Converting AAHRPP Requirements into Your Ongoing Quality Improvement Program

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Mayo Clinic

Elements of a Quality Management System

- Management Commitment
- Culture
- Customer Service & Satisfaction
- Measurement & Analysis
- Competence, Awareness & Training
- Documentation System
- Continuous Improvement

Mayo Clinic Human Research Subjects Protection Program
Institutional Review Board

2012 Quality Plan
Purpose and Content of Quality Plan

- Overarching Goals for the Office
- Use QMS to support daily operations as a management tool and basis for CI
- Monitor KPIs, collect customer feedback & identify non-conforming events
- Identify & Self-Monitor IRB processes
- Use data for corrective & preventive action planning

QMS Self-Monitoring Program

- Part of Annual Quality Plan
- Finalize monitoring focus on quarterly basis
- Prioritize monitoring based on:
  - Perceived risk
  - Uncertainty in our process among IRB staff
  - Previous history of problems
  - Response to AAHRPP required monitoring and status reports

Event Management Program

- Purpose – To identify areas for improvement
- Information captured from:
  - Operations problems, staff reports
  - Self-monitoring program
  - Voice of the Customer – surveys & concerns
  - Regulatory or compliance findings
- Process for event reporting, tracking, review, improvement and communication
Charge of HRPP Oversight Group

- To provide operational oversight to Mayo Clinic’s HRPP
- To evaluate the quality, resources, effectiveness and outreach of the HRPP
- To direct the implementation of planned improvements to the HRPP based on evaluation findings
- Ensure maintenance of AAHRPP Accreditation
Components of Mayo Clinic’s Human Research Protection Program

HRPP Component Reviews

- Developed tool to assess business processes of major components of HRPP
  - System to measure effectiveness of process
  - Measure against targeted performance
  - Training and Orientation
  - Internal and External Audits and Findings
  - Challenges performing HRPP related business processes

Summary

- QMS adds value to IRB & HRPP operations
- Quality Plan serves as guide & framework
- Provides simple and organized approach
- Monitoring and Event Management help in decision-making
- Flexibility important in model for oversight of HRPP
Thank You

- Mayo Clinic IRB Staff
- Mayo Clinic Office of Research Quality Management Services
Converting AAHRPP Requirements into Your Ongoing Quality Improvement Program… in the VA

Making the Regulations Work for You: It’s a Process

- Why?
- What?
- How?

Why We Have to! per VHA Handbook 1200.05

- Any VA facility with an FWA must have obtained Full Accreditation of its HRPP

- After Full Accreditation of its HRPP, it must adhere to the Accrediting Organization’s requirements for maintaining accreditation.
Resistance is Futile!

Research \[\rightarrow\] Regulations \[\rightarrow\] Accreditation

What it Means?

per VHA Handbook 1200.05

**Accreditation.**
- process of obtaining independent recognition that a HRPP affords protection to human subjects
- meeting and exceeding the prevailing ethical, professional, and regulatory requirements
- HRPP engages in continuous quality improvement.

What it Really Means for You?

- AAHRPP Accreditation Process and your HRPP
  - Rigorous and consuming
  - Requires long hours and attention to detail
  - Requires resources
  - Exhaustive…. and exhausting

- It is also…. a great way to revisit your program and processes from a global all encompassing perspective
A Systematic Approach is the Key!

- What you know
  - Accreditation (every 5 yrs.)
  - Annual accreditation report
  - Annual HRPP review
  - “Surveys” “Assessments” by...
- Who you know
  - Organizations i.e. FDA, ORO/RIPP, OIG, OI&T/ITOC, and on and on.... and on....
  - Key personnel

AAHRPP Requirements are not NOVEL

- Remember the Regulations!...
  - The Common Rule:
    - DHHS: Title 45 part 46 Protection of Human Subjects
    - Dept. of VA: Title 38 part 16 Protection of Human Subjects
    - FDA: Title 21 part 50 Protection of Human Subjects
  - OHRP
  - FDA
  - VA
    - VHA Handbooks:
      - 1200.05
      - 1200.01
      - Etc... Too many to list!
  - AAHRPP

Work Smarter

- Many of the Regulations overlap between regulatory bodies/agencies
  - Use one method to fulfill all requirements
    - e.g. Security Assessments
      - AAHRPP
      - ORO/RIPP
      - ITOC
      - ISO
      - PO
Work Smarter…

- Many regulations have common themes within them or one committee/person is tasked with the oversight.
  - i.e. "must be reviewed/evaluated/assessed annually"
  - Use one process that incorporates all annual requirements.

Annual Evaluation of the HRPP

- Provide a global view of the program … in a snapshot.
- Allows us to see progress from previous year
- Provides the opportunity for feedback
- Allows us to see areas of improvement
  - Great time to incorporate topics that require similar attention:
    - Outreach
    - Credentialing/Scopes
    - WOC

“The times they are a changing….”

- Regulations/accreditation standards change or are modified often!
  - Know your documents/resident expert on documents and make consistent updates.
- Use this as a time to educate/re-educate staff
  - Boards/committees
  - Update/Notification emails to Research Staff
  - “What’s new” folder
Share the Love!

- Delegate/defer to the experts… this is not easy!
  - ACOS or C/R&D
  - IRB Admin/IRB
  - R&D
  - SRS
  - RCO

☑ Involved staff = educated staff = invested staff!

Accreditation Facilitates Quality Improvement

- The accreditation process should be seen as an OPPORTUNITY
- Gives you guidelines
- Regulations provide provisions
- Requirements help provide context and schema

In Summary

- Understand the process
- Consolidate the work
- Keep up with changes
- Share the responsibility
Questions?

- Contact info:
  Shayma.Khalil@va.gov
  Research Office: 828-299-5909
  Direct: 828-298-7911 x 5788
  Charles George VA Medical Center
  1100 Tunnel Rd. (151)
  Asheville, NC 28805
After Site Visitors Leave or Preparatory to a Site Visit

- What happens next?
- What elements and standards need enhancing?
- Opportunity for ongoing CQI

Continuous Quality Improvement

Know your system

- Outputs: What do we make?
- Customers: Who do we make it for?
- Customer knowledge: What do we know about them? How do they judge us?
- Community needs: What is the underlying need for what we make?
- Processes: What processes do we use to make what we make?
- Inputs: What comes in and is transformed to make what we make?
- Suppliers: Who provides inputs?
- Vision: What is our aim?
- Plan to improve: What is important to improve?
What is important to improve?

- Overall program
- Start small
- Use the AAHRPP standards and elements

AAHRPP Standards and Elements

- Great starting place
- Separated into broad areas (standards)
- Further separated into small areas (elements)
- Even further (many items in each of the elements)

Standards and Elements: Use the Evaluation Instrument

Processes: (“change” is an event; “process” is the transition)
- Define the process, current process first
- Decide on a beginning and an end
- Start at a high level as the backbone and other charts will follow
Areas of Improvement

- What changes did/can you make?
- How did you report it to AAHRPP?
- How are you measuring it?
- Did it work?

Example: Element I.4.B Community Outreach

- 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.

What do you currently do?

- Volunteer brochures
- Website
- Social media
What can you add or change?

Pick a change that is measurable

- Visits to health fairs
- Presentations at churches, community centers, etc.
- On campus/off campus activities (malls, etc.)
- Change an existing venue
- Addition of a “suggestion box”

How do you know the change is an improvement?

- Flow out the process
- Eliminate non-value added steps
- Collect data over time

What would an improvement look like?

- Element I.4.B: Increase in awareness
  - Increase in enrollment or attendance at a venue
  - Increase in complaints, inquires or suggestions
Periodic Assessment of the Element

- Look at all the activities under the element
- Website
- Suggestion box
- Is it working?
- Do you add something to the program?

What next?

- Repeat for every element
- Start with ones that are identified as needing improvement
- Move to all of the elements gradually
- Look at any areas of distinction to use as models

Remember

- The AAHRPP standards and elements are comprehensive
- If you integrate them into your CQI, you will have a strong HRPP program
Thank you

Questions?
Strategies for Negotiating AAHRPP Required Language into Contracts

What’s the issue?
In sponsored research, both the sponsor or its agents, and the Organization have obligations to protect research participants. These obligations include the ethical conduct of the research, dissemination of knowledge gained from the research, and that the interests, health and safety of current and future research participants are protected.

What’s the element?
- Element I.8.A. The Organization has a written agreement with the Sponsor that addresses medical care for research participants with a research-related injury, when appropriate.
What’s the element?

- 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.

What’s the element?

- 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.

What’s the element?

- Element I.8.D. Before initiating research, the Organization has a written agreement with the Sponsor about plans for disseminating findings from the research and the roles that Researchers and Sponsors will play in the publication or disclosure of results.
What’s the element?

- 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.

What might you consider?

- What does your organization’s contract template language
- What happens when the sponsor provides its own template document
- What happens if a sponsor resists including required human protections language in contracts

What might you consider?

- Is the requirement that the IRB approve the data and safety monitoring plan addressed
- How are research findings disseminated
- How is consistency between the contract and consent document verified
What materials will be looked for?

- Executed contracts
- Consent documents
- Contract templates
- Master agreements

Characteristics of 129 Policies for Injuries to Research Volunteers at 102 Academic Medical Centers in the United States

<table>
<thead>
<tr>
<th>Policy Provision</th>
<th>Policies (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free care not provided</td>
<td>66</td>
</tr>
<tr>
<td>Medical treatment billed at usual and customary fees</td>
<td>54</td>
</tr>
<tr>
<td>Emergency or immediate treatment billed at usual and customary fees</td>
<td>12</td>
</tr>
<tr>
<td>Free care provided</td>
<td>21</td>
</tr>
<tr>
<td>Medical treatment</td>
<td>10</td>
</tr>
<tr>
<td>Emergency or immediate care</td>
<td>11</td>
</tr>
<tr>
<td>Care billed to insurance first; free for those without insurance</td>
<td>13</td>
</tr>
<tr>
<td>Medical treatment</td>
<td>9</td>
</tr>
<tr>
<td>Emergency or immediate care</td>
<td>4</td>
</tr>
<tr>
<td>Care billed on a case-by-case basis</td>
<td>5</td>
</tr>
<tr>
<td>No publicly accessible information</td>
<td>24</td>
</tr>
</tbody>
</table>

NEJM 2006;354:1871

Differences in Perception of Restrictive Provision in Clinical Trial Agreements

<table>
<thead>
<tr>
<th>% Judging Provision Acceptable</th>
<th>RA (n)</th>
<th>CT (n)</th>
<th>OR (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Industry sponsor will own the data produced by the research</td>
<td>80</td>
<td>42</td>
<td>18</td>
</tr>
<tr>
<td>Faculty investigator in an industry-sponsored trial is not permitted to alter the study design after the agreement is executed</td>
<td>68</td>
<td>62</td>
<td>N/A</td>
</tr>
<tr>
<td>Industry sponsor may review manuscript written by the investigators for an agreed-on period before publication</td>
<td>96</td>
<td>47</td>
<td>N/A</td>
</tr>
<tr>
<td>Industry sponsor may decide that the results should not be published</td>
<td>9</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Industry sponsor may make revisions to a manuscript written by the investigators, other than revisions relating to the protection of proprietary information</td>
<td>6</td>
<td>38</td>
<td>23</td>
</tr>
<tr>
<td>Industry sponsor may delay publication beyond the agreed-on time for manuscript review while a patent application is filed</td>
<td>87</td>
<td>46</td>
<td>N/A</td>
</tr>
<tr>
<td>Industry sponsor may prohibit individual site investigators in a multi-center trial from publishing manuscripts independently of the sponsor or group</td>
<td>10</td>
<td>48</td>
<td>N/A</td>
</tr>
<tr>
<td>Industry sponsor will write up the results for publication and the investigators may review the manuscript and suggest revisions</td>
<td>50</td>
<td>56</td>
<td>29</td>
</tr>
<tr>
<td>After the trial is over, the investigators may not discuss research results (including presentations at scientific meetings) until the sponsor consents to dissemination</td>
<td>21</td>
<td>38</td>
<td>29</td>
</tr>
<tr>
<td>After the trial is over, the industry sponsor may prohibit investigators from sharing raw research data with third parties</td>
<td>41</td>
<td>48</td>
<td>29</td>
</tr>
</tbody>
</table>

RA = research administrators (107); CT = clinical trialists (593); OR = other researchers (291)
Investigator Perceptions of Office of Research Administration

- Investigator rating of research administration’s ability to maintain ethical standards when negotiating clinical research contracts
  - 48% very high; 32% high; 8% medium; 2% low; 10% don’t know
- 35% of investigators felt office was overprotective: 63% felt it was about right; 2% felt it was underprotective
- 36% often felt some of the provisions the research office wanted were unnecessary
- 49% felt that it often or always took too long to negotiate and execute agreements

Investigator Perceptions of Office of Research Administration

- 30% of investigators felt office of research administration had stricter standards for what should be in a CTA than they did
  - 13% believed they had stricter standards; 57% thought the standards were the same
- 91% of research administrators felt their office had stricter standards than the investigator; none felt the investigator had higher standards

Perceived Difficulty of Research Administrators Negotiating Provisions of Multicenter Trial Agreements with Industry Sponsors

<table>
<thead>
<tr>
<th>Provision Negotiated</th>
<th>Response (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Very Difficult</td>
</tr>
<tr>
<td>Ownership of inventions and intellectual property</td>
<td>31</td>
</tr>
<tr>
<td>Ownership of the data produced by the research</td>
<td>25</td>
</tr>
<tr>
<td>Indemnification issues</td>
<td>17</td>
</tr>
<tr>
<td>Confidentiality of the data produced by the research</td>
<td>15</td>
</tr>
<tr>
<td>Rights to publish</td>
<td>15</td>
</tr>
<tr>
<td>Rights to disseminate study results</td>
<td>15</td>
</tr>
<tr>
<td>Confidentiality of trial participants’ records and information</td>
<td>7</td>
</tr>
</tbody>
</table>
Prevalence of Disputes with Industry Sponsors of Clinical Trials

<table>
<thead>
<tr>
<th>Subject of Dispute</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Payment</td>
<td>62 (55)</td>
</tr>
<tr>
<td>Intellectual property</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Data control</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Indemnification</td>
<td>7 (6)</td>
</tr>
<tr>
<td>Publication</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Personnel</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Confidentiality</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Misconduct</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Enrollment of subjects</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Control of study</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Problem with IRB</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (4)</td>
</tr>
</tbody>
</table>

Policies, Tools, and Structures Used to Facilitate Negotiations Concerning Clinical-Trial Agreements – Negotiation Tools

<table>
<thead>
<tr>
<th>Tool</th>
<th>Overall (N=107)</th>
<th>High-Volume Institutions (N=55)</th>
<th>Low-Volume Institutions (N=51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written general statement of ethical or legal principles to which the institution adheres</td>
<td>65%</td>
<td>74%</td>
<td>57%</td>
</tr>
<tr>
<td>Written checklist of topics that clinical-trial agreements should cover</td>
<td>77%</td>
<td>89%</td>
<td>67%</td>
</tr>
<tr>
<td>Written list of specific provisions that agreements should contain</td>
<td>76%</td>
<td>82%</td>
<td>69%</td>
</tr>
<tr>
<td>Written list of specific provisions that are unacceptable</td>
<td>67%</td>
<td>76%</td>
<td>57%</td>
</tr>
<tr>
<td>Written boilerplate agreement to use as a starting point in negotiations</td>
<td>84%</td>
<td>100%</td>
<td>68%</td>
</tr>
</tbody>
</table>

Investigator Awareness of Tools

- 67% - statement of institutional ethical or legal principles
- 37% – checklist of topics that CTAs should cover
- 37% - list of specific provisions that CTAs should contain
- 30% boilerplate agreement
- 28% - list of unacceptable provisions
### Policies, Tools, and Structures Used to Facilitate Negotiations Concerning Clinical-Trial Agreements – Negotiation Practices

<table>
<thead>
<tr>
<th>Practice</th>
<th>Overall (N=107)</th>
<th>High-Volume Institutions (N=55)</th>
<th>Low-Volume Institutions (N=51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Often or sometimes consult with counterparts in the offices of sponsored research at other schools or hospitals about policies and standards</td>
<td>78%</td>
<td>87%</td>
<td>67%</td>
</tr>
<tr>
<td>All, most, or some frontline negotiators handling clinical-trial agreements have law degrees</td>
<td>41%</td>
<td>54%</td>
<td>29%</td>
</tr>
<tr>
<td>Draft clinical-trial agreements always or usually signed or reviewed by a lawyer</td>
<td>34%</td>
<td>34%</td>
<td>35%</td>
</tr>
<tr>
<td>Draft clinical-trial agreements always or usually signed or reviewed by a senior research administrator</td>
<td>79%</td>
<td>70%</td>
<td>88%</td>
</tr>
<tr>
<td>Draft clinical-trial agreements always or usually signed or reviewed by the faculty principal investigator</td>
<td>91%</td>
<td>89%</td>
<td>92%</td>
</tr>
</tbody>
</table>

NEJM 2005;352:2202

### COMPLIANCE SCORES FOR SITE AGREEMENTS BETWEEN MEDICAL SCHOOLS AND INDUSTRY SPONSORS OF MULTICENTER CLINICAL TRIALS

<table>
<thead>
<tr>
<th>Item</th>
<th>Survey Median Score (IQR)</th>
<th>Mediation Study Median Score (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement addresses plan for data collection and monitoring</td>
<td>100 (75–100)</td>
<td>100 (75–100)</td>
</tr>
<tr>
<td>Agreement requires an independent data and safety monitoring board</td>
<td>100 (0–13)</td>
<td>100 (0–13)</td>
</tr>
<tr>
<td>Agreement requires access to all data for authors of reports on multicenter trials</td>
<td>100 (0–21)</td>
<td>100 (0–21)</td>
</tr>
<tr>
<td>Agreement allows site investigators to analyze and publish site data</td>
<td>100 (0–25)</td>
<td>100 (0–25)</td>
</tr>
<tr>
<td>Agreement requires publication of trial results</td>
<td>100 (0–10)</td>
<td>100 (0–10)</td>
</tr>
<tr>
<td>Agreement contains provision that prevents confidentiality clause from restricting investigators’ publication rights</td>
<td>100 (0–10)</td>
<td>100 (0–10)</td>
</tr>
<tr>
<td>Agreement explicitly requires institution to follow protocol</td>
<td>100 (0–10)</td>
<td>100 (0–10)</td>
</tr>
<tr>
<td>Agreement explicitly requires sponsor to follow protocol</td>
<td>100 (0–25)</td>
<td>100 (0–25)</td>
</tr>
</tbody>
</table>

NEJM 2002;347:1335

### Strategies

- Include the required language your contract template
  - Establish the range of acceptable terms
- Develop talking points or an information for sponsors to help them understand the requirements
- Educate
  - Staff who negotiate contracts and funding agreements
  - Investigators
  - IRB members
Strategies

- Develop a checklist for the required language to be used to each contract or funding agreement
  - Indicate whether each item of required language is present; not applicable (with justification) or that the sponsor refused to include the language (with evidence attached)
- Check with the sponsor if they have contract language which has been approved by AAHRPP
- Develop a process to inform senior officials or general counsel when the sponsor refuses
- Monitor
SELF-ASSESSMENT PROCESS AND PRODUCT
Strategies for Sharing the Work, Soliciting Input, and Promoting Buy-In

TOPICS

- Timelines
- Evaluation Instrument
- Gap Analysis
- Evaluate Polices and Procedures
- Evaluate Practice

HUMAN SUBJECTS PROTECTION PROGRAM
### AAHRPP Accreditation Process

#### AAHRPP Evaluation Instrument

Each element contains four parts:
- **Commentary**
- **Regulatory and Guidance Reference**
  - US Federal Agencies, ICH GCP (E6)
- **Required Written Materials**
  - Policies and Procedures including SOPs, policy statements, procedure descriptions, checklists, guidelines, educational materials, job descriptions, forms, templates, websites, charters, mission statements etc.
- **Common Materials to Meet Requirement**
- **Outcome**

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#### Evaluation Instrument

<table>
<thead>
<tr>
<th>Organization</th>
<th>Institutional Review Board</th>
<th>Researcher and Research Staff</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Standard I.1 (6)</td>
<td>- Standard II.1 (5)</td>
<td>- Standard III.1 (6)</td>
</tr>
<tr>
<td>- Standard I.2</td>
<td>- Standard II.2 (7)</td>
<td>- Standard III.2 (4)</td>
</tr>
<tr>
<td>- Standard I.3</td>
<td>- Standard II.3 (6)</td>
<td></td>
</tr>
<tr>
<td>- Standard I.4 (3)</td>
<td>- Standard II.4 (3)</td>
<td></td>
</tr>
<tr>
<td>- Standard I.5 (4)</td>
<td>- Standard II.5 (3)</td>
<td></td>
</tr>
<tr>
<td>- Standard I.6 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Standard I.7 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Standard I.8 (5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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[www.aahrpp.org](http://www.aahrpp.org)
RESOURCES

- AAHRPP Website (www.aahrpp.org)
  - Tip Sheets
- Other Accredited HRPPs
  - AAHRPP Website
- Consultants
- Commercially available SOPs

RESISTANCE TO CHANGE

- We don’t need to do this, because the problem it solves, doesn’t exist.
- Okay, a problem exists, but your solution is not a good one.
- Okay, a problem exists and your solution is a good one, but it will never work here.

John P Kotter, Buy In – Saving Your good Idea from Getting Shot Down
PROJECT LEAD

- Appoint a project leader
- Appoint teams
- Appoint team leaders
- Identify people who will write policies and procedures
- Identify people who will audit records

TEAMS (example)

| HRPP PLAN | IRB REVIEW | IRB OPERATIONS |
| CONTRACTS | ANCILLARY (COI, Scientific Review, Safety Review etc) | RESEARCHERS |

TEAM MEMBERS

- Team leader
- Subject matter expert
- Representative from group the change will most impact
- Project lead or representative
- Team scribe
MATERIALS FOR TEAM

- Charge to team
- Current policies and procedures
- Relevant elements from AAHRPP Evaluation Instrument
- Relevant AAHRPP Tip Sheets
- Links to resources – contact numbers, websites etc.

SELF ASSESSMENT

- Consider and address each element of the Accreditation Standards
  - Do you have the Required Written Materials?
  - Do you follow the practice described in the Required Written Materials?
  - Do your activities achieve the Outcomes?

AAHRPP ACCREDITATION PROCESS

EVALUATE POLICIES AND PROCEDURES
WRITTEN MATERIALS

- Policy - a strategy, goal, or objective. It defines an expectation regarding a behavior or course of action.
- Procedure - a method by which a policy can be accomplished. Should describe the operational steps that are followed to meet regulatory requirements.
- Procedures should include:
  - An explanation of how key regulatory terms are interpreted,
  - The actions that are taken,
  - The title of the person, office, or entity responsible for taking the action, and
  - The timing of actions.

www.aahrpp.org

EVALUATE POLICIES AND PROCEDURES

- For each AAHRPP element – identify the relevant policies and procedures
- If written documents exist:
  - Evaluate whether the policies and procedures meet all the requirements of the element
  - Make revisions to policy if needed
- If there aren’t any policies and procedures:
  - Identify the people who conduct the specific process
  - Map the process – evaluate if process meets requirements of the element
  - Develop written documents

Evaluate Policies and Procedures – an Example

- Element 1.5.3 - 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.
PROCESS MAPPING

- Determine which clinical site task needs mapping.
- Lay out all the steps currently used to complete that task.
- “Mapping” involves taking each step in the task and making it more efficient and easier to follow.


PROCESS MAPPING – PRIMARY STEPS

MAKING COFFEE

Ensure Coffee Maker is Ready
Add Coffee
Add Water
Turn Machine On
Serve Coffee

PROCESS MAPPING – SECONDARY STEPS

Ensure Coffee maker is ready
Add the coffee
Add the water
Turn on the machine
Serve the coffee
Purpose
The SOP ensures that any company employee wanting to make coffee does so appropriately and according to company standards, thus ensuring a drinkable brew that satisfies and gives pleasure.

Scope
This SOP applies to all employees of the company and pertains only to use of the approved machine to make coffee. Coffee may be made only by employees who have been trained on the machine and are approved to make coffee.

Procedure
1. Ensure coffee maker is plugged in and the carafe is clean and empty.
2. Place a filter in the coffee receptacle and add an appropriate amount of coffee.
3. Fill the carafe with the desired level of water and pour the water in the reservoir.
4. Place the carafe on the heating element and turn the machine on. When the coffee has stopped dripping into the carafe, it is ready to serve.

Regulation and Guidance
- ICH Good Coffee Practice Guideline

References
- Coffee Maker Manual
- Guidance: Making Coffee

Attachments
- Guideline: Making Coffee


**Guidance: Making Coffee**

Effective date: Jan 1, 2011

Ensure coffee maker is ready:
- Plug is located at the end of the cord attached at the back of the machine.
- Outlet is on wall directly to the right of the machine.
- Insert plug into wall outlet, matching large side of plug to larger hole in outlet.
- Be sure the plug is inserted firmly and completely.

Wash carafe:
- Dishwashing soap is located in the cabinet under the sink.
- Use hot water and a small amount of soap.
- Brush with small brush located on hook under sink.
- Rinse thoroughly with hot water.


**PROCESS MAPPING** (example)

**IRB REVIEW PROCESS - EXEMPTIONS**

Submission – what to submit, how to submit, when to submit

Pre-screening

Assigning for review

Review process to determine if it meet exemption criteria

Determine if additional protections are needed

Communication of outcome
TYPES OF DOCUMENTS

- Some organizations choose to have a two-tiered system that includes both policies, procedures and guidelines.

CONSENT POLICY

- Review Procedure
- Consent Guidelines
- Elements Checklist
- Consent Templates
- Glossary
- Simple Words
- Interactive Website for Reading Level

STEPS IN DEVELOPMENT

- Assemble Team
- List of Documents
- Develop Templates
- Final Version
- Group Review
- Assign Writing to Experts
- Disseminate and Educate
- Document Management

Adapted from http://www.standardoperatingproceduretemplates.com

IRB POLICIES AND PROCEDURES (example)

- IRB Membership
  - IRB Composition
  - Conflict of Interest
- IRB Review Process
  - Initial Review
  - Continuing Review
  - Amendments
  - Exempt Review
  - Expedited Review
  - Unanticipated Problems
- Additional Protections
  - Research involving Children
  - Research involving Pregnant Women
  - Research involving Prisoners
  - Research involving Cognitively Impaired Persons
- IRB Meetings
  - Compliance
  - Noncompliance
  - Suspensions and Terminations
  - Post approval Monitoring
  - Appeal Process
  - Subject Complaints
  - Reporting
- Special Topics
  - Investigational Drugs
  - Investigational Devices
  - Humanitarian Use Devices
  - Emergency Exception from Informed Consent
  - Emergency Use
AAHRPP ACCREDITATION PROCESS

EVALUATE PRACTICE

Identify major processes and outline an evaluation plan:

- Exemption
- Expedited review
- IRB application
- Continuing Review
- Amendment
- Consent forms
- Waiver of consent or documentation
- Minutes - SR/NSR
- Protocol specific determinations
- Vulnerable subjects
- UPs
- Noncompliance
- Suspensions / Terminations
- Complaints from subjects

... etc

EVALUATE PRACTICE

WHAT REALLY HAPPENS AT IRB MEETINGS...
EVALUATE PRACTICE – an Example

- Example – evaluating exemptions:
  - Did PI provide adequate information to the IRB?
  - Individual conducting exemption review and approval had authorization?
  - Is there documentation of category of exemption?
  - Does the proposal meet exemption criteria?
  - Were additional protections considered?
  - Did the IRB send the PI a written outcome letter?

FINAL WORDS

- Define the objectives
- Set deadlines
- Stay on schedule
- Avoid scope creep
- Don’t re-invent the wheel

THANK YOU!
After Accreditation: Strategies for the “In Between” Years and Preparing for the Next Self-Assessment

Is This YOUR Research Organization?

T-minus 1,095 (1,825) Days: You Are AAHRPP Accredited!!
T-minus 1,094 (1,824) Days: 
(aka the NEXT Day)

T-minus 730 (1460) Days: 
(aka ONE year later…)

T-minus 365 Days: 
(aka Application Due Date…)
Yearly Effort - Accreditation

Keys to the “In-Between” Years

- Review Policies & Procedures on a regular/continual basis
- Stay up-to-date with requirements/best practices
- Make accreditation part of daily routine
- Maintain engagement of entire HRPP
- Keep communication open

The “In-Between” Years – Achieving Continuous Readiness
Engagement: Debriefing

- Assemble participants to provide feedback and results of accreditation process
- Get buy-in for continued engagement
  - Organizational leaders (HRPP leadership)
  - IRB/EC Staff
  - IRB/EC members
  - Researchers/Research Staff
  - Sponsors

Planning (Strategic)

- “Simply put, strategic planning determines where an organization is going over the next year or more, how it’s going to get there and how it’ll know if it got there or not.”

Free Management Library
http://managementhelp.org/strategicplanning/index.html#anchor1234

Strategic Planning

- Review your mission statement
  - What is your basic purpose
- Create a vision
  - where you want your HRPP to be at next application – your “future state”
- Set goals (short- and long-term)
  - 2/4 year roadmap (application due 12 months prior to Council date)
Strategic Planning

- Best: integrate into overall strategic planning for your research organization
- Many models – pick one that fits your organization and needs
- **BUT** – Don’t let the “modeling” get in the way of DOING something

Actions

- Create action item(s) to achieve each goal
  - Multiple small actions = continuous improvement!
  - Include education as a component

Actions

- Develop a timeline for each action item
  - Integrate with other major organizational initiatives
  - Think about complexities, resources if major changes close in time proximity to reaccreditation
Actions

- Engage others – staff, IRB members, all HRPP personnel
- Define who is accountable for the project
  - Track action plans
  - Review outcomes
  - Integrate with Evaluation

Evaluation

- Identify how to assess each goal/action item
  - Descriptive
  - Qualitative
  - Quantitative
- Create report(s) of evaluation outcomes
  - One-time
  - Ongoing – “Dashboards”
  - Graphics!

Feedback

- Take results of evaluations and give them back to those involved in the actions/goals
  - Educational
  - Gets buy-in
- Remember to include successes!
Feedback

- Turn feedback into ongoing educational opportunities
  - Look at trends
  - What are the findings?
  - Is this what we intended?
  - What should we do with these findings?
  - Continuous monitoring or episodic?

Engagement

- Create communication/dissemination plan
  - Who
    - Organizational Leaders
    - HRPP key stakeholders
  - What
    - Goals
    - Summary of Action plans
    - Results of Evaluations
    - Update on Strategic Plan and Next Steps

Engagement

- When
  - Identify regular “touch-base” time points
    - Annual
    - Quarterly
    - More frequently as needed
  - Allow for flexibility – may need to engage in the middle of an action plan if major change occurs (new regulations)
Example Goal 1

- Educate IRB members in review using the Criteria for Approval
  - Ability to identify the criteria for review
  - Ability to correlate the info in the myIRB application to the criterion of approval
  - Ability to correlate the Reviewer Sheet to the criteria of approval
  - Ability to express concerns regarding a study in terms of criteria of approval

Example Goal 2:

- Maintain Policies
  - Update policies whenever changes occur
  - Create monitoring plan for new information
    - Regulatory changes
    - Guidance changes
    - Accreditation information
    - State/Local laws

Example Goal 2:

- Update COI policies to new regulations
Example Goal 4:

- Review/Audit IRB Procedures
Plan for Presentation

- Review procedures leading up to site visit
- Provide some perspective from someone who has been a frequent site visitor

Current Model of AAHRPP Accreditation 2 Step Process

- Step 1 Review of Application Materials
  - Self evaluation using AAHRPP standards
  - Preparation of Step 1 application
    - Policies and procedures
    - Work with AAHRPP accreditation staff
- Step 2 submission
  - Within one year after submitting Step 1
  - Site visit scheduled, usually within 3 months after Step 2 app received
Main Purpose of Site Visit

- Assess how well practice conforms to policy

Site Visitors

- 2-6 visitors depending on size of org
  - Work in pairs
- Varying backgrounds
  - HRPP professionals/consultants
  - Researchers (biomedical, S & B)
  - IRB chairs/members
  - Some from accredited places, some not
Site Visitors (cont.)

- Team leader
  - Either member of Council on Accreditation or experienced site visitor
- No AAHRPP staff on site visit
  - Team leader talks to AAHRPP AD by phone before, during and after SV
- No COI
  - Visitor/immediate family not related to site (as employee, student, consultant) in last 2 yr.

Site Visitors (cont.)

- Confidentiality
  - All visitors sign confidentiality agreements
  - We don’t disclose our specific destination and purpose of trip
  - We are instructed not to sign additional confidentiality agreements on site.

Site Visitors (cont.)

- Site visitors now get training – on line slide show, site visitor newsletter
- Site visitors encouraged to focus on outcomes in subject protection, not details of process employed
  - “That’s not the way we do it” – not what you want to hear from a site visitor
4-8 Weeks Before Site Visit

- Draft agenda, prepared by AAHRPP staff
  - Based on application and protocol list
- Site visitor list
- Request for logistic/travel info
- Request for rooms
  - Visitors work in teams of 2

Education (Staff, IRB, researchers)
Pre Site Visit

- Probably makes sense as you move from self evaluation through step 1 and step 2, to have a plan for orienting organization to the AAHRPP process
  - Special meetings
  - sessions at IRB meetings
  - Email/online resources
- Focus on areas where you think you may be deficient
- Session H6 on Friday!

One Week Before Site Visit

- Final agenda
- Travel/logistic details for SV
- “Documents to pull”
  - IRB files for protocols (representative samples)
  - Minutes
Site Visit

- Introduction
- Program overview
  - Can give short presentation about your site, but don’t have to
- Records review
- Interviews
- Daily closeout
- At end: Lead contact review/final closeout

Records Review

Who will we interview?

- Set up by AAHRPP, but team leader can ask for changes pre-visit
- HRPP staff
- IRB chairs and members (scientist, non-scientist, nonaffiliated)
- Researchers/research staff
- Ancillary committees/persons (COI, legal, pharmacy, contracts)
- Leadership
Electronic IRB System Issues

- Figure out how visitors will be able to access materials
  - Full/partial system access
  - Downloads to USB drive
  - Site staff-driven access
  - Print-outs
- Visitors almost always have laptops, but you may prefer we use yours

Phone Interviews

- Almost always need to do a few, sometimes a lot
- Make sure we have conferencing phones or speakerphones that work

Don’t

- Ask visitors if you will be accredited
  - Not up to site visit team alone
- Ask to take pictures, videos
- Ask visitors out to dinner
- Contact site visitors after visit is over
The Real Close-out Session
Preventing for an AAHRPP Site Visit

Who am I? Why am I here?

- Background at Indiana University
- Background with AAHRPP
- My Role Today—the Social/Behavioral Perspective
- Approach to Today’s Talk

What Happens Before the Site Visit

- Website—first impressions
- Application
  - Overview and Organizational Structure
  - Policies and Procedures
  - Elements and Social/Behavioral Research
  - Roster(s) and Minutes
  - Records to Pull List
  - Site Visit Agenda
The Site Visit—Day One

- Program Overview and Organizational Questions
- Records Review—Social/Behavioral Perspective
- Interviews with Researchers
- Interviews with IRB Members
- The Daily Closeout Meeting

The Site Visit—Day Two

- Interviews with IRB Chairs and Vice Chairs
- Interviews with Research Coordinators
- Interviews with HRPP Office Staff
- Interviews with Department Chairs, Directors, and Deans
- Interviews with Chairs of Committees Relevant to HRPP

The Site Visit—Day Three

- Interviews with Senior Officials
- Interview with Legal Counsel
- Interview with Contracts and Funding Agreements Representative
- Interviews with Representatives of Affiliated Organizations
- Lead Contact Review and Closeout
Points to Ponder—The Highlights

- Social/Behavioral Research and the HRPP
- Representation
- Education
- Communication
- Process
- Final Thoughts
Basic Overview of the DHHS Regulations Related to Protecting Human Research Participants

DHHS Regulations for Protecting Human Research Participants

AAHRPP Element I.1.A:
1. Define "research involving human participants"
2. Define process for providing determinations

Tip Sheet: #2 Determining Whether an Activity is Research Involving Human Participants (DHHS 45 CFR 46.102)

What is research?
- Definition includes regulatory definitions
- "Systematic investigation"
- "Generalizable knowledge"
- Explain WHO, HOW, and WHEN determination is made
AAHRPP Element I.1.C.: Authority and Independence of the IRB or EC
- Approve, require modifications, or disapprove research
- Suspend or terminate IRB or EC approval
- Observe or have a third party observe, the consent process, conduct of research
- Ensure that research does not commence until approved
(DHHS 45CFR 46.109); AAHRPP Tip Sheet 12

AAHRPP Element I.1.D.
- Define roles, responsibilities, and the laws, regulations, codes, and guidance requirements.
- Assurances: May extend Subpart A and Subparts B, C, D to all research
- Describe the “equivalent protections”
(DHHS 45CFR 46.103)

AAHRPP Element I.1.F.
- Scientific or Scholarly Validity
- “Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk”
- “Importance of the knowledge that may reasonably be expected to result”
(DHHS 45 CFR 46.111)
Element I.1.G.

- Determining who is a child “under applicable law of the jurisdiction where the research will take place”
  - State law, emancipation, wards
- Determining who may serve as legally authorized representative
  - Describe the process, use of legal counsel
- Additional laws and protections:
  - Identify state and local laws that apply
  - Jurisdictional issues
  - Border states, multiple sites, foreign sites

DHHS 45 CFR 46.101, 102, 402

Standard I-2, Standard I-3

Adequate Resources

Knowledge of local laws, customs, culture

Local approval

(DHHS 45 CFR 46.103, 114)
Tip Sheet # 19

Element I.4.A.

- Respond to concerns:
  - Provide an explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject (45 CFR 46.116)
Element I.5.D: Non-Compliance

- Define, Identify, Decide, Report:
  - Non-compliance
  - Serious Non-compliance
  - Continuing Non-compliance
- Actions:
  - Suspension
  - Termination
  - Notification

Non-Compliance Management

- Modification of research protocol
- Modification of information disclosed during consent process
- Provide additional information
- Notification and re-consent process
- Modification of review schedule
- Monitoring research, consent process

AAHRPP Tip Sheet 14; Guidance (June 30, 2011)

Reporting Requirements

- Guidance on reporting to OHRP
**Standard I-6: Conflict of Interest**

- Financial interests are disclosed
- Financial interests are evaluated
- Financial interests are managed
- DEFINITIONS: financial interests, immediate family, significant, institutional responsibilities
- AAHRPP Tip Sheets 10, 13
- Evaluation Instrument

**Element I.7.C**

- DHHS:
  - ✔ Planned Emergency Research
  - ✔ (Data obtained from patients is not human participants research)
- Emergency uses of investigational or unlicensed test articles follow regulations or laws

**Standard I-8**

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<td>Safety Reporting</td>
<td>Data and Safety Monitoring</td>
<td>Publications</td>
<td>Safety issues after a study has closed</td>
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<td>Tip Sheet 25: DHHS 45CFR46.116</td>
<td>Include required language</td>
<td>Develop checklists</td>
<td>Maintain communication</td>
<td>Work with sponsors</td>
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Domain II

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<td>Evaluation of Protocol</td>
<td>Approval Criteria</td>
<td>Additional Protections</td>
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<td>Multi-Site</td>
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Guidance

- Guidance on Reporting Incidents
- Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events

Domain III

- Researchers and research staff knowledge
- Conflicts of interest
- Study design and minimizing risk
- Resources to protect participants
- Equitable selection
- Informed consent
- Response to complaints and concerns
- Oversight, delegation, and reporting
Helpful Tips

1. Stay in touch
   ✓ With your AAHRPP Accreditation Director and ask for advice.
2. Check out the AAHRPP Tip Sheets
3. Review OHRP Guidance

Questions?
Response to Site Visit Reports and Status Reports

Response to Draft Site Visit Reports

Three step process:

1. Review the report
2. Prepare your response
3. Submit your response

Step One:
Review the Draft Site Visit Report

- Cover letter
  - Note date response is due in AAHRPP office
  - Note whom to contact with questions
- Draft Site Visit Report
  - Review site visit team’s observations and areas of concern
  - Check for accuracy (review for inaccuracies)
  - Note site team’s suggestions are not included
- Instructions
Domain II: Institutional Review Board or Ethics Committee

Standard II-6: The IRB or Ethics Committee maintains documentation of its activities.

Draft Site Visit Report

Observations:

- IRB records included all required information and were retained for the required time period. IRB records were accessible for inspection and copying by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner. Records were stored safely and in a way that maintained confidentiality.

Areas of Concern:

- When an investigational device was evaluated for its safety or effectiveness, the IRB did not always record in the minutes the determination of the significant risk or non-significant risk status of the device. (Element 3.7.5c)

Initial Determination:

Pending
Step Two: Response Preparation

- Understand the documented area of concern.
  - Make sure area of concern is correct.
  - Check with assigned AAHRPP Accreditation Director as needed.
- The response will differ for concerns related to
  - Knowledge versus
  - Practice.

Concerns Regarding Knowledge

- Prepare an education plan for the appropriate people which includes:
  - Who was (or will be) educated (by type(s) of person)
  - Summary of the content of the education
- If education occurred prior to the submission of the response, also provide:
  - The date(s) it occurred
- If education has not occurred indicate, also provide:
  - The date it will be completed

Council expects education to begin within 30 days of the receipt of the Draft Site Visit Report and to be completed within five months of receipt of the report.

Concerns Regarding Practice

Response must include the following:

- Description and copies of changes made to written materials
- Education plan (see previous slide)
- Monitoring plan related to area of concern
  - When and how often will monitoring occur
  - What will be monitored
  - Who will monitor
Monitoring

- If monitoring is completed prior to the submission of the response:
  - Provide a summary of the results of the monitoring in narrative or statistical form
  - Do not submit names of researchers or protocols
- If monitoring has begun but is not completed or is planned:
  - Provide a plan for monitoring

Council expects monitoring to begin within 30 days of the receipt of the Draft Site Visit Report and to be completed within five months of receipt of the report.

Step Three: Submit the Response

- Response should be comprised of two sections.
  - Section A: Response
  - Section B: Supporting documents

Section A - Response

- Provide a written response for each element listed under Areas of Concern
- Begin the response with a brief summary of the changes, followed by a list of revised documents submitted
- In the response, refer to the supporting documents that are listed in section B
- Format is similar to application
Section B – Supporting Documents

- Include a copy of each supporting document ordered by reference number.
- Use highlighted or tracked changes to point out specific revisions.
- For long document with a few changes, provide only the changed pages with changes indicated.
Assembly and Mailing

- Formatting
  - Submit original cover letter signed by the organizational official who signed the original application form
  - Use 12pt font with single space blocked paragraph
  - Format to letter sized paper

- Paper Copies
  - Submit two fully collated printed copies of the response

- Electronic Copy
  - Submit the electronic on CR-ROM as a single PDF file.

AAHRPP Council Determinations

- The council determinations are based on a decision as whether a standard is
  - Met,
  - Met with a status report requested, or
  - Not met.

Helpful Tips

1. Stay in touch!
   - With your AAHRPP Accreditation Director and ask for advice. Submit draft response to AAHRPP Accreditation Director and ask if it is reasonable.
   - Talk to sites similar to yours that are accredited and ask for advice


3. Don’t go it alone!
Questions? Suggestions?
Basic Overview of the FDA Regulations Related to Protecting Human Research Participants

Additional Requirements When Following FDA Regulations

- Domain I
- Domain II
- Domain III

Define When the Use of a Drug or Device is Research Involving Human Participants (Elements I.1.A. and III.1.A.)

- Definition of "research involving human participants" includes:
  - Clinical investigation (21 CFR 50.3(c))
  - Human subject (21 CFR 56.102(g))
- Researchers and research staff know when research falls under FDA regulations.
Definition of Clinical Investigation

- Any experiment involving a test article and one or more human subjects that:
  - Must meet requirements for prior submission to FDA, or
  - Results of experiments intended to be submitted to FDA as part of an application for research or marketing permission (21 CFR 812.3(p))

Definition of Human Subject

- Individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient (21 CFR 50.3(g)).
  - Includes an individual on whose specimen an investigational device is used.

Conflicts of Interest in FDA-regulated Research (Elements I.6.B. and III.1.B.)

- Define who must disclose interests:
  - At least annual disclosures by researchers and research staff, immediate family members, IRB members.
  - Update disclosure within 30 days of acquisition or discovery.
- Describe process to educate researchers about disclosure requirements.
  - Disclosure threshold is $50,000 for FDA-regulated research.
Define When Researchers and Staff have a Conflict of Interest

- Ownership interest, stock options, or other financial interest related to the research unless it meets four tests:
  - Does not exceed $50,000 when aggregated for the immediate family.
  - Publicly traded on a stock exchange.
  - No arrangement has been entered into where the value of the ownership interests will be affected by the outcome of the research.
  - Does not exceed 5% interest in any one single entity when aggregated for the immediate family.
- Compensation related to the research unless it meets two tests:
  - Does not exceed $25,000 in the past year when aggregated for the immediate family.
  - No arrangement has been entered into where the amount of compensation will be affected by the outcome of the research.
- Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.

Describe Process to Evaluate and Manage Conflicts of Interest

- Describe process to evaluate conflicts of interest
  - When review is conducted by someone other than the IRB or EC, describe communication of the results to the IRB or EC.
- Describe process to manage conflicts of interest, including monitoring of management plans.
  - The IRB or EC has final authority to approve management plans.

Define When Drugs Must have Regulatory Approval or Meet Exemptions (Elements I.7.A. and III.1.A.)

- When research involves the use of a drug other than marketed drug in medical practice:
  - Define when an IND is required.
  - Define when the drug meets an exemption from the requirement to have an IND (21 CFR 312.2(b)).
- Researchers and research staff know when an IND is required and how to obtain an IND.
Define When Devices Must have Regulatory Approval or Meet Exemptions (Elements I.7.A. and III.1.A.)

- When research is conducted to determine the safety or effectiveness of a device:
  - Define when an IND is required.
  - Define when the device meets requirements for an abbreviated IDE (21 CFR 812.2(b)(1)).
  - Define when the research meets an exemption (21 CFR 812.2(c)).
- Researchers understand when an IDE is required and how to obtain an IDE.

Describe a Process to Verify the IND or IDE is Correct (Element I.7.A.)

- Specify the individual who verifies the IND or IDE.
  - Does not need to be the IRB or EC.
- An investigator’s brochure should not be used to verify the IND or IDE:
  - One investigator brochure often covers multiple INDs or IDEs.

Ways of Verifying the IND or IDE (Element I.7.A.)

- Number imprinted on the Sponsor protocol.
- Communication from the sponsor with the IND/IDE linked to the specific protocol.
- Communication from the FDA.
  - When the researcher holds the IND or IDE.
Describe the Process to Review the Researcher’s Plans for Control of Test Articles (Element I.7.B.)

- Describe the process for handling investigational or unlicensed test articles so that they are used only in approved protocols and under the direction of approved Researchers
  - Organizational control.
  - Protocol-by-protocol review and approval.
- Policies apply to all research settings.

Define Emergency Use of a Test Article (Element I.7.C.)

- Single use of a test article in an emergency situation without prior IRB review.
  - Different from planned emergency research.
- Emergency use of a test article is a clinical investigation.
  - May not be considered research involving human participants under 45 CFR 46.
- Define criteria for emergency use.

Describe Process for Review of Emergency Use of a Test Article (Element I.7.C.)

- Describe who reviews emergency use of a test article to determine whether the use met FDA regulations:
  - Indicate who reviews five-day reports of the circumstances of the emergency use.
  - If consent is not obtained, indicate who confirms whether the circumstances permitted an exemption from consent.
Additional Requirements When the IRB Reviews FDA-regulated Research

- Conflict of interest of IRB members – same as for researchers and research staff.
- Equitable participant selection.
  - Advertising and recruitment.
- Consent.
  - Waivers and alterations of consent.
- Review of research involving children.
- Reporting requirements.

Additional Requirements to Ensure Equitable Selection of Participants (Elements II.3.C. and III.1.E.)

- IRB reviews advertising to make sure they do not:
  - Make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.
  - Use terms, such as "new treatment," "new medication," or "new drug," without explaining that the test article is investigational.
  - Allow compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

Additional Requirements for Consent (Element II.3.F. and III.1.F.)

- Consent includes required and additional elements of disclosure:
  - FDA may inspect the research records.
  - Results of the research will be posted on clinicaltrials.gov
  - The participant or legally authorized representative (LAR) will sign and date the consent document
  - The researcher will give the participant or LAR an opportunity to read the consent.
- Use of the short form meets regulatory requirements.
Additional Requirements for Consent, continued (Element II.3.F.)

- With regard to data collection:
  - Consent documents cannot give participants the option of having data removed from the study if they withdraw from the research.
  - Researchers must obtain consent for limited follow-up if participants withdraw, if this was not included in the original consent.
    - If the participant withdraws and does not consent to continued follow-up the researcher must not access medical records without the participants consent.

Waivers and Alterations of Consent (Elements II.3.G. and III.1.F.)

- Not permitted except:
  - Waiver of Documentation of the Consent Process for Minimal Risk Research
    - The research presents no more than minimal risk of harm to participants.
    - The research involves no procedures for which written document of the consent process is normally required outside of the research context.
    - The IRB considers having researchers provide participants with a written statement about the research.
      - The IRB reviews the written statement.

Exception From Informed Consent for Studies Conducted in Emergency Settings (Element II.4.C.)

- Limited circumstance allowing for waiver of requirements for consent for planned emergency research.
  - Additional regulatory requirements, including:
    - Prior approval by the FDA.
    - Community involvement.
Review of Research Involving Children (Element II.4.B. and III.1.F.)

- When following Subpart D, the IRB makes protocol-specific determinations:
  - Permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child, or the permission of one parent is sufficient.
  - Additional requirements apply if research is more than minimal risk with no prospect of direct benefit.

Review of Research Involving Children (Element II.4.B. and III.1.F.)

- When following Subpart D, the IRB or EC makes protocol-specific determinations:
  - Whether assent is a requirement of all children, some children, no children.
    • The IRB or EC determines and documents which children are not required to assent.
  - When the IRB or EC determines assent is not a requirement, it makes protocol specific documentation that certain criteria are met.

Reporting Requirements When Following FDA Regulations (Elements I.5.D., II.2.F., II.2.G.)

- Describe who provides reports to the FDA and the timeframe for reporting:
  - Suspensions, terminations.
  - Unanticipated problems involving risks to participants or others.
  - Non-compliance.
Researcher Responsibilities

  - Note: state law can require researchers to have medical licenses to perform treatments and procedures in the research.