



Managing a Centralized Research Compliance Program in a Decentralized Environment

**HCCA Research Compliance Conference –
October 19, 2009**

DRAFT 3/08 DRAFT

1

Presenters

Luanna Putney, Ph.D., CHC, CCEP

*Director of Research Compliance
Ethics and Compliance Department
University of California*

Andra M. Popa, J.D., LLM

*Consultant
Meade & Roach, LLP*

DRAFT 3/08

2

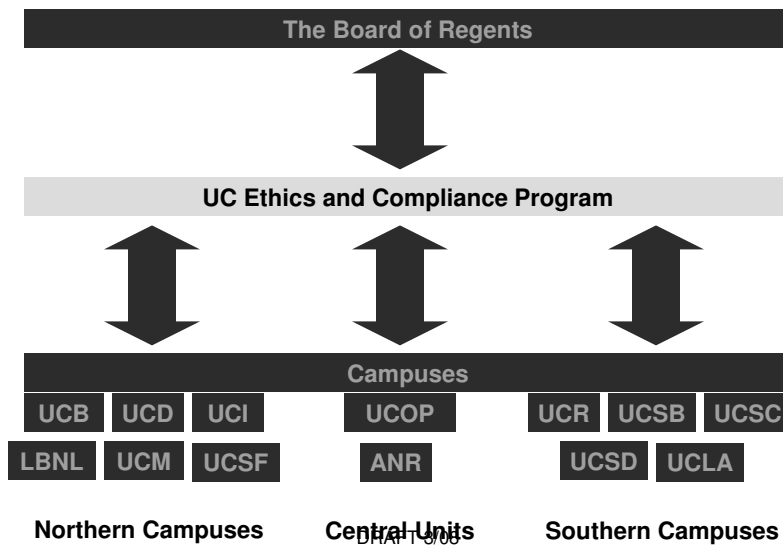
Presentation Goals

- Identify goals, priorities, gaps and alignments in systemwide and campus-based compliance programs
- Learn processes to support and integrate conflict of interest and other research compliance priorities in a distributed system
- Learn practical ways to incorporate AAHRPP accreditation requirements, VA research, Stark, anti-kickback, and research billing requirements
- Learn how to develop audit tools and form templates and take away samples

DRAFT 3/08

3

UC Systemwide Ethics and Compliance Program



DRAFT 3/08

4

UC Systemwide Ethics and Compliance Program: Mission Statement

The UC Ethics and Compliance Program **enhances** the University's duty to perform its public responsibilities in an ethics and compliance-based environment where applicable legal, regulatory, Regental and UC Policy are followed and in which the public trust is maintained.

Sample of Compliance Obligations including but not limited to the below

Anti-kickback/Sponsorship Laws	Equal Employment Opportunity	Grants and Contracts Rules	Human Subjects Protection	Conflicts of Interest
Anti-trust/ Competition Laws	Affirmative Action	Animal Research	HIPAA Privacy	Compensation & Tax (IRS)
Pricing & Reimbursement	Sexual Harassment	Environmental Health & Safety	Good Clinical/Lab Practices (GCP)	Information Security
Promotional Activities	Benefits Fiduciary Obligations	Import/Export Controls	Licensure	
	NCAA			

DRAFT 3/08

5

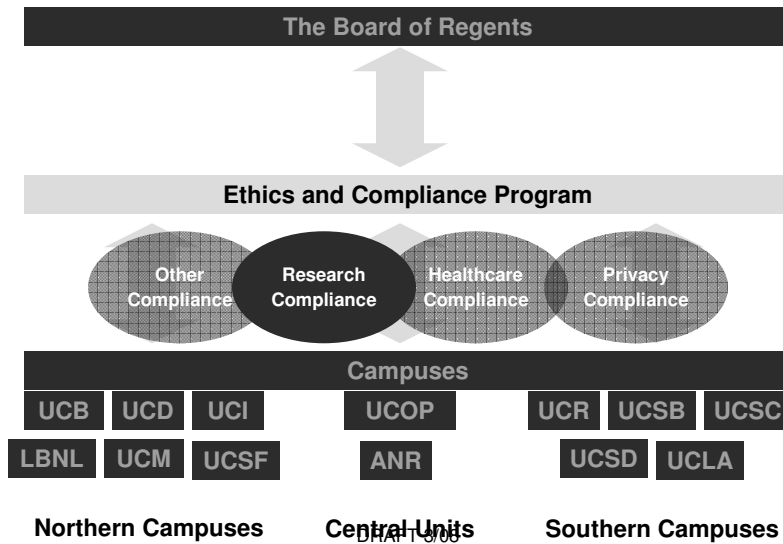
Roles of the Systemwide Office

- Assist locations in establishing effective Ethics and Compliance Risk Committees, i.e., provide tools, performance metrics, benchmarking, etc.
- Coordinate/collaborate with locations on identification of compliance risks and mitigation efforts
- Develop mandatory training (i.e., Sexual Harassment, Compliance/COI Briefings, HIPAA)
- Facilitate accountability through development of central policy statements (i.e., enforcement policies)
- Report overall activities and performance metrics to the Compliance and Audit Committee of the Board of Regents

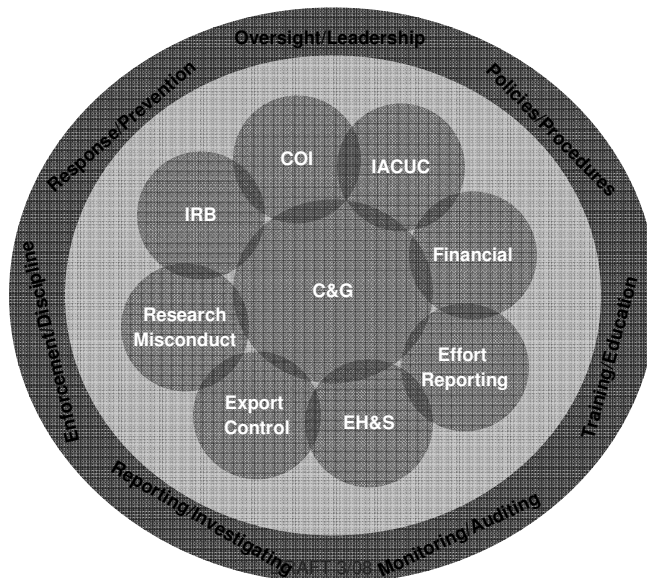
DRAFT 3/08

6

UC Systemwide Ethics and Compliance Program: Research Compliance Unit



Creating an Effective Systemwide Research Compliance Program



Systemwide Research Compliance Program

- Goals
 - Prevent systemwide non-compliance
 - Enhance public trust
 - Meet expectations of external constituents and The Regents
- Priorities
 - Focus on high risk research compliance areas that threaten more than one campus: FY10 priorities include Effort Reporting, Conflict of Interest, ARRA Monitoring
 - Activities focus on preventing non-compliance in high risk areas through: Education/training, Auditing/monitoring and Assurances

DRAFT 3/08

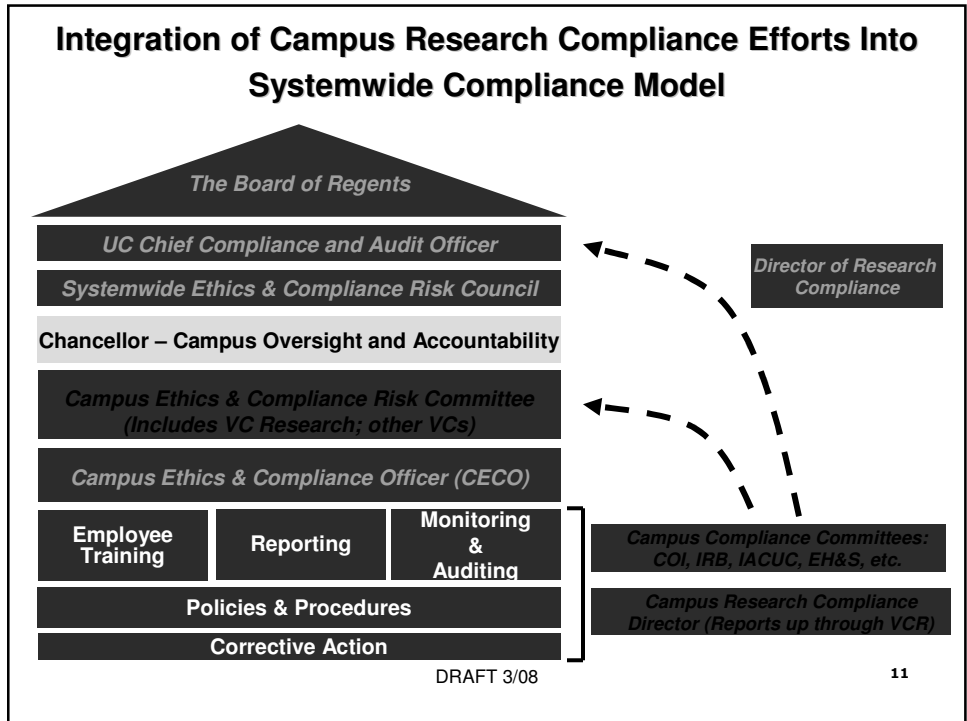
9

Campus Research Compliance Program

- Goals
 - Prevent campus non-compliance
- Priorities
 - Focus on high risk research compliance areas that threaten individual campus: i.e., ARRA Monitoring, Animal Activism, Effort Reporting
 - Activities focus on preventing non-compliance in high risk areas through: Policies/Procedures, Education/Training, Advisory Services

DRAFT 3/08

10

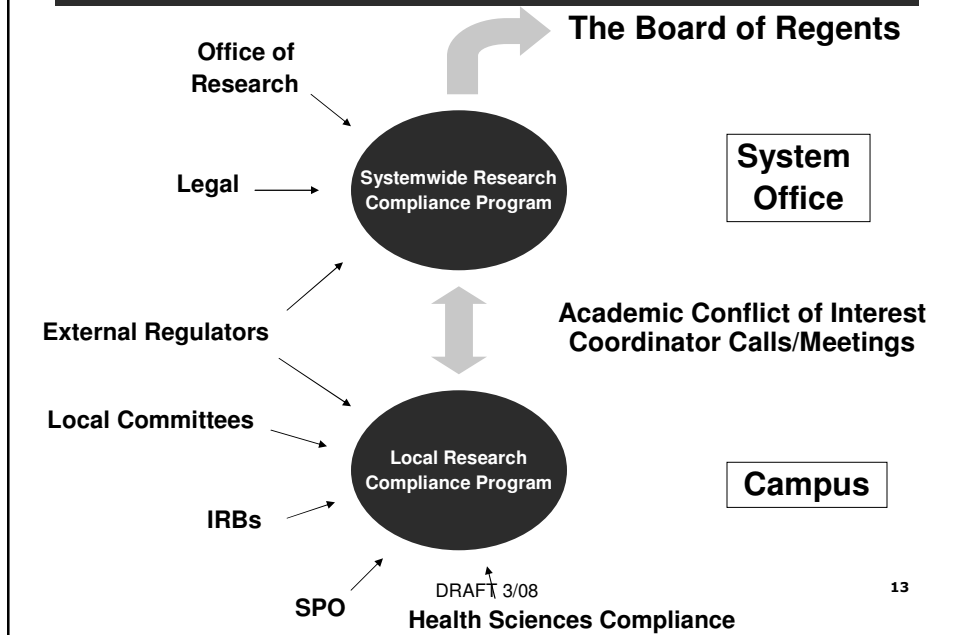


Research Compliance: Conflict of Interest

- Potential expansion of federal regulations covering COI in PHS-funded research to broaden scope of reportable interests, enact new requirements regarding management of COI, address institutional COI
- Potential regulation/increased scrutiny of COI in clinical enterprise
 - Senator Grassley inquiries
 - Federal legislation (Physicians Payment Sunshine Act)
- UC Initiating discussion regarding merit/feasibility of annual reporting requirements (to supplement transaction-based reporting)

DRAFT 3/08 12

Example: Conflict of Interest Communication



Recent Topics at UC Systemwide COI Meeting

- Annual Financial Interest Reporting by Investigators
- Coordinating Conflict of Commitment and COI Reporting
- Mandatory COI Training for Researchers
- Determining Who Meets the “Design, Conduct or Reporting” Standard
- Consent Form Disclosures - Individual Financial Interest & Moore Clause
- Institutional Financial Interest Disclosure in the Consent Form
- Panel Discussion - COI Issues in Licensing and Research with Inventor-Owned Companies

DRAFT 3/08

14

Summary: Systemwide vs. Campus Research Compliance Programs

- Gaps –
 - Campus monitoring efforts (i.e. COI, Export Control, Clinical Research QA)
 - Systemwide information about campus compliance reports, audits, external regulator visits, etc.
- Alignments –
 - Prevention of non-compliance
 - Focus on education/training

DRAFT 3/08

15

Case Study: Integrating a Human Research Compliance Program

- In a three-step process, this presentation will outline the integration of a hypothetical human subjects protection program as a case study.

Overview of Requirements

Key Operational Choices

Practical Tips for Integration

- Apply this three-step model to other types of research, including animal research.

DRAFT 3/08

16

Research Review Model

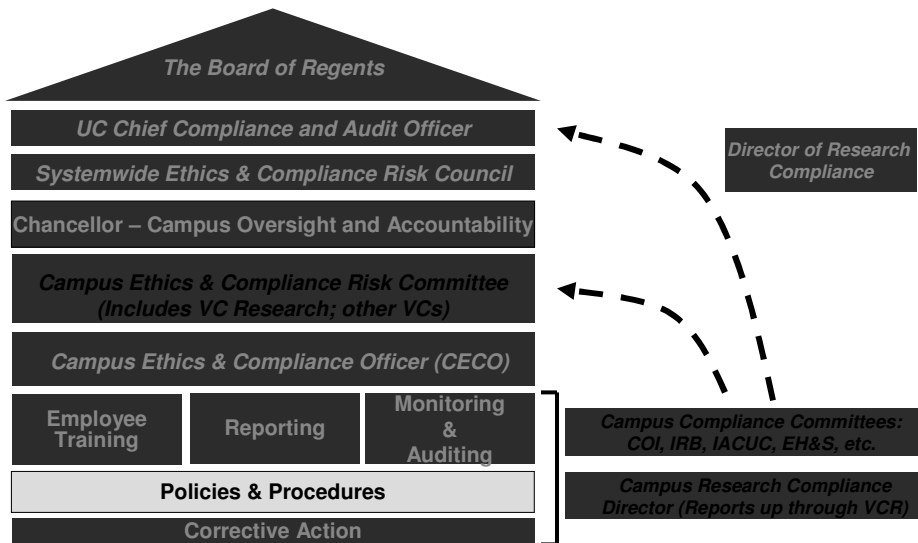
- A continuum exists as to how institutions structure their research review models.
- All types of institutional models need to develop a research compliance program that contains both required elements and elements relative to institutional needs



DRAFT 3/08

17

(Note: Slide from Dr. Luanna Putney's Presentation)



DRAFT 3/08

18

Policies and Procedures

Separate policy from procedure statements

Overview of Requirements

Policy statements

- Curate library of federal and state regulations and laws; VHA Handbooks & Directives
- Institutional policies that may affect human research:
 - Classified research
 - Reporting requirements for payments over \$600
 - Planned emergency use

Key Operational Choices

- Institutional interpretation of certain laws and regulations
- State law as related to research
- Beyond the baseline requirements
- Flexibility in the regulations
- Procedures: Describe how the institution carries out the policy statements

Practical Tips for Integration

Separating the policy from the procedure in a document requires an institution to work through how to implement the requirements and to work with other departments in a decentralized system to identify and delegate responsibilities.

19

Policies and Procedures: Myth vs. Reality

Myth:

- It was better before when we did not know every requirement; now we have more work.
- Policies are both a sword and a shield.
- Its best that we not detail how we do things to avoid violating our own procedures.
- We will just copy another institution's policies and procedures.
- We will just copy the regulations to create a policy and procedure document.
- It is always important to state the law and requirements in your own words.
- It is important to provide the history of the requirements in the policy.
- We did not follow the policy and procedure because we could not understand it (although we had the opportunity to comment).
- We did not follow the policy and procedure because our priority is processing letters.

Reality:

- Reference: 45 CFR 46.103(b)(4) and (5) require institutions to have written IRB procedures for a wide range of topics
- *OHRP Guidance on Written IRB Procedures*, January 15, 2007
- *OHRP Recent Compliance Oversight Determinations*, Item #39, February 4, 2009
- Corrective action plan requirements
- OHRP Determination Letters
- AAHRPP requirements
- State and federal laws and regulations still apply
- The policy decisions may be unique to a particular institution or to certain state laws; procedures are unique
- Research mix differs between institutions
- Well written policies and procedures improve efficiency, improve the quality of submissions, and help create uniformity
- Find greater flexibility in the regulations
- Tip: Staff can cut and paste policy and procedure into letters or use as a reference for phone calls

DRAFT 3/08

20

OHRP Guidance on Specificity of Written Procedures

- “OHRP has not developed a model written IRB procedures document for institutions to adapt because procedures appropriately can vary significantly among institutions as the result of differences in institution size, type of research activities, institutional administrative practices, number of IRBs, and local and state laws and regulations.”
- “For each required element [in 45 CFR 46.103(b)(4) and (5)], the written IRB procedures **should** provide sufficient step-by-step operational details so that an independent observer can understand how an IRB operates and conducts its major functions.” (emphasis added)

Further Reading: *OHRP Guidance on Written IRB Procedures*, dated January 15, 2007.

DRAFT 3/08

21

The Signatory Official, The Institutional Official & The Human Protections Administrator

Overview of Requirements

- **The Signatory Official “must be legally authorized to represent the Institution.”**
 - Ensures proper allocation of resources and education
 - Appropriate knowledge of local research context
 - Institutional official function may be delegated
 - Be cautious with delegation in a decentralized program
- The Human Protections Administrator oversees the day to day management of the human participant protection program

Key Operational Choices

- Consider whether your current IO and HPA selection are appropriate to your human subjects protection program and the size and scope of your program and institution.

Practical Tips for Integration

- Clearly identify individuals and roles publicly
- Specify responsibilities in policies and procedures
- Schedule standing meetings for the IO to discuss research review resources with the HPA

Further Reading: *Assurance Training Modules: Regulations & Institutional Responsibilities*; *FDA Warning Letter*, dated September 30, 2008; *OHRP Guidance, Knowledge of Local Research Context*, dated August 27, 2008.

Terms of the Assurance

Overview of Requirements

- All institutions that are *engaged* in human subjects research that is not exempt from the regulations and supported by an HHS agency must provide a written assurance of compliance to OHRP
- Before reviewing or developing policies and procedures, review the terms of your federal wide assurance
 - Single Project Assurances
 - Department of Defense/ Navy: Addendum

Key Operational Choices

- Determine whether the choices listed on your federal wide assurance as to non-federally funded research are appropriate for your institution and research mix
- Determine whether the assurance correctly reflects reliance on IRBs of other institutions or on an independent IRB; the institution should submit changes to OHRP as applicable
- Designating additional IRBs under the FWA requires that the institution provide prior notice and obtain approval from OHRP

Practical Tips for Integration

- Develop all policies and procedures, applications, and forms with the terms of the federalwide assurance, as well as all other assurances, as the framework.

Further Reading: *OHRP Determination Letter in Re: Human Subject Protections Under Federalwide Assurance - 6252*, dated June 29, 2007; OHRP FWA FAQs, FAQs #11 and #35; *OHRP Guidance on Engagement of Institutions in Humans Subjects Research*, dated October 16, 2008. 23

Memorandum of Understanding / IRB Authorization Agreement

Overview of Requirements

- "Reliance on the IRB of another institution or organization or an independent IRB must be documented by a written agreement that is available for review by OHRP upon request."
- An IRB must not begin reviewing the research of another institution without a written agreement in place
- Memorandum of Understanding is recommended
- Sample IRB Authorization Agreement is on the OHRP web site, but not recommended

Key Operational Choices

- Determine whether certain types of research should be reviewed by an external IRB
- Remains the responsibility of the institutional official

Practical Tips for Integration

- A separate MOU or IAA is needed for each legal entity
- IAA is not the preferred choice because it is just one page and very general
- Exercise caution with similar, but not identical, institutional names
- For IRBs that are the IRB of record for a VA Medical Center:
 - Consider forming a committee with various HPAs/IOs at different institutions if more than one institution is involved to make sure that the institutions are communicating properly and to direct audits

DRAFT 3/08

24

Engaged or Not Engaged/ Multi-Center Studies

Overview of Requirements

- Institutions considered engaged in HHS supported non-exempt human research would need to hold or obtain an OHRP approved FWA and certify IRB review and approval to HHS when the involvement of their employees or agents in that project rises to *engaged* status

Key Operational Choices

- Engagement can be used as criteria to establish education requirements
- Determine treatment of adjunct faculty who do not engage the institution
- Determine whether the institution applies the OHRP guidance applied to non-federally funded research if the FWA does not elect OHRP jurisdiction over such research
- Determine scope of NIH sponsored research educational requirements

Practical Tips for Integration

- Coordinate with NIH sponsored research educational requirements
- Devise a method to verify completion of the educational requirements
- IRB administrative staff pre-review the investigator's submission and verify that all educational requirements are met
- IRB members confirm whether requirements are fulfilled

Further Reading: OHRP Guidance on Engagement of Institutions in Humans Subjects Research, Item 25 #40, dated October 16, 2008. DRAFT 3/08

Human Subjects | Research | Exempt

Overview of Requirements

- The FDA and OHRP have different definitions for "research" and "human subjects."
- VA Research on human biological samples requires IRB review (VHA Handbook 1058.03)
- If the research involving only human biological specimens is found to be exempt by an IRB, then the VA R&D Committee is still responsible for review
- Ensure that the investigator does not make the final determination as to whether something is research, concerns human subjects, or exempt
- Exempt research must still be conducted in accordance with the ethical principles of the Belmont Report

Key Operational Choices

- Operational choices as to how to track which protocols are exempt
- Even if research is exempt from the regulations, the ethical principles of the Belmont Report still apply
 - Operational decisions need to be made as to the contents of the investigator application, treatment of amendments to the protocol, educational requirements, pre-review scope, and review guide contents
 - Operational choices rest on how to implement the ethical principles of the Belmont Report. For example, what information does the institution request from the investigator? An informed consent? A protocol?
 - Operational choices as to time period that an exemption can be granted

Practical Tips for Integration

- Provide education to staff and investigators as to the difference between expedited review and exempt review

DRAFT 3/08

26

Conflict of Interest

Overview of Requirements

- Different conflict management requirements and procedures
 - PI/ Research Coordinator
 - Office Staff
 - Institutional conflicts
 - IRB Members

Key Operational Choices

- Operational choices need to ensure that COI are identified and sent to the IRB when necessary in a timely manner
- Process mapping to ensure there are no gaps in the procedure section
- Create different forms and processes for PI/Research Coordinator, IRB members, and office staff
- Create a database containing conflicts of interest information
- Identify how the institution will apply COI parameters for non-federally funded research

Practical Tips for Integration

- If the institution has a conflicts of interest office, meaningfully involve this office in the process of developing a policy and procedure and forms specific to the IRB review process, IRB members, and the office staff
- Ensure that any the primary institutional policy and procedure is reflected in any human research specific policy and procedure

DRAFT 3/08

27

Core Policies and Procedures: Initial and Continuing Review

Overview of Requirements

- "Assurances applicable to federally supported or conducted research shall at a minimum include . . . written procedures for which the IRB will follow for conducting its initial and continuing review of research."

Key Operational Choices

- Decisions need to be made as to the content development and design of applications, forms, and review guides, as well as supplementary materials. In addition, the documentation system needs to be worked through to ensure that it is seamless, from expedited review to convened review.

Practical Tips for Integration

- OHRP and AAHRPP require that continuing review be substantive. Apply the same regulations at 45 CFR 46.111 and subparts B, C, and D, when applicable, as well as the informed consent requirements. Apply the regulations to the facts that have developed over the course of the IRB approval period. The criteria are the same on continuing review and expedited review.
- Develop a pre-review process that identifies missing or improper documents or incomplete applications before the submission arrives at the IRB level
- Develop initial and continuing review applications that collect sufficient information from which the IRB can make its determination
- Develop review guides for IRB members that list each approval criterion individually

DRAFT 3/08

28

Core Policies and Procedures: More than Annual Review | Verification

Overview of Requirements

- “Assurances applicable to federally supported or conducted research shall at a minimum include . . . written procedures which the IRB will follow . . . for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.”

Key Operational Choices

- Operational decisions need to be made as to how and where to incorporate these matters into IRB review materials and how to develop these abstract principles into procedures.

Practical Tips for Integration

- Provide education to staff and IRB members as to documentation requirements and case studies providing the practical application of verification from other sources.

DRAFT 3/08

29

Core Policies and Procedures: Investigator Prompt Reporting

Overview of Requirements

“Assurances applicable to federally supported or conducted research shall at a minimum include . . . written procedures . . . for ensuring prompt reporting to the IRB of proposed changes in a research activity.”

- Changes to research initiated without prior IRB approval

Key Operational Choices

- Determine time period for your institution
- Create prompt reporting forms that investigators submit
- Identify personnel who will assess and triage the report
- Map process for prompt reporting from intake to IRB Chair to IRB members

Practical Tips for Integration

- Send investigators a summary of prompt reporting responsibilities along with IRB approval letter
- Educational sessions for investigators and research coordinators

DRAFT 3/08

30

Core Policies and Procedures: Institutional Reporting

Overview of Requirements

“Assurances applicable to federally supported or conducted research shall at a minimum include . . . for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with [45 CFR 46] or the requirements or determinations of the IRB.”

Key Operational Choices

- Map the office process for identification and management of noncompliance
- Provide definitions of serious noncompliance and continuing noncompliance
- Create template noncompliance letters

Practical Tips for Integration

- Provide targeted education to IRB members and administrators

DRAFT 3/08

31

Core Policies and Procedures: Lapses in IRB Approval

Overview of Requirements

- Lapses in IRB approval constitute noncompliance
 - OHRP has indicated this concept in several previous determination letters and most recently and most clearly in a determination letter dated June 9, 2009
 - The IRB, IRB Chair, or designee must make a noncompliance determination as to lapses in IRB approval, as appropriate
 - The IRB, IRB Chair, or designee must determine whether each individual lapse is serious and/or continuing noncompliance, as appropriate

Key Operational Choices

- Operational decisions as to: (1) lapse prevention, (2) method to identify lapsed protocols, (3) procedures to be followed after lapse in IRB approval, (4) identification of individuals who are notified of lapse, (5) procedures to follow if the investigator has left the institution, (6) time frame of when protocols are closed, and (7) consequences of lapse in IRB approval for investigators.

Practical Tips for Integration

- One of the most difficult areas to implement; obtain feedback from various levels of administrative staff, IRB members, and all IRB chairs. Provide education and flow diagrams.

Further Reading: OHRP Determination Letter to Carle Clinic Association and Carle Foundation Hospital, dated June 9, 2009, available on OHRP website. DRAFT 3/08

32

Core Policies and Procedures: Lapses in IRB Approval Cont.

Overview of Requirements

- "Assurances applicable to federally supported or conducted research shall at a minimum include . . . written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of . . . any suspension or termination of IRB approval."
- A lapse in IRB approval is distinct from the termination or suspension of IRB approval

Key Operational Choices

- Identify how lapses in IRB approval will be tracked
- Create a process to prevent lapses in IRB approval, such as 90, 60, 30 day reminder letters
- For minimal risk research, determine whether protocols that have lapsed in IRB approval will be closed immediately or whether investigators have a few days to submit the continuing review application or final report application before the institution closes the research
- Develop a process for greater than minimal risk research
- Develop a form and procedure for managing protocol exceptions after lapse in IRB approval
- Audit the IRB administration office to ensure that noncompliance determinations are being made as to each lapsed protocol
- Ensure that serious and/or continuing noncompliance is being reported to the appropriate agencies
- Audit the investigator to ensure that no recruitment, enrollment, or any other research is occurring after IRB approval has lapsed.

Practical Tips for Integration

33

- Provide targeted education to IRB members and IRB administrative staff

Core Policies and Procedures: Reporting to Outside Agencies

Overview of Requirements

- "Assurances applicable to federally supported or conducted research shall at a minimum include . . . written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval."

Key Operational Choices

- An institution that has not extended its FWA to non-federally funded research needs to consider whether it will report non-federally funded events to OHRP. An institution could determine that this will be decided on a case by case basis
- Note that the FDA reporting requirements and all other requirements apply whether the research is federally funded or not
- Determine who needs to receive a copy of the reporting letter

Practical Tips for Integration

- Provide a copy of the reporting letter to a broad spectrum of individuals for a variety of reasons, such as the department head or supervisor, compliance, and the IRB Chairs

Citation: OHRP Determination Letter to Carle Clinic Association and Carle Foundation Hospital, dated June 9, 2009, available on OHRP website.

DRAFT 3/08

34

Core Policies and Procedures: Sufficient Resources

Overview of Requirements

- Sufficient Meeting space
- Sufficient support staff
- Appropriate selection of IRB members

Key Operational Choices

- A best practice is to include compliance with requirements when evaluating productivity of staff turnover of protocols
- Run reports as to how many protocols each IRB processes
- Run reports as to the subject mix of the protocols
- Separate exempt protocols

Practical Tips for Integration

- Again, establish a standing meeting on a regular basis where the IO and the HPA can review compliance and productivity reports and discuss this matter, along with other relevant staff.

DRAFT 3/08

35

Scientific and Scholarly Review

Overview of Requirements

- Investigational drug service
 - Cancer committee
 - Radiation safety
- VA R&D Committee
 - Biosafety (rDNA)
 - Multi-Center Studies
- Departmental Review
- Faculty Sponsor Review
 - Radioactive Drug

Key Operational Choices

- Ensure that policies and procedures are clear as to which scientific and scholarly review committees must approve research before the protocol is reviewed by the IRB
- Captured on the application that the investigator completes
- Pre-reviewer should verify that the application contains the applicable review forms

Practical Tips for Integration

- Incorporate review committee requirements in the application that the investigator must complete and require that the investigator obtain appropriate review before submitting the application to the IRB office

DRAFT 3/08

36

Criteria for Approval of Research

Overview of Requirements

- The application for IRB review must gather enough information from the investigator to allow the IRB to make determinations as to the criteria for IRB review at 45 CFR 46.111
- Legally effective informed consent requirements
- HIPAA requirements
- FDA requirements
- Institutional requirements
- Other requirements, including other Common Rule agency requirements
- State laws
- IRB must have sufficient experience as to the local research context to make the 45 CFR 46.111 criteria determinations and applicable subparts

Key Operational Choices

•Operational decisions include design and content of applications, pre-review guides, meeting minute templates, and posters. The content should reflect the operational practices and responsibility allocation.

Practical Tips for Integration

- When applicable, collaborate with counsel, privacy officer, compliance, and billing and coding to ensure that the same definitions are being used and to ensure consistency among departments
- Audit review guides and meeting minutes; compliance should attend IRB meetings for assessment

Further Reading: *OHRP Recent Compliance Overview Determinations*, dated February 4, 2009, Items #4, #40. 37

Wards

Overview of Requirements

- A ward of the state generally includes but is not limited to, a child placed by a court under the guardianship of DCFS. In some states, that state's DCFS has a review board that must approve the research before the IRB reviews the research
- Research state law definition for a foster child and guardianship of the person of a minor.
- Research state law limitations on certain types of research on wards of the state, such as experimental drugs.
- Note that federal regulations place limitations on when children who are wards of the state can be included for "406" or "407" research
- Note that for "406" or "407" research, the IRB must require the appointment of an advocate for each child who is a ward for research subject to OHRP regulations.

Key Operational Choices

•Wards are a population where the regulations still apply even if they are incidental to the research, so think through whether approval letters for all research involving children should have a statement that the IRB approval does not include approval for wards

Practical Tips for Integration

- Ensure that the initial application captures wards as a separate population to alert the IRB
- Ensure that the pre-review verifies whether DCFS review board documentation is present
- Ensure that the IRB has review guides that detail the intricacies of the state and applicable federal requirements

Children

Overview of Requirements

- One of the most complex areas in terms of state law requirements
- AAHRPP requires that key definitions for "child," "guardian," and "minor" be articulated, and this is an important step regardless of whether you are seeking accreditation or not as it will inform the review
- Research circumstances where minors can consent for themselves, and establish the parameters for what they can consent for. For example, emancipated minors, mature minors, married minors, and pregnant minors may have varying abilities to consent per state law.
- Assent and parental permission requirements should be listed, as well as requirements for waiver
- Research additional protections for children in research via the funding source. For example, in addition to IRB approval and R&D Committee approval, a waiver from the VA Chief Research and Development Office (CRADO) in Washington is required for research involving children
- Ensure that the IRB makes the determination as to the category of research involving children
- Include provisions for obtaining permission from parents or legal guardians, as well as waiver

Key Operational Choices

- The institution should determine whether it permits all categories of research involving children
- Work with counsel to determine whether to apply state laws related to medical treatment to research
- The institution will need to think through how to manage children who become adults during the course of the research, as well as how to manage instances where children refuse to assent

Practical Tips for Integration

- Once policies and procedures are finalized, design applications, pre-review guides, and review guides to capture the requirements at different operational levels
- Create a log of lapses with the outcome and provide to the IRB so that the continuing noncompliance determination can be based on facts

DRAFT 3/08

39

Decisionally Impaired/ Cognitively Impaired

Overview of Requirements

- Important to define terms, such as "cognitively impaired," "competence," "decisional capacity," "guardian," "incapacity," "incompetent," and "legally authorized representative." Research applicable state law.
- Ensure that the priority of surrogates list for your state is included in your policy and procedures
- Note that some funding sources, such as the VA, have different priority list for surrogates

Key Operational Choices

- The institution must work out the risk and benefit consideration in accordance with its own mission, other relevant policies and procedures, and apply ethical principles
- The institution will need to think through how to treat individuals with fluctuating capacity
- The institution also needs to consider how to manage individuals who are incompetent to consent but resist participating in research approved by their authorized representatives
- Work through when it is appropriate for investigators to obtain consent from the legally authorized representative of a subject and what documentation must be on file

Practical Tips for Integration

- Important to work with other entities in the organization to create a uniform policy as to having advance directives and guardianship documentation on file
- Audit investigator records for documentation concerning legally authorized representatives

Further reading: OHRP Institutional Review Board (IRB) Policy Manual, Chapter 6, Section D).

40

Pregnant Women, Human Fetuses, Neonates

Overview of Requirements

- Refer to all definitions including "delivery," "fetus," "neonate," and "nonviable neonate" in 45 CFR 46.202
- Research state laws concerning pregnant minors
- Note VA Handbooks prohibit research in which the subject is a fetus, in-utero or ex-utero (including human fetal tissue), research involving IVF, and additional requirements must be met for research to involve pregnant women.
- Additional federal requirements must be considered and met for IRB approval, as applicable, for pregnant women, neonates of uncertain viability, and nonviable neonates
- Research your state's anatomical gift act, since this may apply to research involving after delivery, placenta and other tissue

Key Operational Choices

- The institution needs to think through how to treat studies in which pregnancy is coincidental to subject selection
- The institution needs to consider how to treat research that is not otherwise approvable under the federal regulations, if it has chosen not to extend its federal wide assurance to non-federally funded research. For example, should the IO and HPA personally review this research or should an ad hoc panel be created? What requirements should be considered?

Practical Tips for Integration

- Once policies and procedures are finalized, operationalize them by incorporating the requirements in the application, pre-review, and review guides.
- Audit IRB review guides and meeting minutes to determine whether the appropriate determinations are being made

DRAFT 3/08

41

Prisoners/ Other Vulnerable Populations

Overview of Requirements

- "When an IRB is reviewing a protocol in which a prisoner is a subject, the IRB must make, in addition to other requirements . . . **seven additional findings.**"
- Category of research must be documented in the review guide or meeting minutes
- Prisoner representative must be an IRB member and not a consultant
- OHRP definition of "minimal risk" as to prisoners is different from non-prisoner research
- Work with counsel to verify whether state laws prohibit certain types of research with prisoners
- For example, Illinois state law prohibits the use of committed persons in "medical, cosmetic, or pharmaceutical experiments."
- For federally funded research, the institution must certify to the HHS Secretary through OHRP that the IRB is in compliance. In addition, the Secretary must determine that the proposed research falls within the categories permitted. Note that this may apply to all research if the FWA is extended.
- Important to note that other categories of prospective participants may be vulnerable to coercion or undue influence, such as the terminally ill
- The Federal Bureau of Prisons places additional restrictions on research that takes place in the Bureau of Prisons
- State departments of corrections may also have additional requirements for certain research

Key Operational Choices

- Require immediate reporting to the IRB once the investigator becomes aware if the IRB did not specifically approve prisoner population
- Provide definition of who is and who is not a prisoner, with various examples such as house arrest
- Develop policy and procedures for participants who become prisoners while on social behavioral and biomedical trials, particularly if certain biomedical research is prohibited by state law
- For non-federally funded research, the institution may want to permit expedited review if the research is in data analysis, depending on the terms of its FWA
- If the institution has not extended its FWA, it should note that certification is not required, but it may want to consider whether some categories require additional oversight by the HPA in the form of an *ad hoc* panel.

Practical Tips for Integration

- Ensure that the application appropriately reflect all requirements
- Ensure that the IRB is making all prisoner regulation determinations in the category.
- Incorporate prisoner regulation requirements in the IRB meeting minute template
- Ensure that documents capture that if a minor is also a prisoner, then both the children requirements and prisoner requirements apply

42

Informed Consent Process

Overview of Requirements

- Recruitment and payment are part of the informed consent process
- Subject injury language in the template form is important for clinical trial billing
- Basic and additional elements of informed consent apply to both biomedical and social behavioral research
- Research additional FDA requirements
- Additional requirements for the VA, particularly with respect to recruitment
- Research involving deception requires an alteration of informed consent
- Note that the FDA does not recognize the same concept of waiver of informed consent as OHRP
- The FDA has recognizes limited circumstances: in vitro diagnostic device investigations of leftover human specimens with devices that are exempt from IDE regulations and emergency use of a test article
- Note documentation requirements for waiver of the informed consent process, alteration of the informed consent process, or documentation of informed consent

Key Operational Choices

- The institution should consider consent options for prospective subjects who are non-English speaking, illiterate English-speaking, physically unable to talk or write, blind, and/or those with motor difficulties.
- Consider implications for both social behavioral and biomedical research
- Carefully consider implications of template informed consent language concerning benefit to research billing
- Establish a process to ensure that the informed consent matches the clinical trial agreement and protocol

Practical Tips for Integration

- Create informed consent template for investigators, incorporate questions on the application, provide review guides with basic and additional elements of informed consent, and clearly identify who will check whether the elements are present

DRAFT 3/08

43

Further Reading: OHRP Determination Letter re: Human Research Protections under Federalwide Assurances FWA-176, FWA-2247, FWA-9025, dated May 27, 2009; OHRP Determination Letter re: Human Research Protections under Federalwide Assurance FWA-13356, dated February 19, 2009.

Other Requirements

Overview of Requirements

- Identify requirements of agencies that fund research at the institution. For example: DOE; DOD (Navy); DOD (Army); VA
- One AAHRPP element is community outreach. If you are going to create a registry of your trials, pay close attention to the information that is permitted to be listed in a registry before IRB approval is required
- Ensure that the institution has an adequate procedure established with the pharmacy that receive, investigational drugs
- Ensure that tissue banking requirements are captured
- Sponsor-investigator holding an IDE/IND
- Emergency use of a test article
- Humanitarian Use Devices

Key Operational Choices

- For example, Veterans Administration research has a significant amount of other and different requirements, and therefore, it may be advised to create separate pre-review, review guides, and supplementary materials
- Determine what protections to apply in specific cases. For example, the DOE has adopted Subpart D (children), while the National Science Foundation has not
- The institution needs to determine whether it is acceptable for the sponsor-investigator is permitted to hold his or her own IND or IDE, as well as establish necessary precautions
- The institution needs to assess whether it will permit planned emergency use

Practical Tips for Integration

- Incorporate requirements on the IRB member review guides
- Use the policies and procedures as the foundation of the review guides, supplementary materials, and

Further Reading: VHA Handbook 1200.1; VHA Handbook 1200.05; ORO; FAQ: *Banking of Human Biological Specimens for Research*, dated 8/14/09; VA-Approved Tissue Banks; OHRP Guidance on IRB Review of Clinical Trial Websites

DRAFT 3/08

44

HIPAA

Overview of Requirements

- HIPAA
- FERPA
- Carefully research state laws to determine if some state law preempts HIPAA
- In cases where state law is more restrictive, follow state law
- If a state law is more restrictive, carefully assess whether waiver of authorization is appropriate for subjects that the state law governs
- Examples of state law topics that may preempt HIPAA include but are not limited to: HIV/AIDS status, genetic testing, and mental health information
- For example, waiver of authorization may not be permitted in certain states for retrospective chart reviews of HIV/AIDS status of patients

Key Operational Choices

- Determine who will assess whether PHI is present in the research
- Please consider state law HIPAA preemption concerns when weighing whether to implement creative solutions that other institutions may be implementing on seemingly unrelated topics

Practical Tips for Integration

- Incorporate HIPAA requirements and restrictions in review guides and create applications that collect all information necessary to accurately make an assessment

DRAFT 3/08

45

Anti-Kickback and Stark

Overview of Requirements

- Anti-kickback provisions of the Physician Self Referral Law and Stark II
- Work with counsel to find and apply state law requirements

Key Operational Choices

- Consider prohibiting finder's fees in the context of referring individuals to research trials
- The office that manages the human participant protection program needs to determine how involved it will be with interacting with other departments as to this issue

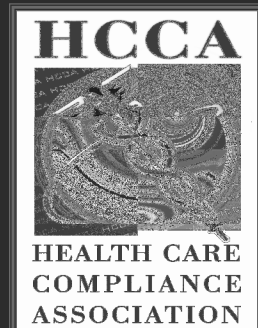
Practical Tips for Integration

- Work with counsel and compliance to share information that may be applicable
- Incorporate a question asking the investigator to explain if the investigator received money for performing the research, but never initiated the research, on the final report application
- Coordinate with grants and contracts
- Share information from the grant, CV, and/or with the appropriate office that would manage anti-kickback violations

DRAFT 3/08

46

Question & Answer Portion



Thank you!

Contact Information:

Luanna Putney, Ph.D., CHC, CCEP

luanna.putney@ucop.edu

510-987-0028

Andra Popa, J.D., LLM

apopa@meaderoach.com

312-933-2800