

Developing a Research Compliance Program in the Context of Corrective Actions to an OHRP Investigation

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Overview

- Brief history of investigation
- Some immediate concerns
- Critical regulations regarding your IRBs
- Some interesting OHRP interpretations
- Lessons learned
- Mobilization
- Organizational response

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Brief History

- OHRP investigational letter 1/16/09
 - Response due 2/2/09
- Second OHRP investigational letter 1/22/09
 - Response due 2/19/09
- First OHRP determination letter 6/9/09 (included follow-up questions, required actions, and recommendations)
 - Response due 7/7/09 (got 1-week extension)
- NCI suspends accrual 6/11/09
- OHRP site visit (with NCI) 7/20 – 22/09
- Second OHRP determination letter 9/21/09 (follow-up questions, required actions, and recommendations)
 - Response due 10/27/09
- Third determination letter 12/16/09 (follow-up questions)
 - Response due 1/13/10
- FDA investigator on-site late November to mid-January
- NCI site visit (with OHRP investigator) 2/1 and 2/10

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Some Immediate Concerns

- HPA was PI on NCI grant
- Signatory Official not intimately involved in research enterprise
- Grant PI was Study-PI on all CCOP studies
 - About 200
- External IRB not functioning well
- Lack of focus by institution on what external IRB was doing
- Policies and procedures not adequate

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IAA

- One page IAA sample agreement
 - Misleading?
 - Creates impression this is all you need to do to use an external IRB?
 - Inadequate for long-term relationship with external IRB

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IRB Meeting Minutes

- 45 CFR 46.115(a)(2) specifies what must be in minutes
 - Attendance
 - Actions taken
 - Vote on actions (including for, against, abstaining)
 - Basis for requiring changes in or disapproving research
 - Summary of discussion of controverted issues and resolution of same

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IRB Minutes

- Are you receiving copies of minutes or auditing copies of minutes?
- If not, how do you know the minutes satisfy the regulation?
- If they don't, it is the institution that gets cited by OHRP.

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Criteria for Approval of Studies

- 45 CFR 46.111(a) specifies criteria for approval
 - 7 criteria must be considered by IRB in order for it to approve a study
- Note, the fact that the IRB considered these criteria is not required to be reflected in the minutes
- Even if getting copies of minutes or auditing minutes, how do you know these criteria were considered for each study approved by the IRB?

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Reporting to OHRP (45 CFR 46.103(b)(5))

- Unanticipated problems that present risk of harm to subjects or others
 - Not known AEs
- Serious non-compliance
 - Whether presents risk of harm or not
- Continuing non-compliance
 - Whether “serious” or not or presents risk of harm

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Planned Deviations

- Current OHRP position: all of these are “amendments” to research that must receive prior IRB approval before being implemented
 - Regardless of whether the deviation presents a risk of harm to the subject or affects the subject’s rights
 - E.g., subject in 5th year of long-term follow-up wants to schedule annual physical one week outside window allowed by protocol because she winters in Florida

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Federal Grants

- Who “owns” the grant?
 - Grants typically awarded to the institution, not the individual named as PI on the grant
- Cultural issues

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Subjects or Patients

- Individuals enrolled in a clinical trial are subjects
 - The investigator cannot just decide to do what is in the individual’s best interests from a clinical standpoint
 - Subject cannot decide what appointments he/she will keep and what tests he/she will have done
- Can be a particular problem at affiliates

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