Peeling Back the Onion

CASE STUDIES IN RESEARCH COMPLIANCE
HCCA RESEARCH COMPLIANCE CONFERENCE

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Focus of Presentation

➢ How should a compliance office tackle some of the variety of matters that come its way?

Points for consideration

- Issue Spotting
- Applicable Rules
- Possible Corrective Action
- Communications & Training

Case 1

FDA has announced a routine inspection of your IRB. Two inspectors will visit your site. They have stated that they will be on-site two days from their call. They want minutes from meetings for the past 6 months. They have requested that they be permitted to interview (1) the chair, (2) an unaffiliated IRB member, and (3) one other member of the site’s choosing.

They have also provided a list of 4 studies they would like to review:

- A device study
- A drug study
- A study using a dietary supplement
- A study using a dehydrated amniotic membrane
FDA IRB Inspections –
The Basics

- Records & Record-keeping
- SOPs
- IRB composition & conduct of meetings
- Meeting minutes
- Type of Review
  - Vulnerable populations
- Classification of protocols
  - Drug v. device
- Type of Review: Full Board v. Expedited

Consent Templates
- Dating
- Non-English Speaking Subjects
- Required statements

Continuing Review
- Timing & method

Safety reports

Reporting to FDA

Review of Device Studies

- IDE v. Abbreviated IDE v. IDE Exempt
- Significant v. Non-Significant Risk Determination
- What questions should IRB be asking and how should this be documented?
- What needs to be reflected in the minutes?
Review of Drug Studies
- IND v. IND exempt
- How to document that exemption criteria are met? Distinguishing between drugs and devices
  - Can IRB always rely on the PI?
  - Check the prescribing information

Review of Study Using Dietary Supplement
- Regulation of dietary supplements.
- When is a dietary supplement a drug?
- What claims are being made in the protocol?
- What should the review process be at the IRB?

Review of a Study Using Dehydrated Amniotic Membrane
- Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)
- Regulation as biologic v. regulation under Section 361 of PHS
- Companies marketing products have received warning letters.
- What's permissible in the protocol?
Case 2

HRSA announces that they are coming to do a routine audit of the 340B program at your infectious disease clinic. The clinic receives grant funding through the Ryan White Program. The clinic dispenses 340B medications on-site via physician dispensing. The clinic also contracts with an outside pharmacy that dispenses 340B drugs to patients by mail order. The outside pharmacy also provides mail order prescription services outside of the 340B program as well. The auditor has asked for clinic records for the past 6 months and site visits to the clinic and outside pharmacy. The auditor wants to interview (1) the program administrator, (2) Ryan White grant PI, and (3) outside pharmacy administrator.

Ryan White Programs & 340B – The Basics

- Ryan White Programs – HRSA funded program to provide HIV/AIDS medical care and support programs for person with insufficient resources/health care coverage.
- Participants in Ryan White Program can participate in 340B Program.
- 340B = HRSA administered drug pricing program. Buy from pharma companies at deeply discounted price for dispensing to eligible patients.

What Documentation Will Clinic be Expected to Provide in Advance?

- Dispensing Records
  - 340B and non-340B
- Drug purchase orders
- List of contract pharmacies
- Contracts
- Medicare Carve-in or Carve-out
- Monitoring reports for contract pharmacy
- Org chart and site bio
- Software used for 340B purchases and dispensing
Audit Focus

Areas of Possible “Drug Diversion”

- 340B drugs going to patients who are not 340B Eligible

- Established relationship with clinic (seen at least 1x every 12 months) + receives care from legally qualified provider at clinic + receives health care service or range of services for which clinic receives grant funding under Ryan White + not a Medicaid beneficiary

Audit Focus

- Documentation of process for determining patient eligibility.

- 340B eligibility v. eligibility for access to medical care and services funded by Ryan White Program

Audit Focus

- Areas of Possible “Duplicate Discounts”

- Provision of discounted 340B program price and Medicaid rebate discount for the same drug.

- Carve-in v. carve out
Audit Focus

- Eligible providers
  - What providers are covered by the clinic's program?
  - Is referral for HIV/AIDS specialty treatment?
  - Is referral for treatment being overseen by clinic?
  - Is referral for treatment unrelated to treatment at clinic?

Audit Focus

Contract Pharmacy

- Does contract meet HRSA’s “essential elements”? (Note: The list seems incomplete and might be missing key points. Please provide more details.)
  - Ship to, Bill to
  - Patient’s freedom to choose pharmacy
  - Reports and tracking system
  - Separation of 340B stock
  - Process to verify patient eligibility
  - Audits and monitoring

Audit Focus

- Policies and procedures
  - Detail is expected!!!

- Policies listed on “340B University” site are a starting point, not the finish line.

- Training on policies must be documented.
Audit Focus

- In-house dispensing
- Dispensing logs are critical
- Documentation of process for ensuring all patients are 340B eligible is critical
- Remember state pharmacy laws usually govern in-house dispensing by physicians

Case 3

A faculty member contacts you about an email received from a journal concerning a paper published online and scheduled for hard-copy publication in a journal. The journal received notice from a faculty member at another university that he developed the survey used to collect the data for the paper, but was not consulted and not listed as an author. He also alleges that the tool was improperly used in a way that would skew the data. The journal has advised your faculty member that if the two institutions cannot resolve this matter, they will retract the online article.

Classifying the Matter

- Classification of issues
  - Authorship dispute?
  - Research misconduct
  - Both?
  - Human Subjects Research?
What Policies are Involved?

- Research misconduct policy
- Authorship criteria
- Journal
- Institutional
- Do policies have associated processes?
- Who administers the process?

Multiple Institutions

- Whose process governs?
- What if institutions agree on joint committee, but disputing parties do not?
- Can institutions require parties to participate in process not contemplated by each institution’s policy?
- What about faculty members who have since left the institution?

Working with Journals

- Who should correspond with the journal?
- How deeply should journal be involved?
- What is journal suggests solution that is in not in conformity with its own authorship guidelines?
- What happens if there is no follow-through in implementing recommendations stemming from dispute resolution?
Case 4

An office administrator calls the compliance hotline and reports that she is new to the job and is surprised to find the physician’s research files in considerable disarray. The physician has three research studies, one industry sponsored drug study, one investigator-initiated study in which the physician holds the IND, and one federal grant for genetic research on donated tissue samples. She has been asked to “tidy up” the tissue study. The samples are donated by the physician’s patients. The hotline caller claims she can only find 5 informed consent forms from 22 donors. When she raised this as an issue to the physician, he told her “You are being a worry wart. Just organize what you can find.”

Case 5

Dr. Jones is practicing medicine in your State on a provisional license set to expire December 31. He is the principal investigator on three studies: (a) an investigator-initiated retrospective study; (b) a Phase III industry-sponsored drug study; (c) a Phase II cancer cooperative group study. On March 15 the Medical Staff Office alerts you that Dr. Jones forgot to renew the provisional license and has been practicing without a license. While everyone works on curing the lapse, Dr. Jones will not be performing clinical services. The medical staff office expects the new license will not be in place until June 1. Dr. Jones consented a subject on January 2 and February 18. Dr. Jones’ study coordinator calls you soon afterwards and tells you a patient is scheduled tomorrow in Dr. Jones’ practice group who is planning to be consented for screening in the two prospective studies.

Case 6

It is Friday afternoon before a three-day holiday weekend. At your regularly scheduled monthly catch-up meeting with the clinical trials contracting officer director, you learn that Executive Director of the Alzheimer’s Research Center has been signing “side budget” agreements with 2 sponsors that no one in the institution knew about. The contracting office director shows you a budget agreement for a study which states “The payments set out in this Letter Agreement cover all costs associated with the study-related services, including overhead.” The contracting office director also shows you the active coverage analysis for the study which shows all protocol services should be billed to insurance.
Case 7

Study 123 is a comparative study between two approved drugs. The study requires the subjects receive a physical exam every 2 months for 3 years. The physical exam at this frequency is conventional care for managing patients receiving these drugs. In conducting a routine regulatory audit of Study 123, one of your analysts reviews the Informed Consent Form and notes in her report that the institution promises to waive the subject’s co-pays and deductibles for the physical exams as well as provide a $25 pre-loaded Visa card every time a subject shows up for the study-required physical exam.