unanticipated Problems Involving Risks to Participants or Others

- Each unanticipated problem involving more than minimal risks to participants or others is reviewed by the convened IRB or EC.
- Sufficient information is provided to primary reviewers and all other IRB or EC members.
Unanticipated Problems - Board Determinations/Considerations

- Suspension of the research.
- Termination of the research.
- Notification of current participants when such information may relate to participants’ willingness to continue to take part in the research.
- Non-compliance

Documenting Sponsor Requirements

When reviewing research sponsored by:
- Department of Defense
- Department of Justice
- Department of Education
- Department of Energy
- Environmental Protection Agency (EPA)
- Or when the sponsor contract requires the organization to follow ICH-GCP (E6)
- All required determinations must be met and documented.

Sponsor Requirements Example - EPA

For research conducted or supported by the EPA:
- The research do not involve the intentional exposure of pregnant women, nursing women, or children to any substance.
- 40 CFR 26 Subparts C and D are followed to provide additional protections to pregnant women and children as participants in observational research, i.e., research that do not involve intentional exposure to any substance.
Sponsor Requirements – Example DOJ

Department of Justice:
For research conducted within the Bureau of Prisons, the Organization, IRB, and researchers and research staff follows the requirements of 28 CFR 512, including:
- The project does not involve medical experimentation, cosmetic research, or pharmaceutical testing.
- The research design is compatible with both the operation of prison facilities and protection of human participants. The researcher observed the rules of the institution or office in which the research is conducted.
- Any researcher who is a non-employee of the Bureau signed a statement in which the researcher agreed to adhere to the provisions of 28 CFR 512.
- All research proposals are reviews by the Bureau Research Review Board.

Sponsor Requirements – Example DOD

Department of Defense:
- Researchers include additional safeguards for research conducted with international populations:
  - Researchers have permission to conduct research in that country by certification, or local ethics review.
  - Researchers follow all local laws, regulations, customs, and practices.

What are the Challenges with Element II.5.B?

Site Visitor Observations:
- Meeting minutes are not clear
- Difficult to re-construct meeting
- Failure to document discussions of controverted issues
- Failure to document determinations
- Over reliance on checklists – no substantive review recorded
- Failure to recognize & determine noncompliance
What are the Challenges with Element II.5.B?

Site Visitor Observations:
- No process for identifying required determinations (i.e. vulnerable populations, DOD studies) prior to meeting
- Staff recording minutes not always adequately trained
- Difficult to discern insufficient knowledge of regulations from failure to document
- IRB staff not used as consultants at meetings

Site Visitor Observations Subpart D – Children Additional Determinations

When research involves children, the following IRB decisions are documented:
- Applicable regulation - plus
- Whether the permission of one parent/guardian is sufficient or if permission from both parents/guardians is required and why?
- How assent is to be solicited or obtained, unless waived.

Site Visitor Observations Subpart B – Additional Considerations

- (e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
Suggestions on Ways to Meet Element II.5.B

- Identify required determinations before meeting and add them to the agenda
- Identify who has a COI before the meeting
- Develop review templates for studies that are enrolling vulnerable populations
- Develop review templates for studies sponsored by EPA, DOD, DOJ, DOE, etc. incorporate these into the review done by primary reviewer

Suggestions on Ways to Meet Element II.5.B

- Primary Review
- Substantive reviews
- If you use reviewer checklist that forces regulatory determinations then have the reviewer present his/her review from these at the meeting discussing the regulatory requirements for approval
- Consent form review

Contact Information

Kathleen Lawry
MetroHealth Medical Center
2500 MetroHealth Drive
Cleveland, Ohio 44109
216-778-2077
klawry@metrohealth.org
In the Beginning – Brief Perspective

- Accreditation of HRPPs was a new experience for those applying, site visitors and council members
  - All site visitors were from unaccredited institutions
  - Many council members were from unaccredited institutions
    - Now all are from accredited institutions

Attention to Consistency

- AAHRPP strives for consistency in application or interpretation of the Accreditation Standards
  - Training for Site Visitors
  - Training for Team Leaders
  - Training for Council Members
Effects of Change on Standards

- Must keep abreast of regulatory changes that might require revisions in standards
  - May result in Standard I-6 revisions
- Must be able to apply standards across a broad range of entities, domestic and international
  - Was part of changes in Standards ~two years ago (Some were not regulatory-related)

Rumors About AAHRPP Accreditation
Myth, Truth or Somewhere in Between

- We will present rumors we have heard
- We want to discuss them with you
- If you have one, tell us what it is

Rumor #1

- The success of the site visit depends on who the site visitors are.
Rumor #2

- Site visitors have to find something, even if it’s picky; otherwise, it would look like they were not doing their job.

Rumor #3

- AAHRPP is inflexible
  - With how/if standards are met
  - With scheduling site visits
  - With the site visit agenda

Rumor #4

- There’s a new focus every year or every couple years.
  
  Example – Institutions should focus on making sure IRB members and chairs are familiar with unanticipated problems, non-compliance and suspensions and terminations
Rumor #5

- Site visitors base their findings on a single instance of a deficiency or a single incorrect response from an interviewee.

Rumor #6

- The accreditation process leads organizations to do considerably more than is required by the regulations.
  - Example – You have to create checklists that you wouldn’t otherwise use.

Rumor #7

- Site visitors intentionally try to intimidate interviewees or trip them up by asking questions without a clear purpose.
  - Example – No clear order to the questions.
Rumor #8

AAHRPP will mold your policies (presumably in Step 1) to fit their expectations, even if they won't work for your site.

Rumor #9

Researchers assume (or were told) that site visitors will:
- Be asking specific questions about their studies
- Will ask to look at investigator study records
- Will be testing them on their knowledge of the regulations

Rumor #10

IRB members will be tested on their knowledge of the regulations.
Rumor #11

- If an institution has an electronic system, it is preferable that they print out copies of requested documents.

Rumor #12

- AAHRPP is easier on organizations applying for initial accreditation and the first re-accreditation visit is very tough with organizations being held to much higher standards than at the initial visit.

Rumor #13

- Although AAHRPP expects organizations to have QA/QI processes in place, it does not have them in place for itself.
Other Rumors?

- What have you heard?

Conclusion

- AAHRPP strives for consistency and transparency.
- The standards are spelled out as clearly as AAHRPP knows how. If a standard or element is not clear, or the rationale is not clear, ask for clarification.
- AAHRPP site visitors are peers and have been through the process. They know how much work is involved and they want you to do well.
- AAHRPP welcomes your feedback and suggestions.