Clinical Research and Compliance

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1

1

Goals

- Define research compliance in clinical research
- Analyze regulations in research compliance
- Evaluate current enforcement and challenges sites face

2

2

Our task in 75 minutes

3

3

Can We Get There?

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Let's just focus on the shoe bag

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5

Define Research Compliance in Clinical Research

- We will stick to the "big ones":
  - Clinical research billing compliance
  - Human subject protection compliance
- From these two points, many principles can be extrapolated for other areas of research compliance:
  - Grants compliance (False Claims Act as background)
  - FDA compliance as a site for external sponsor or when the P.I. is the sponsor
- But first we should discuss one of the biggest challenges in research compliance: the language of research compliance

6

6

Language and Communication Challenges

- Communication and clarity remain a challenge in research compliance
- Physicians tend to focus just on the clinical aspects of research and care
- The "regulations" assume good care but tend to be focused on other matters:
  - Accuracy of claims to federal health care programs (insurance perspective)
  - Data and scientific integrity (review by FDA to make a decision on whether something is "safe and effective")
  - Protecting human subjects (patient/subject perspective)
  - Managing conflicts of interest (financial, non-financial)
  - Failing to remember that the research/experiment is performed on "people" who are often desperate for options

7

7

Language and Communication Challenges

- Keep in mind that you may be managing or assessing regulations that are not understood by the people they regulate
- Watch out for regulations that use the same word differently and understand how the regulated population is using a word
- Examples of language problems in research compliance:
  - *First stop:* Is there a difference between a "clinical research study" and a "clinical trial"?
  - Yes! A clinical trial is a subset of clinical research studies – a clinical trial investigates a "thing" or technique.
  - For example, FDA only regulates clinical research studies that involve "drugs" and "devices" (and "biologics")
    - FDA frequently also uses the term "investigation" instead of "trial"
  - There are many clinical research studies that FDA does not regulate (e.g., observational studies to determine whether people over 50 from Illinois or South Carolina tend to wear shoes with laces versus slip-ons when going to the physician's office).

8

8

Language and Communication Challenges

- More Examples of Language:
  - Medicare's NCD 310.1:
    - CMS refers to this as the **"Clinical Trial Policy"**
    - But the NCD refers to more than just "clinical trials" – there are many government funded "clinical research studies" that are "Qualifying Clinical Trials" under NCD 310.1
  - Medicare versus FDA definition of **"inpatient"**:
    - FDA: "A person who is hospitalized for **at least one night** to receive treatment or participate in a study."
    - CMS: "Generally, a patient is considered an inpatient if formally admitted as inpatient with the expectation that he or she will require hospital care that is expected to span **at least two midnights**…."

9

9

Clinical Research Billing

- The number of federal laws addressing Clinical Research Billing ("CRB") has been growing:
  - Medicare:
    - Government and/or drug trials: NCD 310.1
    - Device trials: 42 CFR 405.201-405.215
  - Medicaid:
    - 42 U.S. Code § 1396d(a)(30)
    - Plus State requirements
  - Commercial Insurance:
    - 42 U.S.C. 300gg–8
    - Plus State requirements
    - Plus contractual terms & health care benefit plans/medical management policies

10

10

Clinical Research Billing

- Organizations generally use the Medicare rules as a baseline for CRB analysis but in denial of claims appeals, providers need to refer to the rules that govern the specific payor for the patient

- General CRB compliance points:
  - Avoid billing items and services paid by the sponsor
  - Avoid billing items and services promised free to the patient in the Informed Consent Form
  - If billing to insurance, check whether the study is a "Qualifying Clinical Trial"
    - If a study is a Qualifying Clinical Trial, check whether services meet the definition of "routine cost" under NCD 310.1
    - If a study is a device trial, check whether it is a CMS-approved IDE trial (CMS website)
    - Ensure appropriate "information" codes are applied to claims per the payor instructions

11

11

Clinical Research Billing

- Biggest CRB risk points in operations:

  1. Assembling all the information to determine whether items and services are billable
     - A "Coverage Analysis" ("CA") is generally used to bring all the information together in a consistent and transparent manner
     - A CA needs to stay up to date when protocols and CTAs are amended
  2. Sorting charges as to whether each item and service charged for care provided to a subject should be booked against the study or can be billed to insurance

- Leveraging compliance programs for CRB risks:
  - Policies
  - Auditing the risk points
  - Corrective Action Plans if the audits have findings
  - Ensuring education and training is occurring

12

12

Human Subject Protection

- With limited exceptions, research studies involving humans generally need to be approved by an Institutional Review Board ("IRB") and prospective studies need to obtain informed consent from the subject
  - Informed consent is best captured through a written Informed Consent Form ("ICF") approved by the IRB
- Where are the rules? Everywhere!
  - FDA: 21 CFR Part 50
  - OHRP (HHS Common Rule): 45 CFR Part 46
  - Contracts with Sponsors and funding agencies
  - State laws
  - Ethics commitments

13

13

Basic Points on IRBs

- The research "Institution" (site) needs to obtain IRB approval
- The IRB is first and foremost a committee of the Institution
  - First step question: Will the Institution form its own IRB or contract with an outside IRB to perform the IRB function?
  - Keep in mind: An Institution can outsource the IRB function but not the liability (mistakes by the IRB will be attributed to the site)
- Keeping track of who is the approving IRB for a study is important for knowing where to do compliance audits
  - Internal IRB – does the IRB function as if it were separate or as a committee of the Institution?
  - External IRB – does the Institution have a contract with the IRB that spells out information the Institution can get and how to conduct audits?

14

14

Basic Points on IRBs

- Critical for Institutions to have access to the following from external IRBs:
  - Documents and information submitted to the IRB
  - Minutes and votes of the IRB
  - ICFs stamped by IRB for approval (understand how ICFs are "controlled")
  - Approval dates and research expiration dates
  - Reports to the IRB and reports made by the IRB to government agencies

15

15

The Informed Consent Form (ICF)

- Reviewing and approving the ICF is one of the most important tasks of an IRB
- ICF is written at a 6th to 8th grade reading level and interpreted from the perspective of the patient
- There are 25 regulatory parts of an ICF (not all will apply in every research study) 45 CFR 46.116
- *Risk Point*: Where are the signed ICFs kept?

16

16

Human Subject Protection Top Enforcement Issues

- Conducting research without IRB approval
- Not obtaining informed consent from subject
- Up to date IRB procedures (parallel institutional policies)
- Keeping straight FWA filings and which FWA Institution the research is approved to be conducted in
- Clarity of ICF
- Lack of infrastructure at the Institution to monitor outsourced IRB
- Researcher “self-testing”

17

17

Human Subject Risk Areas for Sites

- Processing amendments timely
- Adverse event reporting
- Not valuing the consent process
- Local IRB does not update policies when necessary
- Research vs non-research determinations
- Waiver of consents/Research HIPAA authorizations

18

18

Compliance Program Considerations for Research

- Does the organization conduct research?
  - If someone says the organization doesn't, ask again!
- Does the compliance program have a specific Research Compliance Officer?
  - What are the subject-matters covered by the RCO?
- If there is no specific Research Compliance Officer, is research tagged to a specific individual within the compliance program or is it generally dispersed?
- Who has "authority" and "enforcement" for research matters?

19

19

Compliance Program Considerations for Research

- Does the compliance training contain research components or is education the responsibility of research administration/operations?
  - What topics does it cover?
- Are compliance audits being done on research activities?
  - What topics are being audited?
- Do you know if the organization has a master list of studies and subjects?
  - Where are documents kept and are files kept up to date?
- Has the organization recognized their "risk tolerance" for research activities?
  - What is it?

20

20

Questions?

21