FINANCIAL DISCLOSURES AND CONFLICTS OF INTEREST IN CLINICAL RESEARCH

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"In light of the expansion of Medicare coverage for clinical trials. . .prosecutors will have an increased interest in investigating issues related to billing and recruitment for clinical studies. . . . The rule opens up new areas for potential False Claims Act prosecutions."

Jim Sheehan, Associate U.S. Attorney
DIA Annual Meeting, June 17, 2003

Financial relationships between sponsors and investigators are "out of control."

Dr. Greg Koski, Former Director OHRP
NIH Conference, August 16, 2000

Why is Clinical Research under a Microscope?

- Increasing numbers of individuals involved in human subject research
- Increasing dollars at risk
  - Industry dollars
  - Medicare dollars
- A better government understanding of the pharmaceutical and device industries and the life cycles of a product
- Serious adverse outcomes – regulation through enforcement

The Concern about COIs

- Conflicts may
  - jeopardize the welfare of human subjects
    - influence investigator's judgment in participant recruitment or data collection
    - compromise an institution's review of a research protocol
  - undermine the integrity of research results
  - diminish public trust

The Legal Risk Associated with Conflicts

- Regulatory action
- Beyond the regulations
  - False Claims Act liability
    - Direct
    - Indirect through Medicare reimbursement
  - Anti-Kickback Law Liability

Patchwork of Uncoordinated Guidance
that reaches only certain studies

- Federal Regulations
  - Common Rule
  - PHS, FDA, NSF
- NIH Guidelines
- OHRP Guidance
- Professional Society Statements
  - American Medical Association
  - American Society of Clinical Oncologists
  - Association of Academic Health Centers

Common Rule

- Applies to all federally-funded research, but does not address COI specifically.
  - IRB member protocol review and IRB membership.

PHS Regulations

- **Goal**: promote objectivity in research
- **Target**: institutions that apply for PHS grants or cooperative agreements
  - case-by-case determinations when individual is grant applicant
- **Disclosure of COI**: investigator to institution official, not to PHS. PHS may audit.
- **Focus**: management of conflicts of interest versus prohibition – significant discretion given to institution official
- **Timing**: By the time the application is submitted to PHS, annually or ongoing basis

PHS Requirements

- As prerequisite to receiving grant funds an institution must:
  - maintain and enforce written COI policy
  - inform investigators about COI policy and their disclosure duties under the policy
  - designate official to review investigator's financial disclosures
  - report the existence of COI to grantor agency with assurances that the conflict has been managed, reduced or eliminated (to what?)
  - certify that COI process is in place and enforced and that any new COIs will be handled within 60 days of identification

What must be disclosed?

- "significant financial interest that could directly and significantly affect the design, conduct or reporting of the PHS-funded research."
- Anything of monetary value
  - Salary, royalties and other payments exceeding $10,000 in the aggregate over 12 month period
  - Equity interests exceeding $10,000 and is > 5% ownership interest in single entity
- But, not . . .
  - Salary, royalties or other remuneration from the institution
  - Ownership interest in a SBIR program
  - Income from teaching engagements or service on advisory committees or review panels for public or non-profits of public or non-profits

FDA Regulations

- **Goal**: protect integrity and reliability of clinical data
- **Target**: applicants (e.g., sponsors) of "covered" clinical trials
  - Study of a drug, biologic or device used to:
    - support premarket approval
    - reclassification and establish efficacy or equivalency
    - single investigator significantly contributes to demonstration of safety
- **Disclosure of COI**: investigator to sponsor, sponsor to FDA
- **Focus**: impact of COI on study data, steps taken to minimize bias
- **Timing**: After the trial has been completed, when the data is submitted

What must be disclosed?
by the sponsor

- Financial relationships b/t sponsor and investigator where the outcome of the study could increase the monetary value of the investigator's interest (e.g., explicit compensation arrangements, equity interest in sponsor, royalty interest in product)
- Payment > $25,000 from sponsor to investigator or institution during the trial or within 1 year
- Investigator has Proprietary interest in tested product, including patent, trademark, or copyright
- Investigator has equity interest in sponsor of > $50,000 in publicly held sponsor during the trial and within 1 year
- **Steps taken to minimize bias**

What must be disclosed?
by the sponsor

- Certification that none of the above exists and that each investigator was required to disclose any proprietary or equity interest in the product

OHRP Guidance 2003

- Does not carry the weight of law or regulation, but informs the interpretation of these rules and provides insight to judges and juries.

Medicare/Medicaid Anti-Kickback Law

- Prohibits remuneration from sponsors to researcher/institution for participation in clinical research if intended to induce recipients to purchase drugs/services of sponsor paid for by Medicare/Medicaid.
- Criminal and civil penalties
- 1994 OIG “special fraud alert” targeting “sham” research grants from drug companies.
- Additional incentives?

Medicare/Medicaid Anti-Kickback Law

- 2003 OIG pharmaceutical compliance guidance

Clinical Trials
National Coverage Determination

- Medicare will cover:
  - Routine costs of qualifying trials
  - Reasonable and necessary items and services used to diagnose and treat complications arising from participation in all trials.
- Medicare will not cover:
  - The investigational item or service, itself
  - Items or services
    - that are customarily provided by the sponsor free of charge for any enrollee in the trial
    - provided solely to satisfy data collection needs and that are not used for clinical management of participant

Could the failure to meet the regulatory COI requirements be considered enough to so taint a clinical trial that Medicare would take the position that it should never have paid for services related to the trial?

Conflicts of Interest and the False Claims Act

Past 10 years have seen a dramatic increase in Federal enforcement in the health care industry

- Broad array of enforcement statutes, with significant penalty provisions
- Most significant statute: Federal False Claims Act

Background

- Law dates back to Civil War days -- used to pursue unscrupulous suppliers to the Union Army.
- In the 1980's, used to pursue cases against defense contractors for fraud.
- Now "weapon of choice" for the government in health care enforcement cases.

Provisions of the False Claims Act

- Liability imposed against any person who:
  - Knowingly presents or causes to be presented a false or fraudulent claim to the United States.
  - Knowingly makes, uses, or causes to be made or used a false record or statement to get a false or fraudulent claim paid.
- Liability results in treble damages plus penalties of $5,500 to $11,000 for each false claim submitted.

Definition of “Knowingly”

- Actual knowledge.
- Deliberate ignorance of the truth or falsity of the information.
- In reckless disregard of the truth or falsity of the information.

Theory of Express Certification

Health insurance claim form – HCFA –1500

- Certification statement
  - I certify that the services shown on this form were medically indicated and necessary for the health of the patient and were personally furnished by me or were furnished incident to my professional service by my employee under my immediate personal supervision … .

Examples

- Billing for services not rendered.
- Billing for a higher level of service than that performed.
- Billing for services not medically necessary.
- Billing for services as if furnished “incident to,” but without required supervision.

Application to Research Fraud

U.S. ex rel Cantekin v. University of Pittsburgh

- U.S. Court of Appeals for the 3rd Circuit reversed the dismissal of a False Claims Act case based on a researcher's failure to disclose industry funding on a grant application.
- Based on the Court's review of the application process, there was a genuine issue whether the disclosure of the funding would have had an impact on the award of the government grant application.

Theory of Implied Certification

Ab-Tech Construction, Inc. v. U.S. (1994)

- Submission of claim was implicit certification that *Ab-Tech* complied with SBA 8(a) program.
- *Ab-Tech* failed to obtain approval for dealing with non-minority owned subcontractor.
- Submission of payment vouchers represented implied certification by *Ab-Tech* of continuing compliance necessary for participation in the program.

Application to Healthcare

U.S. ex rel Pogue v. American Healthcorp, Inc. (1996)

- A violation of Medicare anti-kickback and self-referral laws also constituted violation of False Claims Act.
- "Government would not have paid the claims submitted by Defendants if it had been aware of kickback and self-referral violations."

Application to Healthcare

U.S. ex rel Joslin v. Community Home Health of Maryland (1997)

- Court rejected False Claims Act claim in connection with violation of state licensure laws.
  - The Court distinguished between conditions of participation and conditions of payment.
  - "To hold that the mere submission of a claim for payment, without more, always constitutes an 'implied certification' of compliance with the conditions of the Government program seriously undermines this principle by permitting FCA liability potentially to attach every time a document or request for payment is submitted. . .."

Application to Healthcare

U.S. ex rel Mikes v. Straus (2001)

- Second Circuit limited implied false certification to situations where the underlying statute or regulation upon which Plaintiff relies expressly states that a provider must comply in order to be paid.
- ". . . implied certification that a provider will adhere to the standard of care is appropriate if the standard of care is at the 'heart' of the parties' agreement."

Relationship between COI Regulations and Medicare Payment

Trials are subject to those agency regulations, which may include disclosure of conflicts of interest.

- Public Health Service regulation
  - Requires disclosure by investigators of “significant financial interest”
- FDA Conflict of Interest regulations
  - Requires sponsor to disclose financial arrangements between the sponsor and its clinical investigators, and requires the investigator to provide the sponsor with accurate information to enable the sponsor to comply.

Application of Implied Certification to Support FCA Claim

- PHS regulations require investigators to disclose “significant financial interest.”
  - Would failure to disclose trigger potential FCA liability under an implied certification theory?
  - Would the clinical trial fail to “qualify” for Medicare coverage purposes?

Application of Implied Certification to Support FCA Claim

- FDA regulations require the investigator to provide the sponsor with information so that the sponsor may make a certification.
  - If the investigator fails to disclose, is there any potential implied certification liability, where the investigator is not responsible for making a certification?

FCA Liability through the Anti-Kickback Statute

- Separate and apart from FCA liability in connection with disclosure obligations and conflict of interest, the expansion of Medicare coverage for services rendered ancillary to a clinical trial triggers the potential application of the Anti-Kickback Statute to the relationships between the sponsors and investigators.

FCA Liability through the Anti-Kickback Statute

- Kickbacks may take the form of gifts, entertainment, lucrative consulting arrangements, free goods, etc.
- As discussed above, it is already fairly well established that violations of the Anti-Kickback Statute may trigger False Claims Act liability, under the theory that the government would not have paid for the service had it known of the kickback relationship.
- Expanded Medicare coverage carries expanded risk of enforcement actions.

Thank you