Working with Drug and Device Manufacturers

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"A productive collaboration between medicine and commercial interests can expand knowledge, drive innovation, and improve quality of care. However, the relationship also contains a potential divergence of interests."

- Lew Morris
Remarks to the Senate Special Committee on Aging (July 29, 2009)

Health Care Compliance Association
6500 Barrie Road, Suite 250, Minneapolis, MN 55435
888-580-8373 | www.hcca-info.org

Session Rules

- There should be time for Q&A at the end of the session, but please feel free to ask questions throughout
- Please turn your pagers and cell phones to vibrate
- If you need to stretch or step out for awhile please do so quietly
- Usual disclaimers
  - My views are my own, and may not be attributed to my current or former employers.
  - This is an educational session. I am not providing legal advice. Consult with your own attorneys for advice tailored to your individual needs.

Session Overview

- Background
  - Laws, Regulations, Accreditation Standards, Guidance
  - Enforcement
- Consulting Agreements
- Clinical Trial Agreements
- Health Information Privacy & Security
- Hypotheticals

Background

Health Care Compliance Association
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Laws – Regulations – Standards

Selected Federal Laws

- **Referrals and Inducements**
  - Stark Law
  - Anti-Kickback Statute
  - Beneficiary Inducement Ban
- **Health Fraud, False Claims and False Statements**
  - Federal Health Care Fraud
  - False Claims Act/Fraud Enforcement Recovery Act
  - Criminal False Claims
  - OIG Compliance Guidance
- **Food, Drug & Cosmetic Act**
- **Conflict of Interest Regulations and Guidance**

Referrals and Inducements

- **Stark Law**
  - Prohibits a physician who has (or whose family member has) a defined financial relationship with an entity that furnishes (performs or bills for) designated health services from making referrals to that entity for services that may be covered by Medicare, and prohibits the entity from billing for those services – unless a statutory or regulatory exception applies
  - "Strict liability" standard
  - Enforcement (civil) requires no finding of intent
  - 42 USC § 1395nn; 42 CFR part 411
- **Anti-Kickback Statute**
  - Prohibits knowing or willful offer, solicitation, payment, or acceptance of anything of value intended to induce referrals for services payable by federal health care programs
  - Regulators have adopted the "one purpose" test articulated in Greber
  - Enforcement (civil or criminal) requires finding of intent
  - Compliance with statutory exceptions or regulatory safe harbors can mitigate risks
  - 42 USC § 1320a-7b; 42 CFR § 1001.952
- **Beneficiary Inducement Ban**
  - Prohibits remuneration to beneficiaries likely to influence their choices, with VERY limited exceptions (e.g., financial need; *de minimus* non-cash give-aways; preventive care)
  - OIG advisory opinions have approved waiver of co-payments and limited free services in government initiated/funded clinical trials … never in industry-funded studies
  - 42 USC § 1320a-7a(a)(5); 42 CFR § 1003.101; OIG Special Advisory Bulletin (2002): http://oig.hhs.gov/fraud/docs/alertsandbulletins/SABGiftsandInducements.pdf

H. R. 3590

One Hundred Eleventh Congress of the United States of America

AT THE SECOND SESSION

Begun and held at the City of Washington on Tuesday, the fifth day of January, two thousand and ten

An Act

Entitled The Patient Protection and Affordable Care Act.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "Patient Protection and Affordable Care Act".

(b) TABLE OF CONTENTS.—The table of contents of this Act is as follows:

Sec. 1. Short title; table of contents.

TITLE I—QUALITY, AFFORDABLE HEALTH CARE FOR ALL AMERICANS

Health Care Reform (Sec. 6402)

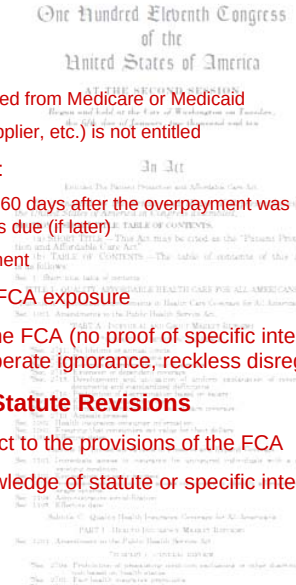
- "Remuneration" (42 USC §1320a-7a) excludes offer or transfer of:
  - I/S for free or less than fair market value if:
    - The I/S are not offered as part of any advertisement or solicitation
    - The I/S are not tied to the provision of other services reimbursed in whole or in part by Medicare or Medicaid
    - There is a reasonable connection between the I/S and the medical care of the individual; and
    - The person provides the I/S after determining in good faith that the individual is in financial need
  - I/S for free or less than fair market value if:
    - The I/S consists of coupons, rebates, or other rewards from a retailer
    - The I/S are offered or transferred on equal terms available to the general public, regardless of insurance status; and
    - The offer or transfer of the I/S is not tied to the provision of other I/S reimbursed in whole or in part by Medicare or Medicaid
  - Any other remuneration which promotes access to care and poses a low risk of harm to patients and Federal health care programs (per regs)

Health Fraud, False Claims, and False Statements

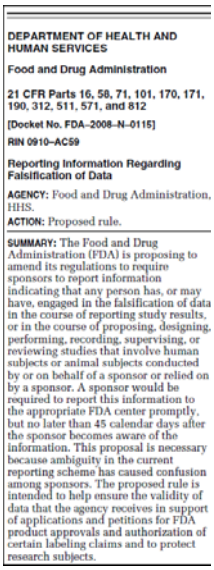
- **Federal Health Care Fraud: 18 USC 1347 (criminal)**
  - Prohibits any scheme or artifice to defraud a health care benefit program or obtain by means of false or fraudulent pretenses, representations, or promises any health care benefit program money or property
  - "Health care benefit program" means "any public or private contract, affecting commerce, under which any medical benefit, item, or service is provided to any individual"
  - Punishable by fines and up to 10 years' imprisonment (20 if serious bodily injury results, life if death results)
- **False Claims Act / Fraud Enforcement Recovery Act: 31 USC § 3729 *et seq.* (civil) and 18 USC § 287 (criminal)**
  - Prohibits the presentment of a false claim to the government or other conduct intended to induce government payments
  - AKS/Stark violations have been "bootstrapped"
  - Enforcement (civil) requires finding of intent (including reckless disregard/deliberate indifference)
- **Criminal False Statements: 18 USC §§ 1001 (general) and 1035 (health care)**
  - Law bars falsification, concealment, cover-ups of material facts; materially false, fictitious, or fraudulent statements; and creation or use of false documents … "in any matter within the jurisdiction of the executive [branch]"
  - Punishable by fines and (generally) 5 years' imprisonment

Health Care Reform (Section 6402)

- **False Claims Act Revisions**
  - Overpayments
    - Include any funds received or retained from Medicare or Medicaid
    - To which the recipient (provider, supplier, etc.) is not entitled
  - A person receiving an overpayment:
    - Must return the overpayment within 60 days after the overpayment was identified, or the date the corresponding cost report is due (if later)
    - Explain the reason for the overpayment
  - Retaining an overpayment triggers FCA exposure
  - Scienter is defined as specified in the FCA (no proof of specific intent to defraud is required): actual knowledge, deliberate ignorance, reckless disregard
- **Health Fraud and Anti-Kickback Statute Revisions**
  - AKS violation is a false claim, subject to the provisions of the FCA
  - A person need not have actual knowledge of statute or specific intent to violate statute as a basis for enforcement



New on the Horizon …
- FDA NPRM on Falsification: 75 Fed. Reg. 7412 (Feb. 19, 2010)



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 16, 58, 71, 101, 170, 171, 190, 312, 511, 571, and 812

[Docket No. FDA–2008–N–0115]

RIN 0910–AC59

Reporting Information Regarding Falsification of Data

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend its regulations to require sponsors to report information indicating that any person has, or may have, engaged in the falsification of data in the course of reporting study results, or in the course of proposing, designing, performing, recording, supervising, or reviewing studies that involve human subjects or animal subjects conducted by or on behalf of a sponsor or relied on by a sponsor. A sponsor would be required to report this information to the appropriate FDA center promptly, but no later than 45 calendar days after the sponsor becomes aware of the information. This proposal is necessary because ambiguity in the current reporting scheme has caused confusion among sponsors. The proposed rule is intended to help ensure the validity of data that the agency receives in support of applications and petitions for FDA product approvals and authorization of certain labeling claims and to protect research subjects.

- **Rule**
  - No new monitoring or supervision obligations but …
  - Sponsors who "become aware of" potential falsification in studies conduct by them or on their behalf, or studies on which they rely must report to FDA promptly (45 days maximum)
  - Applies to IND and IDE studies
  - Reporting mandate is triggered regardless of sponsor's evaluation of researcher's intent
- **See** http://edocket.access.gpo.gov/2010/pdf/2010-3123.pdf (comments due 5/20/2010)

FDA Falsification NPRM (cont'd)

- Definitions
  - Falsification: creating, altering, recording, or omitting data in such a way that the data do not represent what actually occurred (other than transpositional errors), for example:
    - Fabrication, forged signature
    - Alterations (e.g., changing laboratory measurements to a less extreme deviation from normal)
    - Manipulation of specimens or samples, misidentification of specimens or samples
    - Data omissions (e.g., failure to report exclusionary medical history or concomitant medications or treatments)
  - Data: individual facts, tests, specimens, samples, results, statistics, items of information, or statements made by individuals

FDA Falsification NPRM (cont'd)

- **Contracting Challenges**
  - Sponsor reports to FDA during sponsor-initiated studies (issues will arise during monitoring visits)
    - Notice to institution, PI – and opportunity to respond
    - Timing and wording of report to FDA
    - Implications of "findings"
  - Sponsor right to data and reports, even in investigator-initiated studies

- **Internal Challenges**
  - Inconsistency with ORI misconduct regulations (both could apply in an investigator-initiated study funded by NIH)

OIG Concerns (2003 / 2005 Compliance Guidance)

- Data integrity
  - Data on which federal/state governments base payment decisions (particularly pricing data)
- Kickbacks and other illegal remuneration
  - Arrangements that interfere with or skew clinical decisionmaking; or increase risk of overutilization
  - Undermining integrity of formulary process
  - Accurate, complete, and not misleading information to decisionmakers (purchasers, prescribers, patients, payors)
  - Disguised discounts
  - Patient safety/quality of care concerns
  - Educational/research grants – separate grant functions from sales/marketing

- Drug sampling laws
- Increased costs to federal health care programs
- Researcher time and effort reporting, charge allocation on research awards, reporting financial support from other sources (other grant sources, Medicare, etc.)

Food, Drug & Cosmetic Act

- **Civil Enforcement**
  - Inspections
  - FDA-483 (Observations), Warning Letter, NIDPOE
  - Restrictions/Disqualification
- **Office of Criminal Investigations**
  - Off-Label promotion of FDA approved drugs and medical devices
  - Clinical investigator fraud
  - Illegal importation of FDA regulated products

COI Regulations

National Institutes of Health
The Nation's Medical Research Agency

- Regulatory Basis: 42 C.F.R. part 50, subpart F (see also NSF AAG ch. IV.A for NSF application)
- NIH Implementation:
  - Purpose: avoid bias in NIH-funded studies
  - Scope:
    - Institutions applying for NIH grants or cooperative agreements (but not Phase I SBIR/STTR program applications or awards; extends to subrecipients (primary awardees must take "reasonable steps" to ensure subrecipient compliance)
    - PI and anyone else responsible for the design, conduct, or reporting of research funded by NIH, including subgrantees, contractors, and collaborators (includes spouse and dependent children)
  - Threshold: $10,000 or 5% (investigator, spouse, dependent children)
    - Salary/payments for services (e.g., consulting fees/honoraria) over next 12 months, equity interests (e.g., stocks, options, other ownership), IP rights (patents, copyrights, royalties)
    - Excludes salary, royalties, and other **remuneration from the institution**; ownership interests in the institution, if the institution is an SBIR/STTR applicant; income from seminars, lectures, teaching engagements, advisory committees, review panels for public/non-profit entities
  - Record retention: at least 3 years post close-out
- Institutional focus:
  - Development, implementation, training on, and enforcement of policies
  - Investigators' prompt and full disclosure of financial interests that could be implicated in NIH-supported research
  - Sound institutional management of conflicting interests
  - Mandatory reporting to NIH
- Non-compliance exposure includes: program fraud civil remedies: 45 CFR part 79

FDA on COI

- **Scope/Application**
  - Sponsor responsibility: “applicants” who submit “marketing applications” (e.g., NDA, PMA, 510k) and “covered clinical studies” (i.e., studies demonstrating efficacy or where a single investigator makes a significant contribution to the determination of safety)
  - Reportable Interests
    - $25,000 during the time of the study and for 1 year following (exclusive of the costs of conducting the clinical study or other clinical studies)
    - Any equity/ownership interest in a non-publicly traded company or an interest worth > $50,000 in a publicly traded company
    - Compensation that may be influenced by study outcomes
- **Mandate**
  - Identify all clinical investigators (PIs, subinvestigators, spouses, dependent kids)
  - Certify no covered interests or disclose interests (FDA-3455)
  - FDA reviews all disclosed interests for potential bias … may conduct audits, require additional confirmatory studies, or exclude data

Human Subjects Regulations on COI

- Common Rule (OHRP) and Corresponding FDA (21 CFR part 56)
  - No explicit statement re: researcher COI
    - IRB members with conflicts may not participate in the deliberations or vote on a relevant project: 45 CFR 46.107(e)
    - Informed consent rules require disclosure of any benefits to subject or others reasonably expected from the research: 45 CFR 46.116(a)(3)
    - IRB may require additional information to be given to subjects if it would meaningfully add to protection of their rights and welfare: 45 C.F.R. 46.109(b)
  - 2004 HHS Guidance is posted under “policy and guidance” on OHRP website

2004 HHS Guidance on COI

- **References Common Rule and corresponding FDA mandates to:**
  - Minimize risks to subjects
  - Assure risks are reasonable in relation to anticipated benefits
  - Assure equitable subject selection
  - Seek informed consent
  - Minimize coercion/undue influence
- **Recommends that institutions consider:**
  - What financial relationships/interests could cause potential or actual conflicts
  - At what levels should these be managed or eliminated; what are management tactics
  - Is the institution an appropriate site for the research given the conflicts
  - Assure independence of and good communications between COICs and IRBs
- **Recommends that IRBs consider:**
  - Whether proposed management plans are adequate to protect subject rights/welfare
  - Whether other actions are necessary to minimize risks to subjects
  - What additional information should be provided to subjects
- **Recommends that investigators:**
  - Inform prospective subjects of any relevant financial relationships and relevant management
  - Protect the informed consent process by using non-conflicted individuals, consent monitors, etc.

State Activity – Legislation

- Multiple states have passed or are considering mandates to limit and/or disclose industry payments to physicians, sometimes through licensing statutes (see http://www.ncsl.org/programs/health/rxads.htm for more information)
- Requirements vary
  - Not all initiatives address gift prohibitions or mandatory disclosure of gifts
  - Those that do have different thresholds
  - Many address disclosure of clinical trials and results and to the extent addressed by FDAAA are preempted
- PPSA would also create federal pre-emption
- Early experience has been mixed
  - Incomplete disclosures
  - Poor public access/accountability
  - But yield interesting information on scope/breadth of payments

Accreditation (AAHRPP)

- Consistent policies regardless of funding source
- Sponsor contracting standards:
  - Address medical care for participants with research-related injuries "when appropriate"
  - Require sponsor to report to organization findings that could affect participant safety or influence the conduct of the study; and provide DSM reports
  - Include publication plans
  - Provision to update organization or researcher on results after study if participant safety could be directly affected
- COI standards:
  - Disclosure, evaluation, appropriate management (or elimination)
  - Use of objective criteria to identify disclosable conflicts
  - Transparency in process of evaluation and management of conflicts
  - Communication of relevant information to IRBs
  - Documentation

AAMC & AAU on COI

- Recognition of additional "compelling circumstances" permitting a conflicted investigators to participate (e.g., early stage research)
- Determination that low-risk research may not require the same vigilance as riskier research
- Eliminate "de minimus" reporting thresholds but maintain for determining whether to exclude a researcher from a clinical study (designed to avoid inadvertent non-reporting)
- Report on all outside financial interests directly or indirectly related to professional responsibilities to the institution
- Focus on relevant pre-clinical activities
- Specified disclosure requirements to different groups (including subjects of affected clinical trials)
- Addresses reportability/management of IRB member conflicts
- Provides detailed guidance/techniques for management of conflicts
- Calls out but does not address clinical conflicts (medical practice)
- Provides a sample policy for institutional conflicts

IOM Recommendations: (April 2009)

- *Easier Verification*: Build consensus among array of concerned parties to standardize disclosures [reporting] process/forms to allow physician/researchers to fill out a single, standard questionnaire and then the information can be formatted for different institutions and purposes.
- *Public reporting*: Calls for creation of broad public reporting system of spectrum of payments (pharmaceutical, medical device, and biotechnology companies and their foundations)
- *Scope of reporting*: All matter the type or stage of research (clinical or not) *all* researchers should be subject to the institutions reporting policies.
- *Institutional Conflicts*: Responsibility for oversight of institutional conflicts should be lodged in the governing board.

IOM Recommendations (April 2009)

Conflicted individuals:

- General rules should be individuals may not conduct research with human participants if they have a significant financial interest in an existing or potential product or a company that could be affected by the outcome of the research.
- Exceptions to general policy should be
  - Made public
  - Permitted only if the COI committee
    - determines that an individual's participation is **essential** for the conduct of the research (*necessary for the safety, reliability or validity of research*) AND
    - Establishes an effective mechanism for managing the conflict and protecting the integrity of the research
- Applicable to PIs & other others who have "*substantial responsibility*" for design, conduct, or reporting of findings.
- **"In most cases of a conflict of interest no compelling argument that the investigator's participation is essential can be made"**

Health Care Reform (Section 6002)

- Payments and other transfers of value (greater than $10) from manufacturers to physicians and teaching hospitals, as well as ownership interests of physicians and family members
  - Electronic reports in a form to be dictated by DHHS
  - Content to include:
    - Name (and NPI) of recipient
    - Amount of payment or other transfer, description of the form (e.g., cash, in-kind, stock option)
    - Nature of payment (e.g., consulting fee, honorarium, service compensation, research, education, charity, royalty, grant)
    - Name of relevant drug, biological, device, or supply (if payment is for marketing, research, or education related to a particular one)
  - Reporting applies even if payments are redirected to other organizations
- Loophole for payments made through third parties where the manufacturer is unaware of the identity of the recipient
- Penalties for failure to report include significant CMPs

Section 6002 (cont'd)

- Implementation Deadline
  - First reports due March 31, 2013 for payments made during CY 2012
  - DHHS to make information available and searchable via Internet by September 2013 and by June each year thereafter
  - Manufacturers may delay reports until the earlier of
    - Product approval or clearance; or
    - Four (4) calendar years after payment or transfer of value was made
- Preemption
  - Applies to payments or transfers made after 1/1/2012
  - Applies only to "the type" of information required to be reported under the federal standard
  - States may implement additional reporting mandates applicable to others (e.g., recipients, third parties); or for public health surveillance or oversight

Section 6002 (cont'd)

- Exceptions are limited but include:
  - $10 limit applies to all payments made during a calendar year (so two $5 pizza lunches would be reportable)
  - Product samples not intended to be sold and intended for patient use
  - **Educational materials to directly benefit patients or intended for patient use**
  - **Loan of a covered device for a short-term trial period of 90 days or less**
  - Warranty I/S
  - **In-kind payments used for charity care**
  - Discounts, rebates
  - Physician services with respect to a civil or criminal action or administrative proceeding
  - Dividends and other profit distributions from publicly traded securities and mutual funds

About the Enforcement Environment


United States Senate

July 22, 2008

W. Douglas Weaver, M.D., F.A.C.C.
President
American College of Cardiology
Heart House
2400 N Street NW
Washington, DC 20037

Dear Dr. Weaver:

FEBRUARY 2010

EXECUTIVE SUMMARY

IN-HOUSE COUNSEL AND BUSINESS LAW AND GOVERNANCE PRACTICE GROUPS

Alerting the "C-Suite":
The Responsible Corporate Officer Doctrine

Michael W. Peregrine, Esquire*
Joshua T. Buchman, Esquire
McDermott Will & Emery LLP
Chicago, IL

Sample Enforcement Results

Defendant	Laws	Allegations	Result
U. Pitt/Bluestone (1999)	FCA	Failure to disclose industry funding on NIH grant applications	- Judgment
Orphan/Jazz (2007) Dr. Peter Gleason	FDCA, Health Care Fraud	Off-label promotion	- $20 million, criminal plea (against company) - Indictment (against Gleason)
Ortho Mfrs. (9/07)	AKS	Five companies accounting for 95% of hip and knee replacement parts accused of conspiracy and inducement	- DPAs/NPA - $311 million for 4 companies - Publish physician payments to websites
Emory (10/08)	Regulatory/GPS	Failure to report $1.2 million in funding from Glaxo SmithKline	- NIH stops payment on $9.3 million grant - Special award conditions - Institutional assurance of compliance
Eli Lilly (1/09)	AKS, FDCA	Off-label promotion, kickbacks	- $1.2 billion
Pfizer (9/09)	AKS, FDCA	Off-label promotion, kickbacks	- $2.3 billion (3 CIAs since 2002)
Spectranetics (12/2009)	FCA	Illegal imports of unapproved devices, clinical study in violation of regulations, off-label promotion	- CIA (IRO) - $4.9 million, NPA
Guidant/BS (12/09)	AKS	Payment of kickbacks to physicians (post-marketing studies)	- CIA - $22 million - Publish physician payments to website
Dr. Scott Reuben (1/10)	Health care fraud	Fabrication and falsification, uncovered when routine review of research identified no IRB approval for published work	- Guilty plea - Up to 10 years' imprisonment - Up to $250,000 fine and asset forfeiture
Amgen (Pending)	AKS/FCA	Sham consulting contracts, lavish vacations, over-filled vials (Aranesp), encouraged bills to Medicaid for free drugs	- FCA complaint filed - State AGs have intervened
J&J (Pending)	AKS	Predatory marketing tactics to push drugs on nursing home patients	- FCA complaint filed

Enforcement Results: Disclosure

THE NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Accuracy of Conflict-of-Interest Disclosures Reported by Physicians

ABSTRACT

BACKGROUND

The recent public reporting of payments made to physicians by manufacturers of orthopedic devices provides an opportunity to assess the accuracy of physicians' conflict-of-interest disclosures.

METHODS

We analyzed the reports of payments made to physicians by five manufacturers of total hip and knee prostheses in 2007. For each payment recipient who was an author of a presentation or served as a committee member or board member at the 2008 annual meeting of the American Academy of Orthopedic Surgeons, the disclosure statement was reviewed to determine whether the payment had been disclosed. To ascertain the reasons for nondisclosure, a survey was administered to physicians who had received payments that were not disclosed.

RESULTS

The overall rate of disclosure was 71.2% (245 of 344 payments). For payments that were directly related to the topic of the presentation at the meeting, the rate was 79.1% (163 of 206); for payments that were indirectly related, the rate was 50.0% (16 of 32); and for payments that were unrelated, the rate was 49.2% (29 of 59) ($P<0.008$). In the multivariate analysis, payments were also more likely to have been disclosed if they exceeded $10,000 ($P<0.001$), were directed toward an individual physician rather than a company or organization ($P=0.04$), or included an in-kind component ($P=0.002$). Among the 36 physicians who responded to the survey regarding reasons for nondisclosure (response rate, 39.6%), the reasons most commonly given for non-disclosure were that the payment was unrelated to the topic of presentation at the annual meeting (38.9% of respondents) and that the physician had misunderstood the disclosure requirements (13.9%); 11.1% reported that the payment had been disclosed but was mistakenly omitted from the program.

CONCLUSIONS

In this study of self-reported conflict-of-interest disclosure by physicians at a large annual meeting, the rate of disclosure was 79.1% for directly related payments and 50.0% for indirectly related payments.

1466

http://content.nejm.org/cgi/content/short/361/15/1466

- Ortho device settlements (2007)
  - Biomet: http://www.biomet.com/corporate/consultant_disclosure.cfm
  - Depuey: http://www.depuy.com/corporate-information/find-surgeons and http://www.depuyorthopaedics.com/Pages/Transparency.aspx
  - Smith & Nephew: http://www.smithnephewdpacompliance.com
  - Stryker: http://www.stryker.com/meetourconsultants/consultants/consultants.php
  - Zimmer: http://www.zimmer.com/z/ctl/op/global/action/1/id/10373/template/CP/navid/10548

On the Horizon …

- Institutional Accountability
  - *Qui tam* lawyers are examining the possibility of pursuing false claims act cases against sponsors for the acts and omissions of independent site investigators (GCP failures)
  - CTAs typically include indemnification provisions protecting sponsors against liability for certain categories of conduct, including false statements of contracting institutions and their agents

- Individual Accountability
  - Government is increasingly pursuing individuals responsible for corporate misconduct as part of its investigations, including physicians
  - Theories vary
    - Direct participation in crimes or civil fraud
    - Responsible corporate officer doctrine
- Mandated Transparency => Voluntary Transparency
  - Government demands transparency through settlement agreements
  - Congress may require transparency via the Physician Payments Sunshine Act (and many states do this already)
  - Individual institutions are moving toward transparency.


The New York Times

December 3, 2008

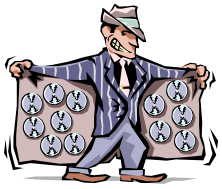
Cleveland Clinic Discloses Doctors' Industry Ties

By REED ABELSON

The Cleveland Clinic plans to announce this week it has begun publicly reporting the business relationships that any of its 1,800 staff doctors and scientists have with drug and device makers.

Best Practices - Policies

- Develop/coordinate policies in all areas, and address the entire institution – *but typically not all at once*
  - Issues
    - Vendor access to facilities
    - Negotiation and execution of purchasing agreements and CTAs
    - Educational grants / seminars
  - Locations
    - Hospital(s) / Clinic(s)
    - Medical School
    - FPP



Consulting Agreements

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Challenges and Opportunities

- **Challenges**
  - Legal/regulatory constraints
  - Conflict of commitment
  - Investigator independence and data integrity
  - Public perceptions
- **Opportunities**
  - Expanded support for clinical research in an age of generally declining and insufficient federal support (not all fundable research is funded)
  - Incremental improvements in and new uses for existing drugs, devices, and procedures
  - Collaborations

Policy Considerations

- Policy options are endless and decisions require input from across the institution
  - Elimination of all conflicts or categories of conflicts
  - Absolute transparency/disclosure
  - Standards tagged to regulatory minimums
- Once policies are set, provide guidance to employees on content of outside activities policies to help them avoid inadvertent violations
  - Acceptability (complete ban, only during release time or off hours, etc.)
  - Reportability (COI disclosures)
  - Acceptable terms and conditions in contracts (e.g., re: ownership of IP) and other relevant considerations
  - Role of institutional counsel

Best Practices – Consulting Agreements

- **Minimize fraud and abuse risk**
  - Avoid situations that implicate Stark unless an exception is clearly met
  - Don't do the deal unless there's a real and documented need for services and the consultant's qualifications/experience meet those needs
  - Describe in reasonable detail all services to be provided
  - Compensation
    - Base consistent with fair market value in an arms-length transaction
    - Package not based on volume or value of past, present, or anticipated future business
    - Royalties only in return for novel, significant, or innovative contributions to the company's products, and calculated to not interfere with clinical objectivity
    - Reimbursement for documented, reasonable and actual expenses incurred and necessary to perform the services
  - Reasonable meeting venues
  - Agreements written and signed by the parties in advance of performing the services
- **Address other business issues**
  - Whose relationship – individual or institution
  - Intellectual property
  - Indemnification

Clinical Trial Agreements

Health Care Compliance Association
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Left Hand – Right Hand

- Ask who (among research team, department administrators, sponsored programs staff, *etc.*):
  - Initiates relationships with industry
  - Negotiates major business terms of agreements
  - Develops, approves budgets
  - Develops, approves final contracts
- Confirm all:
  - Are aware of the relevant legal and regulatory mandates, as well as relevant institutional policies (education / training)
  - Have access to knowledgeable compliance staff / legal counsel to consult on non-standard terms or other novel issues
  - Work together with research teams, one another, and IRB to assure compliant agreements and consistency among various study documents

Allocation of Responsibilities

- **The Challenge**
  - Definitions are critical, e.g. “sponsor” and “Principal investigator”
  - Definitions can (without more) determine both contractual and regulatory obligations
    - Who is responsible for securing any required permits (e.g., IND, IDE)
    - Who is responsible for reporting SAEs and other information to FDA
      - Investigational drugs/devices
      - Approved drugs/devices
- **Response**
  - Clearly define in the agreement who is responsible for what
  - Distinguish (if applicable) between the financial sponsor(s) and the sponsor for FDA purposes
  - Distinguish (if applicable) between the project director (even if an academic investigator) and the site PI or PIs

Participation of Multiple Parties

- **Challenge**
  - Typical contracts:
    - Presume institution/site are one and employ PI
    - Vary tremendously in definition of “parties” and authority to approve amendments
    - Are not well-constructed to address different divisions of responsibilities
  - There is no “typical” and unforeseen circumstances may disrupt smooth conduct of studies
- **Solutions**
  - Clearly define in CTAs, intra-institutional agreements, and/or institutional policies the respective roles and responsibilities of principal investigator, host site, and any involved third parties, e.g.
    - Good clinical practice (compliance with HRP regulations)
    - Clinical research billing
  - Specify in advance what happens in the event of foreseeable but unexpected developments
    - Conflicts among institution, site, and PI
    - Disaffiliation of PI from institution or site
    - Withdrawal of site from project (PI still interested in pursuing)
    - Regulatory developments

Recognizing Fraud and Abuse Risks

- **Recruitment incentives**
  - Rewards to individual investigators or study coordinators for success in meeting targets
    - Problem – can encourage inappropriate enrollment and should be explicitly barred in CTAs
    - Solution – fair market value payment for services actually rendered to recruit/enroll trial participants
  - Payments to research participants
    - Problem – raises ethical as well as potential legal challenges (e.g., beneficiary inducement)
    - Solution – address clearly in CTAs and institutional policies, and require IRB approval for each individual study
- **Other payments for services (of PI, institution, and host facility)**
  - Promote compliance with CMS clinical trial policies and private payor requirements
  - Avoid duplicate claims and payments
  - Avoid Medicare Secondary Payor challenges
  - Assure fair market value

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Health Information Privacy and Security

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Regulatory Background

- **Health Insurance Portability and Accountability Act of 1996 ("HIPAA")**
  - Limitations on Use and Disclosure
    - "Covered entities" may use or disclose "protected health information" only with a patient's written authorization or for specifically designated purposes without written authorization
    - Compound authorization and authorization for "unspecified" future research is invalid
  - Security:
    - Covered entities must assure the confidentiality, integrity, and availability of ePHI
- **Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH)**
  - Prohibition on Sales: Covered entities and business associates may not directly or indirectly receive remuneration for PHI without authorization, unless an exception applies … research exception requires price charged to reflect only costs of preparation and transmittal
  - Breach Notification: Individuals, media, OCR must be notified of certain breaches of "unprotected PHI"

Recruiting/Informed Consent Process

- **Recently seen …**
  - "I donate my information to the sponsor. The sponsor may use or disclose the [tissue] [information] for any purpose."
  - "Sponsor may use my information to analyze study results and for future research and product development."
- **Recommendations**
  - Train IRB staff charged with administratively reviewing ICFs (and, ideally, members) to recognize impermissible language
  - Consider institutional template with opt-in to correlative studies and acceptable language for disclosures to sponsors: "Data the researchers collect may be shared with the sponsor:
    - To report on study activities and findings
    - During on-site inspections
    - For use in reports and applications to FDA

    Once the information is shared with the sponsor, it may no longer be protected by federal privacy regulations."

Commercial Tissue Repositories: HIPAA Raises Sponsors' Fears

CRFs and Adverse Event Reporting

- **Issue**
  - Increasingly sponsors are relying on electronic information systems to collect study data, including direct eCRF entry
  - Information provided to sponsors on CRFs typically qualifies as "limited data set" but not "deidentified"
- **Implications**
  - Covered entities reporting data to sponsors are responsible for the security of ePHI (data transmission policies/standards)
  - Covered entities reporting data to sponsors are responsible for breaches that occur in transmission
- **Recommendations**
  - Assure institutional data security officials understand the nature of these communications with sponsors
  - Include in CRFs sponsor representations and warranties re: compliance of electronic submission systems with HIPAA/HITECH regulations and relevant guidance (e.g., NIST standards for encryption of data in transit)

Monitoring/Site Visits

- **Sponsor Needs**
  - Review study records to assure complete
  - Review source documentation (including medical records) to assure study records are accurate
- **Site Challenges**
  - Stretched staff
  - Frequent monitoring visits and inspections
  - Restrictive privacy/security policies

- **Site Responses**
  - Study coordinator logs in monitor under study coordinator's password and walks away from terminal
- **Recommendations**
  - Assure CTAs include language anticipating monitor access to information systems, if that might occur, and requiring monitor basic education and compliance with site policies
  - Consider issuing limited use/duration IDs and passwords for site monitors
  - Issue routine reports to study coordinators on records accessed and directly audit against informed consent/authorization restrictions

Hypotheticals

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Assuring Participant Compliance With Protocol

- DeviceCo has successfully completed early testing on its new cardiovascular device and is in the process of opening sites across the U.S. and internationally for final testing prior to PMA application. DeviceCo's standard budget assumes Medicare and third-party payment for routine costs associated with the study. DeviceCo will pay for the device itself and for two study-required scans that would not typically be performed as part of conventional care. One of DeviceCo's physician consultants has suggested that DeviceCo pay subject transportation costs and co-payments to help assure subjects show up for study-required visits, where important data will be collected in addition to routine H&P and other procedures.
- Discuss.

Investigator-Initiated Study

- PI approaches PharmCo to supply free drug and provide some financial support to study PharmCo's approved drug off-label. PharmCo agrees and in the proposed agreement specifies that PI is sponsor for regulatory purposes associated with the study.
- What are the implications?
  - IND application (or exemption determination)
  - Collection of CVs and COI disclosures from investigators
  - Monitoring
  - Reporting to FDA
    - Part 312
    - Part 314

PI Disaffiliation

- PharmCo contracts with academic institutions, community hospitals, and large physician practices to perform Phase III studies of its new drug. Dr. Jones has worked with PharmCo for the last ten years. His studies are always well-managed. Recruitment generally meets targets; and monitoring visits and FDA inspections have proceeded smoothly. PharmCo's standard contract is a multi-party agreement PharmCo, the community hospital where Dr. Jones sees his patients, Dr. Jones' group practice, and Dr. Jones himself. All research support for Dr. Jones' studies has been provided in the past by staff employed by his group practice. Dr. Jones announces that he is leaving the group practice and will be employed by a competing community hospital.
- Discuss.

Useful Links – Clinical Trials Contracting

- **Contract Standardization**
  - Institute of Medicine: http://www.iom.edu/Activities/Research/DrugForum/2009-APR-27.aspx
  - National Cancer Institute (START): http://restructuringtrials.cancer.gov/initiatives/standardization/highlights/start
  - National Cancer Institute (Tech Transfer): http://ttc.nci.nih.gov/forms/
  - Federal Demonstration Project: http://www.thefdp.org/
- **Reducing Fraud Risk**
  - http://www.healthcareappraisers.com/AHLA_LifeSciences_0409.pdf
  - http://www.ehcca.com/presentations/ressummit/105b.PDF
- **OIG Advisory Opinions**
  - http://oig.hhs.gov/fraud/advisoryopinions.asp

Useful Links – Conflicts of Interest

- **Federal Efforts**
  - NIH Current: http://grants.nih.gov/grants/policy/coi/
  - NSF Current: http://www.nsf.gov/pubs/policydocs/pappguide/nsf09_1/index.jsp
  - Reports and Proposals
    - Grassley's Sunshine: http://grassley.senate.gov/private/upload/12209.pdf
    - OIG report re: FDA http://oig.hhs.gov/oei/reports/oei-05-07-00730.pdf
    - Emory letter summarizing NIH http://www.osp.emory.edu/compliance/2008.10.10%20FCOI%20Letter%20to%20Research%20Community.pdf
    - MedPac Recommendations (Nov 2008): http://www.medpac.gov/transcripts/Public%20reporting_Nov%2008_public.pdf
- **State Efforts**
  - NCSL: http://www.ncsl.org/programs/health/rxads.htm
  - NCSL (2008 Rx Bills By State): http://www.ncsl.org/programs/health/drugbill08.htm#States
- **Private Initiatives**
  - On-Line Reporting: www.clevelandclinic.org, www.dcri.org/research/coi.jsp, www.psychiatrictiems.com/editorial-board
  - Associations
    - AAMC: http://www.aamc.org/research/coi/start.htm
    - AMSA: http://www.amsascorecard.org/
    - PhRMA: http://www.phrma.org/code_on_interactions_with_healthcare_professionals/
    - AdvaMed: http://www.biomet.com/fileLibrary/corporate/codeOfEthics.pdf