


**RESEARCH  
Compliance  
Conference**

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**IRB Compliance Topics and Tips**

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**What this Presentation will Cover:**

- **Frequent Findings on AAHRPP Accreditation Review**
  - Overview of Accreditation & Accredited Organizations
  - Overview of Standards & Principles for Accreditation
  - Major Accreditation Findings
  
- **Putting it into Practice: Tips for Avoiding Compliance Quagmires**
  - Review Required Documentation
  - Review Process Check-up
  - Assess IRB Meetings



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## Overview of AAHRPP Accreditation

- **Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP®)**
- **Accreditation process is voluntary, peer-driven and educational.**
- **Goals of Accreditation:**
  - Improve the systems that protect the rights and welfare of individuals who participate in research.
  - Help communicate to the public the strength of an organization's commitment to the protection of human research participants.
  - Improve the overall quality of research by consistently applying high standards and practices, raising the global benchmark for human research protection.

## AAHRPP HISTORY: 2002 - 2008

- **Major improvement in the quality of accreditation applications**
  - Annual conference
  - Networks
  - Evaluation Instrument on Accreditation and Tip Sheets
  - Preliminary application
- **More focus from AAHRPP on practice than on written documentation**

## Overview of Accredited Organizations

- **As of September 2008, 138 organizations representing more than 600 entities:**
  - Contract research organizations, hospitals, independent IRBs, research institutes, universities and government agencies
  - Small (fewer than 20 protocols) and large (greater than 6,000 protocols) institutions
  - Clinical and non-clinical research programs
  - International programs: Canada, Singapore, and South Korea



## Overview of Standards and Principles for Accreditation

- **Nine Principles for Accreditation**
  - Principles serve as foundation for structure and content of Accreditation Standards.
- **Accreditation Standards**
  - Structure of Accreditation Standards incorporated Five Domains of a highly developed Human Research Protection Program.
- **Domains**
  - Organization
  - Research Review Unit
  - Investigator
  - Sponsored Research
  - Participant Outreach
- **Elements**
  - Each Accreditation Standard has specific Elements that must be met.

## Major Accreditation Findings

- **Of the 77 elements, 21 pose challenges**
  - Domain I
  - Domain II
  - Domains III - V



## Accreditation Findings – Domain I

- Elements I.3.C, I.3.D, I.3.F
  - **Definition of research involving human subjects (I.3.C)**
    - Missing FDA definitions
    - Definitions inconsistent with federal regulations
  - **Criteria for exemptions (I.3.D)**
    - Do not take into account FDA regulations
    - Do not take into account OHRP guidance
  - **Definitions of legally authorized representative, child, guardian (I.3.F)**
    - Which individuals within your state meet the federal definitions

## Accreditation Findings – Domain I

- Elements I.3.G, I.3.I, I.3.J
  - **Investigator conflict of interest (I.3.G)**
    - Missing FDA and PHS disclosures
    - Missing a procedure that the IRB has the final authority to decide whether the research is approvable
  - **Non-compliance (I.3.I)**
    - Definitions, determinations, actions, reporting
  - **Unanticipated problems involving risks to participants or others (I.3.J)**
    - Process to determine whether a problem is an “unanticipated problem involving risks to participants or others”
    - Reporting

## Accreditation Findings – Domain II

- **Element II.1.D**
  - Missing an evaluation process for the IRB chair and members
  - Missing a requirement to include someone on the IRB who represents the views of participants
- **Element II.2.B**
  - Procedures for review using the expedited procedure
    - Missing applicability criteria
    - Missing definition of “minor”
- **Element II.2.D**
  - Continuing review
    - Missing a status report or status report is incomplete
- **Element II.3.C**
  - Missing documentation of required determinations

## Accreditation Findings – Domain II

- **Element II.4.A**
  - Evaluation of risks and potential benefits
    - Missing the three regulatory criteria
- **Element II.4.B**
  - Evaluation of data and safety monitoring plan
    - Missing an evaluation component
- **Element II.4.D**
  - Suspension and termination of IRB approval
    - Definitions of suspension and termination
    - Consider consequences of suspension or termination for enrolled participants
    - Reporting

## Accreditation Findings – Domain II

- **Element II.6.A**
  - Protection of privacy interests
    - Understanding the difference between privacy and confidentiality
    - Missing as a criterion for approval of research
- **Elements II.7.A – F**
  - Missing evaluation of the consent process
  - Missing required disclosure elements
  - Missing FDA requirements pertaining to consent
  - Confusion between waiver of the consent process and waiver of documentation of the consent process
  - Confusion of requirements for implementing the exception to obtain consent in emergency situations

## Addressing the Accreditation Standards

- Use the Evaluation Instrument for Accreditation
- Talk to other accredited organizations
- Develop a procedure that works for your organization

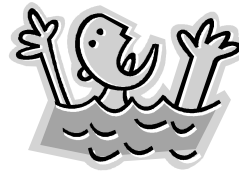
## High-Quality Human Research Protection Programs



- **Elements met with distinction**
  - I.1.A - strong integrated plan for human research protection
  - I.1.B - strong program for scientific review
  - I.1.C - strong and highly motivated organizational leader
  - I.2.A - program for review of resources for the HRPP
  - I.2.B - research specific IRBs
  - I.2.D - strong network of communication among units
  - I.3.H - policy and procedure to identify and manage organizational conflict of interest
  - I.3.L - strong quality improvement programs
  - I.4.A - strong education programs for researchers and staff
  - II.1.D - highly competent IRB chairs, members, or staff
  - V.2.A - impressive educational materials for the community

## Putting it into Practice: Tips for Avoiding IRB Compliance Quagmires

- Review Required Documentation
- Review Process Check-up
- Assessing IRB Meetings



## Required Documentation

- Required Governmental Paperwork
  - Federalwide Assurance (FWA)
  - IRB Registration
  - Extending FWAs and Working with Multiple IRBs

## Required Documentation: Federalwide Assurance (FWA)

- **FWA:** Written document that certifies compliance with the Common Rule. **Not required by FDA.**
- **What to Watch for:**
  - **Checking the Box:** Institution voluntarily agrees that Common Rule will apply to all of its Human Subjects Research and/or that it will also apply the additional protections for research involving pregnant women, human fetuses and neonates prisoners or children.
  - **From FWA Form:** “*Optional:* This Institution elects to apply the following to all of its human subjects research regardless of the source of support, except for research that is covered by a separate assurance:
    - **The Common Rule (see section 3 of the Terms of the FWA for Institutions Within the United States for a list of departments and agencies that have adopted the Common Rule and the applicable citations to the Code of Federal Regulations)**
    - **The Common Rule and subparts B, C, and D of the HHS regulations at 45 CFR part 46”**
- **What happens when you check the box?**
  - OHRP then has authority over all Human Subjects Research conducted by the institution whether or not it is federally conducted or supported.

## Required Documentation: IRB Registration

- **IRB Registration:** Each institution that files an FWA must designate an IRB(s) responsible for review of institution’s Human Subjects Research. The designated IRB(s) must register with OHRP.
- **What to Watch for:**
  - REMEMBER FWA AND IRB REGISTRATION MUST BE RENEWED EVERY 3 YEARS or UPDATED within 90 days of any changes.
  - CALENDAR DUE DATES
  - OHRP Website lists all approved FWA and currently registered IRBs:  
<http://ohrp.cit.nih.gov/search/asearch.asp#ASUR>



## Required Documentation: Extending FWAs

- **Extending FWAs:** When working on HHS-funded research that involves collaborators at other institutions, collaborators must be covered by an FWA.
- **What to Watch for:**
  - Check OHRP website to verify FWA/registration of collaborating site.
  - If collaborating site does not have FWA, then principal site can extend its FWA to cover:
    - A collaborating individual investigator who is doing collaborative research with the FWA Site, but is not doing the research in FWA Site's facilities; is not an employee/agent of the FWA Site; and is not an employee of another institution with respect to his/her involvement in the research.
    - A collaborating institutional investigator who is doing collaborative research with the FWA Site, but is not doing the research in the FWA Site's facilities; is not an employee/agent of the FWA Site; and is an employee/agent of another institution that does not hold an FWA and does not routinely conduct Human Subjects Research.
  - Draft written agreement. to document this extension of the FWA. See sample at: <http://www.hhs.gov/ohrp/humansubjects/assurance/unafisup.rtf>
- **REMEMBER:** FWA Site is responsible for ensuring that collaborator follows the rules.

## Required Documentation: Working with Multiple IRBs

- **Options for Working with Multiple IRBs**
  - Have each IRB do a full and completely independent review.
    - No worries regarding “local context”
    - No additional paperwork necessary
    - BUT frustrating for investigators.
  - Work out Authorization Agreements with Other IRBs
    - Institution with FWA and IRB relies on another Institution's IRB for review of certain research
    - Authorization agreement should be used. See sample at: <http://www.hhs.gov/ohrp/humansubjects/assurance/iprotsup.rtf>
  - FDA – Cooperative Research Agreements
    - Guidance at <http://www.fda.gov/oc/ohrt/irbs/research.html>. Clinical investigator and research site retain primary responsibility for conduct of clinical investigation.

## Required Documentation: Multiple IRBs

- **What to Watch for:**

- REMEMBER: Authorization Agreement doesn't let the "relying" institution off the hook
- UPDATE FWA – it must list every IRB upon which an institution relies.



## Required Records: Documentation & Record Retention

- **Documentation Requirements:**

- FDA - 21 CFR 56.115; Common Rule - 45 CFR 46.115

- **Types of Documents that Must be Retained under FDA and Common Rule**

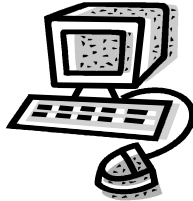
- Research proposals and scientific reviews
- Sample consent documents
- Progress reports
- Subject injury reports
- All correspondence with investigators
- IRB Roster, Minutes and Written Procedures
- Statement of significant new findings provided to subjects that relate to subject's willingness to continue in study

- **Record Retention Period:** 3 years, or, if related to research that is conducted, 3 years after completion of research

## Required Records: Documentation & Record Retention

- **What to Watch for:**

- **Electronic Records for FDA Studies:** Determine up front if electronic documents meet documentation requirements – REMEMBER for FDA studies, 21 CFR Part 11 requirements must be met if electronic documents are primarily relied upon.
  - If using electronic records, does your institution meet electronic signature standards?
- **COSTS:** Include cost of IRB document preservation/storage in contracts for research.
  - Offsite storage contracts should include confidentiality provisions and/or meet HIPAA Business Associate Agreement requirements.



## Review Process Check-up

- Be aware of FDA and Common Rule differences.
- Be aware of review requirements for research involving Special Populations.
- Make sure you have a process to ensure that all research documents match up.



## Review Process: FDA and Common Rule Differences

- **Informed Consent:** FDA does not permit IRB to waive informed consent for clinical investigations.
  - FDA does permit emergency use of test articles without informed consent in certain emergency, life-threatening situations.
  - FDA provides for IRB to permit exception to informed consent requirements in certain emergency situations.
- **Expedited Review:** If medical devices or drugs are used, review must encompass specific FDA requirements, e.g., assignment of risk level of device, necessity of having an IND.
- **Exempt Review:** Common Rule Exempt categories do not apply to Clinical Investigations covered by FDA Regulations.
  - In certain circumstances, FDA Regulations do permit emergency use of a test article without IRB approval if reported to IRB within 5 days of use.

## Review Process Check-up: Special Populations

- **Make sure the IRB is adequately considering and documenting special review requirements for special populations such as pregnant women, prisoners, children.**
- **What to Watch for:**
  - **Pregnant Women:** Remember, if you checked box on FWA that adopts Subpart B's requirements for ALL research, then protocols may have to exclude pregnant women, of if possibility exists of pregnant women's participation then IRB will have to document review of all elements specified in this subpart.



## Review Process Check-up: Special Populations

- **What to Watch for: Prisoners –**
  - Common Rule Exempt categories do not apply to research involving prisoners.
  - Composition requirements (Prisoner Representative) must be met for all types of review (initial, continuing, modifications).
  - **Be prepared for situation in which a subject BECOMES a Prisoner while enrolled in protocol that did not receive the regulatory required review:**
    - Investigator must notify IRB.
    - All research interactions (including obtaining private identifiable information) must stop unless principal investigator asserts it is in best interest of the subject to continue participation.
    - If investigator wants prisoner to continue participation, then IRB must re-review the protocol in accordance with the Subpart C requirements.
    - If HHS is involved, certification will have to be sent to HHS and a letter of authorization to proceed received before research with prisoner subject can continue.



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## Review Process Check-up: Special Populations

- **What to Watch for:**
  - **Children:**
    - Look at your state law to determine who is a “Child.”
    - IRB must assign appropriate risk/benefit category.
    - IRB must determine if permission must be obtained from one or both parents.
    - IRB must determine if Assent is required from children participating in research.
    - If a Child is in the custody of a state agency, then the regulatory requirements for Wards of the State must be followed:
      - Check state law regarding status of foster children in the custody of foster parents.



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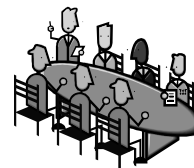
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## Review Process Check-Up: Making Sure Documents Match

- **Consistency between research agreement and informed consent is extremely important, as is ensuring consistency within the informed consent.**
- **What to watch for:**
  - Beware of cut-and-paste consents.
  - Have a process in place between sponsored programs office and IRB for determining who does final match-up.
  - Subject injury language.
    - HOT TOPIC with Medicare and pharmaceutical companies.
  - “Additional costs” text in informed consent.
    - HOT TOPIC in clinical trial billing arena.
    - Look at language regarding payment of costs for uninsured subjects.

## Assessing IRB Meetings

- Elements of a Successful IRB Meeting:
  - **Train the IRB Members & Administrators**
    - Initial and Continuing Training
    - Minute Taking Requirements
    - Changes in Regulations and Determination Letters
  - **Establish Member Composition & Quorum Requirements**
    - General Member Composition Requirements
    - Identifying Members with COIs
    - Tracking the “ins and outs” of the Meeting
    - Special Compositional Requirements
  - **Direct the Discussion**
    - Ensure all Required Review Elements are Covered
      - Checklists
    - Consensus and Opposing opinions
    - Local Context
  - **Committee Actions on Protocols**
    - Pending vs. Deferred
    - Voting



## Assessing IRB Meetings

- **What to Watch For:**
  - **Confidentiality Agreements** – Many sponsored research protocols have confidentiality and non-disclosure requirements; IRB members should sign appropriate non-disclosure agreements.
  - **Coverage of All Review Elements** -- CHECKLISTS are essential.
    - Chair should appropriately frame the motion on which the Committee votes.
  - **Local Context** – If the research is taking place at another site, the IRB must ensure that it considers the local context. Particularly important for international research.
  - **Deferral vs. “Pending” Approval:** One of the most common IRB errors noted in OHRP determination letters is the IRB grant of “Pending” Approval when the protocol requires substantive changes or clarifications. In such cases, the protocol should be Deferred so that it comes back to the Full Committee for review.
    - **REMEMBER:** When “Pending” Approval is granted the approval period runs from the date that the Committee met and voted “Pending” Approval even though the research cannot begin until the IRB has given final approval after reviewing the investigator’s responses to the issues raised.

## QUESTIONS



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