06. Assurances and more: The ABCs of FWAs and SOPs - What they are and when are they needed?

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Assurances And More: the ABCs of FWAs and SOPs – What They Are and When Are They Needed?

OHRP Research Community Forum
Community Engaged Research: Exploring the Unique Community-Academic Relationship

St. Louis, MO
September 26, 2011

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Outline

- HHS Regulatory requirements
- Institutional responsibilities
- Assurance applications
- Written policies and procedures aka "SOPs"
HHS Regulations (45 CFR part 46)

HHS will conduct or support non-exempt human subject research only if:

- the institution has an OHRP-approved assurance,
  and
- the institution has certified to HHS
  - research was reviewed and approved by IRB, and
  - the research will be subject to continuing review

§46.103(b) & (f)
Institutional Responsibilities

Protect Human Subjects in Research

Responsibilities shared by Institutional Officials, IRBs, and Investigators
Institutional Assurance

- Documentation of institution’s commitment to comply with applicable regulations §46.103(b) & (f)
Institutional Assurance

- Required when engaged in non-exempt human subject research
- Principal method of compliance oversight
Institutional Assurance, cont’d.

- Federalwide Assurance (FWA) - only option
- Generally recognized by other federal departments & agencies
- Designate only registered IRB(s)
Assurance Applications – Extending FWA

- **Individual Investigator Agreement**
  - independent investigators
  - investigators at another institution

- Assured institution responsible for oversight of research

Sample agreement and guidance available at OHRP website:

http://www.hhs.gov/ohrp/assurances/forms/unaflsup.rtf
http://www.hhs.gov/ohrp/policy/guidanceonalternativetofwa.html
Assurance Applications – Relying on External IRB

Institution responsibility

- Written agreement
  - IRB authorization agreement
    - http://www.hhs.gov/ohrp/assurances/forms/iprotsup.rtf
- Ensure research conducted per IRB approved plan
- Procedures for reporting to OHRP
Institutional Official’s Responsibilities

Assure compliance with the:

Terms of the Federalwide Assurance
Institutional Official’s Responsibilities (cont’d)

- Determine application of FWA – to “check” or “not to check” the box
Institutional Official’s Responsibilities (cont’d)

- Set the "tone" for an institutional culture promoting ethical conduct of research
- Support IRB actions & determinations
Institutional Official’s Responsibilities (cont’d)

- Ensure that investigators fulfill their responsibilities
- Support training/education opportunities for staff
IRB Written Policies and Procedures
Outline

- “Magnificent 7” required elements & operational procedures
- Procedures necessary to meet other HHS requirements
- Additional considerations
Written Procedures

- "Magnificent 7" required
- Other HHS Requirements
- Additional Considerations
Required Elements of Written IRB Procedures
§ 46.103(b)(4-5)
Required Element 1

Procedures IRB will follow for conducting initial review of research

§46.103(b)(4)(i)
Required Element 2

Procedures IRB will follow for conducting continuing review of research

§46.103(b)(4)(i)
Initial & Continuing Review

Description of

- Method of review
- Reviewer system
- Documents received and distributed for review
- IRB review, findings, & determinations
- Range of possible actions by IRB
- Further review by institution
Method of Review

- Convened IRB Meeting
- Expedited
Convened IRB Meeting

- Convened meeting (telephone, videoconference participation OK)
- Quorum
  - majority of IRB members present
  - at least one non-scientist present
- Approval by majority present
Expedited Review

- Minor changes to previously approved research
- No greater than minimal risk and on “list” at 63 FR 60364-60367:

http://www.hhs.gov/ohrp/policy/expedited98.html
Expedited Review (cont’d)

Description of

- Assignment of reviewers
  - IRB chair designates
  - criteria for assignment
  - IRB chair or experienced IRB member reviews
- Documents distributed for review
- Communication of approval action to all IRB members
Documents for Initial Review

- Protocol summary and/or full protocol
- Proposed informed consent document
- Relevant HHS application or proposal
- Recruitment and data collection materials
- Multi-center trials (HHS supported)
  - complete approved protocol and informed consent document
Documents for Continuing Review

- Protocol summary and/or full protocol, include modifications previously approved
- Current informed consent document
- Status report:
  - number of subjects accrued
  - summary of unanticipated problems, available AE information, withdrawal of subjects, & complaints
  - literature summary, amendments, & modifications since last review
  - relevant multi-center trial reports
- All other documents available
IRB Review, Findings, & Determinations

Description of process:

- Criteria for approval under §46.111 & applicable subparts

- Informed consent considerations
  - basic & additional elements §46.116(a & b)
  - altering or waiving §46.116(c or d), §46.408(c), & §46.101(i)
  - waiving written documentation §46.117(c)
Range of Possible IRB Actions

Description of action:

- Approve research
- Require modifications in order to secure approval
- Disapprove research (convened IRB only)
- Suspend or terminate previously approved research
OHRP recommends institutions have written procedures for documenting IRB findings, determinations, actions, and other IRB requirements.
Further Review by Institution

- Who is responsible for further review
  - institutional committees, e.g., COI, Privacy Board, Radiation, Biosafety
  - other

- Institutional policies relevant to review

- Actions that may be taken by institution
  - institution may *not override* IRB disapproval
Required Element 3

Procedures the IRB will follow for reporting its findings and actions to the investigator and the institution

§46.103(b)(4)(i)
Reporting IRB Actions

To investigator

- Written communication
- Request for modifications or clarifications
- Reviewing and acting upon investigator’s response
Reporting IRB Actions (cont’d)

To institution

- Written communication
- Which institutional official(s) notified
- How notification accomplished
Procedures the IRB will follow for determining which projects require review more often than annually

§46.103(b)(4)(ii)
Determining Frequency of IRB Review

- Specific criteria used to make these determinations
- Document approval period
Required Elements 5

Procedures the IRB will follow for determining which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review

§46.103(b)(4)(ii)
Verifying No Changes Since IRB Review

Specific criteria, e.g.,

- Random selection of projects
- Complexity of project
- History or concerns re: investigator compliance
Required Element 6

Procedures for ensuring prompt reporting to the IRB of proposed changes in a research activity and ensuring that such changes in approved research may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject

§46.103(b)(4)(iii)
Ensuring Protocol Changes Made in Accordance with Regs

- Steps to ensure compliance, e.g.,
  - training programs for investigator;
  - specific directives included in approval letters to investigators,
  - random or targeted audits of research
- Exception - eliminate apparent immediate hazards to subjects
Required Element 7

Procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, the Department or Agency head, and OHRP of any

- unanticipated problems involving risks to subjects or others
- any serious or continuing noncompliance
- any suspension or termination of IRB approval

§46.103(a) and §46.103(b)(5)
Unanticipated Problems

- Unexpected
- Related or possibly related
- Suggests greater risk of harm

Reviewing and Reporting Unanticipated Problems And Adverse Events:
http://www.hhs.gov/ohrp/policy/advevntguid.html
Most Adverse Events are **not** Unanticipated Problems

- Adverse Events
- UPs

**Do Not Report AE that are not UP to OHRP**

**Report all UP**
Reporting Requirement

- Who is responsible for prompt reporting
  - to whom/which office(s) or official(s)
- Time frames for accomplishing reporting requirement
- Range of possible actions taken by the IRB in response to reports

Reporting Incidents to OHRP:

http://www.hhs.gov/ohrp/policy/incidreport_ohrp.html
Key Points - Required Elements of Written IRB Procedures

- Institutions must have written procedures comprised of the seven required elements
- Include step-by-step operational details that are user friendly and effective
- Implement throughout the organization
- OHRP guidance is available
Other HHS Requirements and Additional Considerations
Written Procedures

- "Magnificent 7" required
- Other HHS Requirements
- Additional Considerations
Subparts B, C, and D

- Categories of permissible research
- Research not otherwise approvable
  (Secretarial panel process)
- Additional criteria for IRB approval
- Special requirements for informed consent, parental permission, and assent
Informed Consent Process & Documentation

- Facilitate informed consent
- “Long” and “short-form” consent options and considerations
- Non-English speaking subjects
- Methods for ensuring use of proper informed consent document
- Who may be/must be involved in consent process
Determining Applicability and Exemptions

Considerations:

- Institutional locus (e.g., IRB office)
- Institutional person – someone with good foundation of human subjects’ protection regulations
- Mechanism for ensuring no changes in research
Conflict of Interest (COI)

- Recognize
- Manage

HHS Guidance on Conflict of Interest:

Education

Training and education program considerations for IRB members, investigators, & staff

- Who
- How often
- Documentation
- Resources
Other Issues for Possible Inclusion

- Important definitions
- Preparing for review/meeting
- IRB member selection & retention
- IRB meeting attendance
- IRB member responsibilities
- Research with vulnerable populations
Other Issues for Possible Inclusion (cont’d)

- Relying on an external IRB
- Serving as IRB for other institutions
- Managing allegations of non-compliance
- Minimizing coercion and undue influence
- Other relevant authorities
Key Points - Additional IRB Written Policies and Procedures

- Many institutions develop comprehensive procedures that go beyond what is required
- Provide helpful resource for all involved in human subject research
- Establish institutional expectations
OHRP Contact Information

- Website:  [www.hhs.gov/ohrp](http://www.hhs.gov/ohrp)
- Email:  [OHRP@HHS.GOV](mailto:OHRP@HHS.GOV)
- Toll-free phone #:  1-866-447-4777
- Main phone #:  240-453-6900
- Join Listserv:  [http://www.hhs.gov/ohrp/newsroom](http://www.hhs.gov/ohrp/newsroom)