Strategies to Promote Physician-Investigator GCP Compliance

2018 HCCA Research Compliance Conference

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Objectives

1. Examine common Good Clinical Practice (GCP) compliance errors made by physician-investigators
2. Explore underlying origins of GCP compliance errors
3. Discuss strategies to promote GCP compliance

Common GCP Errors

What are the most common errors made by investigators during the course of conducting a clinical trial?

1) Failure to follow the investigational plan and/or regulations
2) Protocol deviations
3) Inadequate recordkeeping
4) Inadequate accountability for the investigational product
5) Inadequate communication with the IRB
6) Inadequate subject protection – including informed consent issues

FDA BIMO CI Inspection Common Findings (2007 – 2016)

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Failure to follow the investigational plan/agreement or regulations, or both	x	x	x	x	x	x	x	x	x	x
Protocol deviations	x	x	x	x	x	x	x	x	x	x
Inadequate recordkeeping	x	x	x	x	x	x	x	x	x	x
Inadequate subject protection - informed consent issues, failure to report AEs	x	x	x	x	x	x	x	x	x	x
Inadequate accountability for the investigational product	x	x	x	x	x	x	x	x	x	x
Inadequate communication with the IRB					x	x	x	x	x	x
Investigational product represented as safe/effective										x

OHRP Reports of Serious & Continuing Noncompliance

Top 10 Categories of Serious and Continuing Noncompliance reported from 2008 to 2014

2008 to 2014

SNC: Protocol changes	1,515
SNC: Informed consent	970
SNC: Initial and continuing review	684
CNC: Protocol changes	292
SNC: Failure to report	231
CNC: Informed consent	204
CNC: Initial and continuing review	135
SNC: IRB documentation	48
CNC: Failure to report	42
SNC: Expedited review	32

SNC=serious noncompliance
CNC=continuing noncompliance

Understanding Why Errors Occur

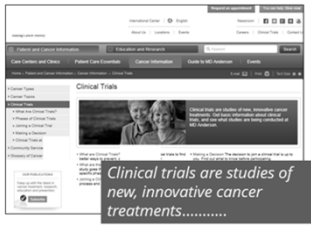
- Research versus the practice of medicine
- Education – Training - Experience
- Support
- Motivation

Research versus the Practice of Medicine

Research is not Treatment: The Therapeutic Misconception

- The goal of clinical research is to generate useful knowledge about human health and illness.
- Clinical medicine aims to provide individual patients with optimal care.
- Benefit to participants is not the purpose of research (although it does occur).
- People are the means to developing useful knowledge; and are thus at risk of exploitation.

Research is not Treatment: The Therapeutic Misconception



Clinical trials are studies of new, innovative cancer treatments……

…the therapeutic orientation to clinical trials obscures the ethically significant differences between clinical research and medical care. As a result, it interferes with informed consent and with the developments of a concept of professional integrity that is appropriate to clinical research.

Miller F, Rosenstein D, The Therapeutic Orientation to Clinical Trials. *NEJM* 348;14 April 3, 2003

Research is not Treatment: Informed Consent Process

- An effective informed consent discussion would typically begin with clinical care options; AND
- Clinical trials frequently include standard of care interventions.

Research is not Treatment: Informed Consent Process

Benefits related to medical care are overestimated by patients

- Objective: Systematic review of all studies that quantitatively assessed patients' expectations of the benefits and/or harms of any treatment, test, or screening test.
- 35 studies involving 27,323 patients
- Conclusions and relevance: "The majority of participants overestimated intervention benefits and underestimated harm."

Education – Training - Experience

Investigator Training & Education

» Investigator training & education opportunities in medical school, residency and fellowship are limited.

» Generally, there are limited requirements to participate as an investigator in hospitals and health systems.

Investigator Training & Education

Why should I check to make sure the patient consented for research, it's the coordinators job?

But I thought that I was doing the right thing……

I wasn't completely certain that the patients death was related to the study so I did not report it

What's the big deal…I missed my continuing review by eight days?

I know the patient's CBC was too low but she really wanted to be in the study

Of course I can deviate from the protocol, the patient doesn't really need that extra CT scan

Privileges and Credentials: The Medical Staff Model

The hospital's Governing Body must ensure that all practitioners who provide a medical level of care and/or conduct surgical procedures in the hospital are individually evaluated by its Medical Staff and that those practitioners possess current qualifications and demonstrated competencies for the privileges granted.

November 2004 CMS letter to State Surveyors

The Two Tiers of the Credentialing and Privileging Process

Tier One: Verification of Primary Credentials and Competence	Tier Two: Delineation of Privileges, Appointment & Reappointment
• Completed application submitted to medical staff services department	• Using evidence-based methodologies, credentials committee reviews application, core competency assessment findings and FPPE (if indicated), and considers request for privileges
• Primary credentials certified	• Credentials committee recommends or denies appointments and delineated privileges
• Core competency evaluation completed	• Governing body approves or denies executive decision
• Focused Professional Practice Evaluation (FPPE) conducted. If applicant lacks documented evidence of competence	• Ongoing Professional Practice Evaluation (OPPE) occurs in a systematic fashion. FPPE is implemented when a member of the medical staff shows signs of being unable to provide safe, quality patient care. • Performance data collected from OPPE and FPPE are applied during the reappointment process in determining whether to continue, limit or revoke existing privileges

Privileges and Credentials: Core Competencies

Harmonized Core Competencies for the Clinical Research Professional: Joint Task Force for Clinical Trial Competency, January, 31, 2014

Support

Support

- Varying levels of support *(institutionally based)*
- Research coordinators
  - Employment relationship
  - Reporting relationship
  - Training requirements
  - Roles & responsibilities
- Study selection - Feasibility
- Grant/Financial management

Motivation

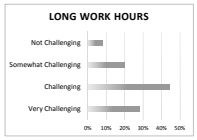
Incentive

Remember:

- Investigators at hospitals are primarily clinicians
- Focus on patient care
- Focus on meeting work RVU requirements
- Motivation to participate in clinical trials:
  - Enhance clinical service offerings
  - Professional interest
  - Financial

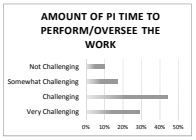
Investigator Perceptions of the Barriers in Conducting FDA-Regulated Drug Trials

A. Corneli et al., One and done: Reasons principal investigators conduct only one FDA-regulated drug trial, Contemporary Clinical Trials Communications 6 (2017) 31-38



72% Challenging-Very Challenging

72% Extremely-Moderately Burdensome



73% Challenging-Very Challenging

Promoting Compliance

Strategies to Promote Compliance

Therapeutic Misconception
- See training & education

Training, Education
- Easily accessible educational offerings (with CME credit)
- Mentorship
- Credentialing/privileging based on defined competencies
- Communication, transparency, oversight, team meetings

Strategies to Promote Compliance

Support
- Invest in the professional development of research coordinators
- Develop and implement feasibility review to help investigators meet enrollment targets
- Centralize certain research functions to allow investigators to focus on conducting the study
  - Budgets/contracts
  - Coverage analysis
  - Invoicing sponsors
  - Revenue reconciliation

Strategies to Promote Compliance

Motivation
- Evaluate the role of clinical trials research in your organization
  - Organizational research mission/vision statement
- Establish consistent and transparent compensation methodologies
  - Work RVUs
  - Research RVUs
  - Administrative time carve out
- Establish consistent and transparent residual fund policies

Questions & Discussion

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