2011 UC Compliance & Audit Symposium

Recent Legal Developments in Academic Research and Clinical Trials

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Session Overview

- Content
  - Industry Relations
  - FDA Regulation of Clinical Trials
  - Fraud and Abuse
  - Insider Trading
  - Information Privacy and Security
  - Clinical Laboratory Improvements Act
  - Time Permitting – Open Q&A

- General Format
  - Basics
  - Recent Developments
  - Potential/Expected Impact on the UC Research Community: Challenges and Opportunities
  - Resources

Industry Relationships

"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

Basics (PHS Grants/Coop Agreements)

- Regulatory Basis: 42 C.F.R. part 50, subpart F
- 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

Basics (cont'd)

- California Political Reform Act
  - Requires specified individuals – including principal investigators – to report on certain financial interests and to be recused from decisionmaking in some instances
- Human Research Protection Programs (OHRP, FDA, AAHRPP)
  - IRB must assure that no members participate in review of projects in which they have conflicting interests, except to provide information requested by the IRB
  - DHHS agency-wide guidance identifies "points to consider" in determining whether specified conflicts may affect the rights and welfare of human subjects participating in research, referencing specific regulations implicated when conflicts arise
  - AAHRPP has published an updated "Tip Sheet"
- NIH-OBA Guidelines
  - Biosafety committee members generally may not participate in review of projects in which they are engaged
  - Investigators must address clinical/research conflicts in their research proposals; OBA provides guidance on language for ICFs regarding financial interests
- And…
  - Professional societies
  - Biomedical journals
  - Funding source policies

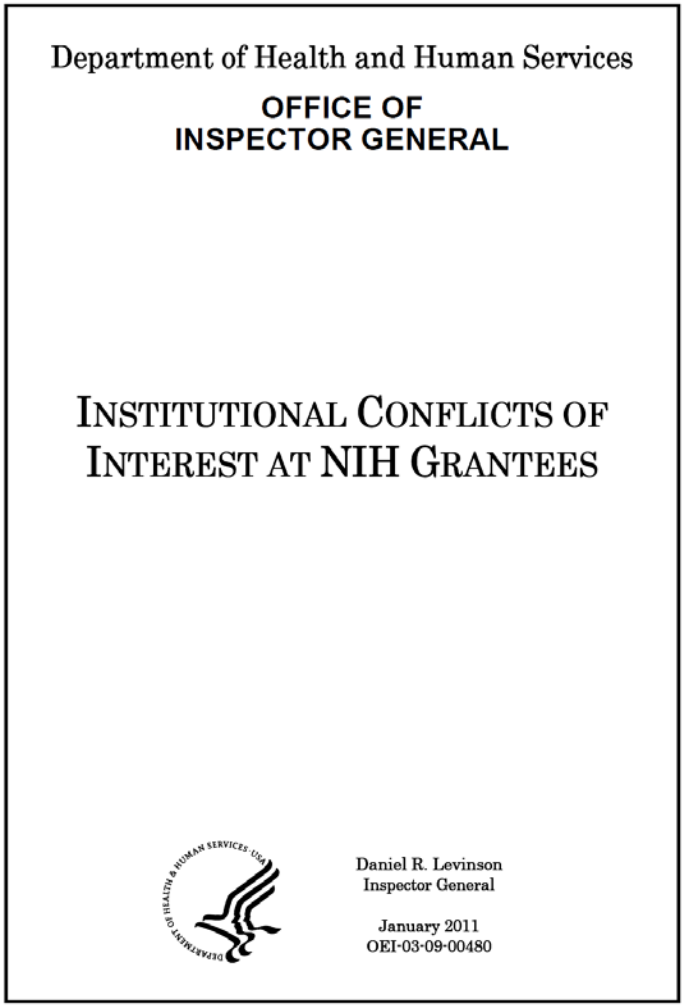
Recent Developments/On the Horizon

Recent Developments/On the Horizon

- PHS Notice of Proposed Rulemaking
  - PI responsibilities
    - Reporting threshold decreases from $10,000 to $5,000
    - SFI is defined to include any equity interest in non-public companies
    - Exceptions previously applicable to public/non-profits will apply only to government agencies and higher ed
    - SBIR/STTR Phase I exception eliminated
    - All SFIs related to investigator's institutional responsibilities must be disclosed to institution (not just those relevant to the project)
  - Institutional responsibilities
    - Determine which SFIs are relevant
    - Develop management plans
    - Report on SFIs to NIH (more detail than previously) and post publicly prior to expenditures; annual updates
    - Biannual training of all investigators
    - Mitigation (corrective action) plans when disclosure failures are identified
  - HHS authority to inquire "clarified"

Recent Developments (cont'd)

- OIG Report on Institutional Conflicts
  - Common Definitions
    - Institutional officials' individual financial interests
    - Equity held by institution in publicly held entities
    - Equity held by institution in non-publicly held entities
  - Major Conclusion
    - Grantee institutions with institutional conflicts policies are more likely than peers to identify institutional conflicts
  - OIG Recommendations
    - NIH should mandate "consistent and uniform" identification, reporting, and management of institutional conflicts
    - Premise: it "is important that NIH know of the existence of such conflicts so it can ensure that the related research is free from any intended or unintended bias"


Department of Health and Human Services

OFFICE OF
INSPECTOR GENERAL

INSTITUTIONAL CONFLICTS OF INTEREST AT NIH GRANTEES

Daniel R. Levinson
Inspector General

January 2011
OEI-03-09-00480

Recent Developments (cont'd)

- External identification of undisclosed or unmanaged conflicts
  - Many sources
    - Malpractice litigation => FPPC complaint
    - Peer reviewers (study sections, RAC, journals)
    - NIH program officers
    - Advocacy groups
  - Creates reputational and financial risk to researchers and the institution
- Executive Order (1/18/11) and Op-Ed on regulatory reform
  - Calls for improved balance between sometimes competing objectives of protecting "public health, welfare, safety, and our environment ... while promoting economic growth, innovation, competitiveness, and job creation."

PRO PUBLICA
Journalism in the public interest

Project On Government Oversight

Exposing Corruption

POGO

Exploring Solutions

CONFLICT OF INTEREST
IN MEDICAL RESEARCH,
EDUCATION, AND PRACTICE

United States Senate
SPECIAL COMMITTEE ON AGING
WASHINGTON, DC 20510-6400
(202) 224-5364

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:

As Chairman of the United States Senate Special Committee on Aging, I take very seriously my responsibility to protect America's seniors. One part of that responsibility is working to ensure that seniors have access to accurate and unbiased information concerning their health care needs. Critical to this goal is the information they receive from their doctors. To that end, the Committee has conducted several hearings studying the financial relationships between physicians and medical device and pharmaceutical manufacturers. This series of hearings led to the drafting of the Physician Payments Sunshine Act, which is currently before the Senate Finance Committee. The legislation would provide for transparency in the relationship between physicians and manufacturers of drugs, devices, or medical supplies for which payment is made under Medicare, Medicaid, or SCHIP.

With that background, I was interested to learn that the American College of Cardiology (ACC) has entered into a five-year partnership with the Cardiovascular Research Foundation (CRF). My understanding is that one of the purposes of this partnership is to develop the component of the ACC Annual Scientific Session concerning catheter based treatments for structural heart diseases. According to its own website, the CRF receives funding from a variety of medical device manufacturers. The potential for this partnership to influence clinical practice raises questions concerning the continued impartiality of your organization. All Americans and particularly seniors need to have confidence in the health recommendations of their physicians. Therefore, the growing links between organizations such as the ACC and industry advocacy groups warrant special attention.

In an effort to learn more about the ACC's relationship with the CRF, I am requesting that your organization provide the following information to the Committee:

1. An explanation of the events and conditions surrounding the establishment of the partnership between the ACC and the CRF.

Web Site: http://aging.senate.gov

tates Senate
MITTEE ON AGING
V., DC 20510-6400
224-5364

nts documenting the terms of the partnership
F.

l exchanges between the ACC and the CRF
accounting should include, but should not

h both the ACC and the CRF are parties.

between the ACC and the CRF.

done at the request of either the ACC or the
a third party. This should include: 1)
by the ACC to the CRF for the benefit of a
sfer requests made by the CRF to the ACC
d party.

or other organizational officers who have
both the ACC and the CRF within the past

tors to your organization who are members
dical device manufacturing industry.

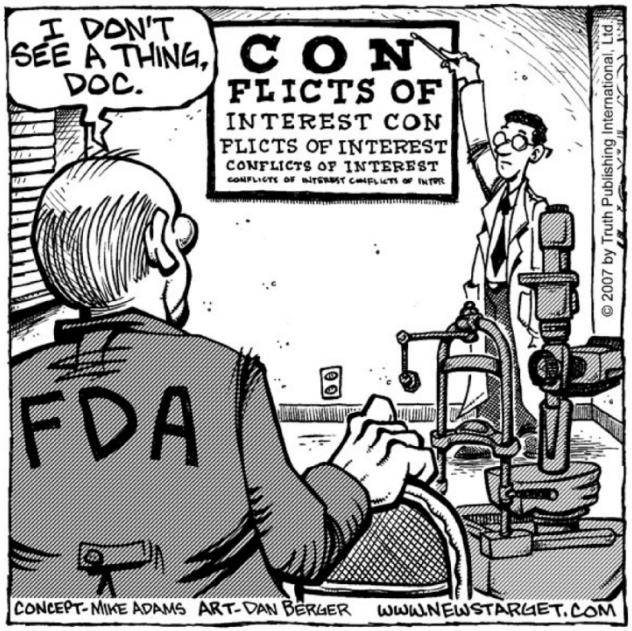
close of business on August 5, 2008. Feel
ll of my staff at (202) 224-5364 with any
est.

ly,

Kohl

ohl
Chairman

COUNTERTHINK "FDA VISION TEST"



H. R. 3590

One Hundred Eleventh Con
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

Protecting Patients, Preserving Integrity, Advancing Health:
Accelerating the Implementation of COI Policies in Human Subjects Research

A Report of the AAMC-AAU Advisory Committee on Financial Conflicts of Interest in Human Subjects Research

February 2008

AAMC

Challenges and Opportunities

- Challenges
  - Money increasingly is equated with waste and even corruption, particularly among government agencies and advocacy groups
  - Amended regulations (likely) will substantially increase administrative burden with no associated increase in administrative support
  - Expectations re: institutional management/oversight of do not necessarily match reality
- Opportunities
  - Relationships with industry, handled appropriately, can facilitate and support research and education in an age of diminishing government investment, speed patient access to new/emerging technologies
  - Advocacy groups have begun to collect publicly available information in a single resource that can be used by auditors and compliance staff to identify inadvertent errors and omissions when there is still time to correct without significant consequence; PPACA will (may?) help

UC Resources

- People
  - Your Conflict of Interest Coordinators: http://www.ucop.edu/ogc/coi/coord.html
  - UC Office of the General Counsel: http://www.ucop.edu/ogc/coi/econinterest.html
  - RPAC: http://www.ucop.edu/research/rpac/rpacstaff.html
  - ECAS: http://www.universityofcalifornia.edu/compaudit/researchcomp/conflict/

- Policies:
  - APM 020 - Special Services to Individuals and Organizations
  - APM 025 - Faculty COI
  - APM 670 - Health Sciences Compensation Plan
  - COI Policy Compendium: http://www.ucop.edu/ucophome/policies/bfb/g39.pdf
  - Conflict of Interest Code – 2011: http://www.ucop.edu/ogc/coi/documents/text.pdf
  - ECAS Compliance Briefing for Researchers: http://www.universityofcalifornia.edu/compaudit/documents/compliance_briefiing_researchers.ppt
  - Guidelines on University-Industry Relations: http://www.ucop.edu/ott/genresources/unindrel.html
  - Healthcare Vendor Relations Policy: http://www.ucop.edu/ucophome/coordrev/policy/PP031208Policy.pdf
  - Industry-University Partnership Resources: http://www.ucop.edu/research/ias/industrylinks.html#policies
  - RAO Operating Guidance 00-08: http://www.ucop.edu/raohome/cgmemos/00-08.html
  - RPAC Links on Integrity and Conflicts of Interest: http://www.ucop.edu/research/policies/integrity.html#coi

External Resources

- NIH Kiosk: http://grants.nih.gov/grants/policy/coi/
- DHHS OIG:
  - DRAFT Grantee Institution Guidance (2005-withdrawn): http://oig.hhs.gov/fraud/docs/complianceguidance/PHS%20Research%20Awards%20Draft%20CPG.pdf
  - Pharmaceutical Industry Guidance (2003): http://oig.hhs.gov/authorities/docs/03/050503FRCPGPharmac.pdf
  - Reports: http://oig.hhs.gov/oei/reports
- Professional Societies/Trade Associations
  - AAHRPP (2011): http://www.aahrpp.org/Documents/D000137.PDF
  - AAMC/AAU (2008): https://services.aamc.org/publications/showfile.cfm?file=version107.pdf&prd_id=220&prv_id=268&pdf_id=107
  - AdvaMed Code (2009): http://www.advamed.org/MemberPortal/About/code
  - ICMJE Guidelines (2009): http://www.icmje.org/ethical_4conflicts.html
  - PhRMA Code (2008): http://www.phrma.org/sites/default/files/369/phrma_marketing_code_2008-1.pdf
- Advocacy Websites
  - POGO: http://pogoblog.typepad.com/pogo/2011/01/the-ugly-underbelly-of-medical-research.html
  - ProPublica: http://projects.propublica.org/docdollars/

FDA Regulation of Clinical Trials

Basics

- FDA regulates drugs (including biologics) and devices under the Food, Drug & Cosmetic Act
- Drugs and devices may be marketed or otherwise commercialized subject to FDA approval and labeling requirements
- New drugs and devices; and approved/cleared products used off-label may be adulterated, misbranded, or both
  - Research exception permits use of "investigational" products in clinical investigations
  - FDA does not regulate medical practice and so does not prohibit physicians from prescribing off-label if appropriate in their clinical judgment
- Clinical investigations are subject to detailed requirements for performance and documentation (referred to collectively as "current good clinical practice" or "cGCP")
  - Sponsors and investigators each have special roles to play
  - Where UC is sponsor, UC assumes sponsor's obligations
  - Where PI is sponsor, PI assumes sponsor's obligations
- FDA has both civil and criminal enforcement authority

Common Citations (Investigators)

- Failure to secure IRB approval, appropriate investigational permits (IND, IDE)
- Consent deficiencies (after screening, wrong version, inconsistent with protocol, opt-in missing for test performed, LEP)
- Protocol deviations; AE/UP reporting
- Missing fCOI disclosure statements; CVs
- Improper delegation, inadequate supervision, inadequate monitoring
- Drug/device accountability
- Documentation deficiencies (inconsistencies between medical and research records; failure to maintain appropriate research records)
- Failure to report (to IRB, sponsor, FDA)
- Fabrication, falsification

1. Failure to ensure that the information given to subjects as part of the informed consent is in accordance with 21 CFR 50.25. [21 CFR 56.109(b)].

The IRB shall require that information given to subjects as part of informed consent is in accordance with 21 CFR 50.25 (21 CFR 56.109(b)). The IRB failed to ensure that the informed consent contained all the information required by 21 CFR 50.25 such as:

- A description of the procedures to be followed and identification of any procedures which are experimental (21 CFR 50.25(a)(1));
- A description of any reasonably foreseeable risks or discomforts to the patient (21 CFR 50.25(a)(2)); and
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might he advantageous to the subject (21 CFR 50.25(a)(4)).

Examples of this failure include, but are not limited to, the following:

a. At the time of the inspection, **(b)(6)** was conducting five clinical trials that involved **(b)(4)** also referred to as **(b)(4)** with over 240 enrolled subjects with **(b)(4)** The informed consent forms for these five studies did not contain all the required basic elements. Specifically:

1. The description of the procedures did not always include **(b)(4)** or **(b)(4)**

2. A statement that explained that this procedure was experimental. The procedures section of most of the studies' informed consent forms erroneously notes the **(b)(4)** has been used for decades.

3. All reasonably foreseeable risks of **(b)(4)** are not described; rather the only risk of **(b)(4)** listed in the consent is **(b)(4)** can also cause **(b)(4)** which may lead to **(b)(4)** and death. In addition, **(b)(4)** can also result in **(b)(4)** and **(b)(4)** as other possible risks.

4. There iis no disclosure statement of appropriate alternative **(b)(4)** or **(b)(4)**.

During the course of the FDA inspection of the IRB facilities the IRB suspended Dr. Tuller's studies and, according to your response letter, after further investigation, these studies were then terminated by the IRB. This response is adequate. In addition, you stated in your response that you are plannin on providing intensive training and have developed tools to assist you in assessing studies and risks. Please provide a description of any completed training and a list of attendees or a projected timeline of planned training.

2. Failure to have written procedures governing the functions and operations of the IRB [21 CFR 56.108].

FDA regulations require that an IRE must prepare, maintain, and follow written procedures that describe the IRB's functions and operations, including: conducting continuing review of research, for determining which projects require review more often than annually and which project needs verification from sources other than the investigator that no material changes have occurred since previous IRB review; ensuring that changes to approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to human subjects; ensuring prompt reporting to the IRB, appropriate institution officials, and the

Common Citations (IRBs)

- Deficient SOPs or failure to follow SOPs
- Inadequate review of records (e.g., approval of problematic consent documents)
- Failure to achieve or maintain quorum for votes
- Documentation deficiencies (adequacy of minutes; retention)
- Inadequate oversight
  - Continuation review
  - Response to red flags

Failure to conduct an investigation according to the signed agreement, the investigational plan, and applicable FDA regulations [21 C.F.R. 812.100 and 812.110(b)]; failure to obtain approval prior to implementing a change to the investigational plan [21 C.F.R. 812.35].

An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicabl FDA regulations. 21 C.F.R. 812.100, and 812.110(b).

- You failed to conduct the investigation in accordance with the investigational plan in that you enrolled subjects who did not meet the eligibility criteria set forth in the investigational plan. Examples of your failure include, but are not limited to the following: The inclusion criteria in the protocol specified that **(b)(4)** were eligible for study enrollment. However, you enrolled **(b)(6)** who were between **(b)(4)** and **(b)(4)** years old and treated them with the investigational device.

Because you are both a clinical investigator as well as the sponsor for this study, you are required to fulfill the responsibilities of each. As a sponsor, you are required to obtain FDA approval and IRB approval when appropriate, and prior to implementing a change to the investigational plan. 21 C.F.R. 812.35.

- You failed to obtain FDA approval for changes to the inclusion criteria.

In your response, you indicate that the age range in the protocol and the IDE was an error, as the intent of the study was to use a minimally invasive method of closure in the pediatric population that had failed to **(b)(4)** in the usual allotted time of **(b)(4)** and would need open **(b)(4)**. You indicatec that in any future studies, the age discrepancy will be corrected. Your response is inadequate in that you did not obtain FDA approval for the changes in the inclusion criteria, nor did you submit any documentation reflecting the corrective or preventive actions you have implemented to ensure that thi deviation does not recur. Please develop procedures that will prevent the above deviation from recurring in future studies. Submit a copy of these procedures, along with documentation demonstrating staff training in these procedures, when you respond to this letter.

No CAPA documentation

Failure to maintain accurate, complete, and current records related to your participation in the investigation. [21 C.F.R. 812.140(a)]

A clinical investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigatior records of receipt, use or disposition of a device that relate to the type and quantity of the device, the dates of its receipt, and the batch number or code mark. 21 C.F.R. 812.140(a)(2)(i).

- You failed to adhere to the above stated regulation. Examples of this failure include, but are not limited to the following: Your device receipt and disposition records were inadequately maintained. You reported that you received enough from not have any documentation of the exact quantity received. You provided a spreadsheet pertaining to device accountability at the close of the inspection; however, it did not state the quantity of device received nor did it provide the date of its receipt.

Your response states that the nurse in the designated **(b)(4)** kept a separate log relating to the quantity, date, and lot number of the device. This log was kept in the cabinet with the devices; however the log and the nurse were not available at the time of the FDA inspection. You stated that you subsequently provided the patient names, lot numbers, and amount given. Your response is inadequate. The spreadsheet you provided did not include the quantity of device received or the date on which they were received. Moreover, your response does not provide substantive corrective actions or any preventive actions to ensure appropriate device accountability and to avoid recurrence of these violations. Please provide us with documentation c a corrective action plan, such as written standard operating procedures (SOPs) and written verification of training received by you and your study staff on study procedures to ensure proper record keeping.

The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical study. It is your responsibility as the study sponsor and clinical investigator to ensure compliance with the Act and applicable regulations.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the sponsor and clinical investigator. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you.

15 day response deadline

You will find information to assist you in understanding your responsibilities at http://www.fda.gov/oc/ohrt/irbs/. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Send your response to: Attention: Linda D. Godfrey, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, WO66 RM3462 G/H, 10903 New Hampshire, Silver Spring, Maryland 20993.

Reference to IRB Info. Sheets

Recent Developments/On the Horizon

Recent Developments/On the Horizon

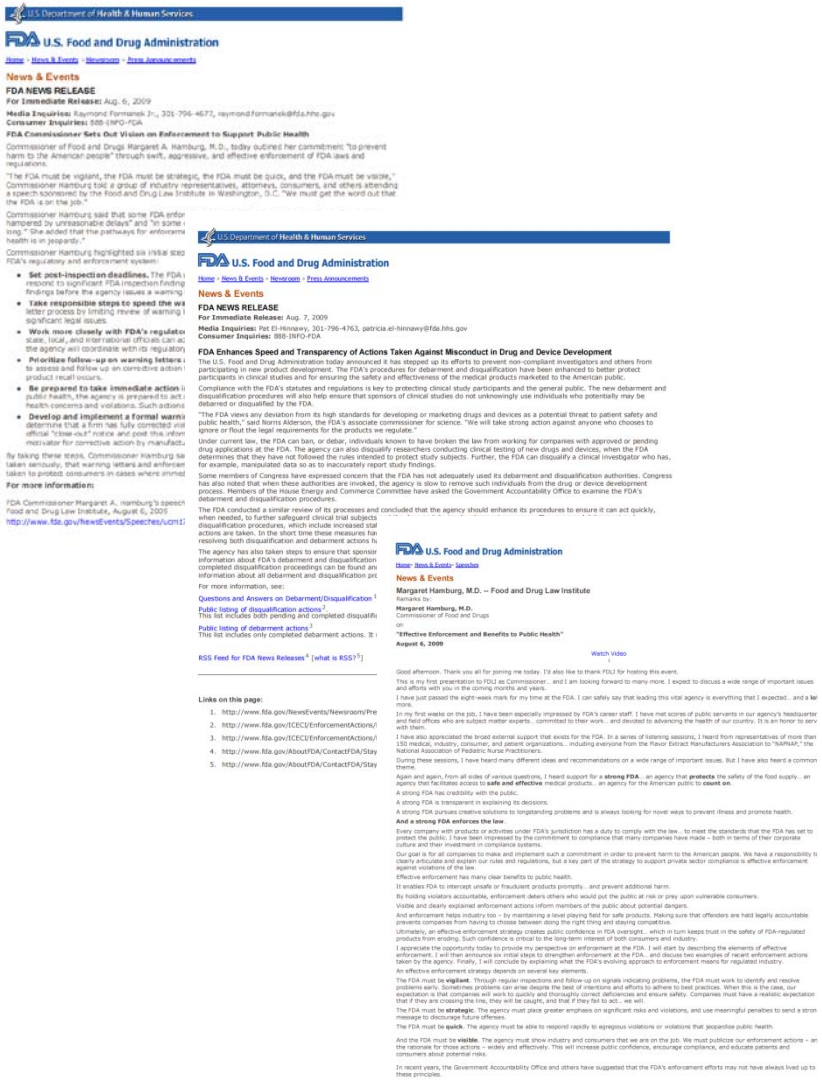
Guidance for Industry

Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects

Additional copies are available from:
Office of Training and Communication
Division of Drug Information, HFD-240
Center for Drug Evaluation and Research
Food and Drug Administration
(Tel) 301-827-4573
http://www.fda.gov/cder/guidance/index.htm
or
Office of Communication, Training and Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
http://www.fda.gov/cber/guidelines.htm.
(Tel) 800-835-4709 or 301-827-1800
or
Office of Health and Industry Programs
Division of Small Manufacturers, International, and Consumer Assistance, HFZ-220
Center for Devices and Radiological Health
Food and Drug Administration
Tel: 1-800-638-2041
www.fda.gov/cdrh

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

Procedural
October 2009



U.S. Department of Health & Human Services

U.S. Food and Drug Administration

Home > News & Events > Newsroom > Press Announcements

News & Events

FDA NEWS RELEASE

For Immediate Release: Aug. 6, 2009

Media Inquiries: Raymond Formanek Jr., 301-796-4677, raymond.formanek@fda.hhs.gov

Consumer Inquiries: 888-INFO-FDA

FDA Commissioner Sets Out Vision on Enforcement to Support Public Health

Commissioner of Food and Drugs Margaret A. Hamburg, M.D., today outlined her commitment "to prevent harm to the American people" through swift, aggressive, and effective enforcement of FDA laws and regulations.

"The FDA must be vigilant, the FDA must be strategic, the FDA must be quick, and the FDA must be visible," Commissioner Hamburg told a group of industry representatives, attorneys, consumers, and others attending a speech sponsored by the Food and Drug Law Institute in Washington, D.C. "We must get the word out that the FDA is on the job."

Commissioner Hamburg said that some FDA enfor
hampered by unreasonable delays" and "in some
long." She added that the pathways for enforcem
health is in jeopardy."

Commissioner Hamburg highlighted six initial step
FDA's regulatory and enforcement system:

- **Set post-inspection deadlines.** The FDA
respond to significant FDA inspection findin
findings before the agency issues a warning
- **Take responsible steps to speed the wa**
letter process by limiting review of warning
significant legal issues.
- **Work more closely with FDA's regulato**
state, local, and international officials can a
the agency will coordinate with its regulato
- **Prioritize follow-up on warning letters**
to assess and follow up on corrective action
product recall occurs.
- **Be prepared to take immediate actions**
public health, the agency is prepared to act
health concerns and violations. Such actions
- **Develop and implement a formal warni**
determine that a firm has fully corrected viol
official "close-out" notice and post this inform
motivator for corrective action by manufactu

By taking these steps, Commissioner Hamburg sa
taken seriously, that warning letters and enforcer
taken to protect consumers in cases where immed

For more information:

FDA Commissioner Margaret A. Hamburg's speech
Food and Drug Law Institute, August 6, 2009
http://www.fda.gov/NewsEvents/Speeches/ucm1

U.S. Department of Health & Human Services

U.S. Food and Drug Administration

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News & Events

FDA NEWS RELEASE

For Immediate Release: Aug. 7, 2009

Media Inquiries: Pat El-Hinnawy, 301-796-4763, patricia.el-hinnawy@fda.hhs.gov

Consumer Inquiries: 888-INFO-FDA

FDA Enhances Speed and Transparency of Actions Taken Against Misconduct in Drug and Device Development

The U.S. Food and Drug Administration today announced it has stepped up its efforts to prevent non-compliant investigators and others from participating in new product development. The FDA's procedures for debarment and disqualification have been enhanced to better protect participants in clinical studies and for ensuring the safety and effectiveness of the medical products marketed to the American public.

Compliance with the FDA's statutes and regulations is key to protecting clinical study participants and the general public. The new debarment and disqualification procedures will also help ensure that sponsors of clinical studies do not unknowingly use individuals who potentially may be debarred or disqualified by the FDA.

"The FDA views any deviation from its high standards for developing or marketing drugs and devices as a potential threat to patient safety and public health," said Norris Alderson, the FDA's associate commissioner for science. "We will take strong action against anyone who chooses to ignore or flout the legal requirements for the products we regulate."

Under current law, the FDA can ban, or debar, individuals known to have broken the law from working for companies with approved or pending drug applications at the FDA. The agency can also disqualify researchers conducting clinical testing of new drugs and devices, when the FDA determines that they have not followed the rules intended to protect study subjects. Further, the FDA can disqualify a clinical investigator who has, for example, manipulated data so as to inaccurately report study findings.

Some members of Congress have expressed concern that the FDA has not adequately used its debarment and disqualification authorities. Congress has also noted that when these authorities are invoked, the agency is slow to remove such individuals from the drug or device development process. Members of the House Energy and Commerce Committee have asked the Government Accountability Office to examine the FDA's debarment and disqualification procedures.

The FDA conducted a similar review of its processes and concluded that the agency should enhance its procedures to ensure it can act quickly, when needed, to further safeguard clinical trial subjects
disqualification procedures, which include increased stal
actions are taken. In the short time these measures ha
resolving both disqualification and debarment actions h

The agency has also taken steps to ensure that sponsor
information about FDA's debarment and disqualification
completed disqualification proceedings can be found an
information about all debarment and disqualification pro

For more information, see:

Questions and Answers on Debarment/Disqualification [1]

Public listing of disqualification actions [2]
This list includes both pending and completed disqualifi

Public listing of debarment actions [3]
This list includes only completed debarment actions. It

RSS Feed for FDA News Releases [4] [what is RSS? [5]]

Links on this page:

1. http://www.fda.gov/NewsEvents/Newsroom/Pre
2. http://www.fda.gov/ICECI/EnforcementActions/
3. http://www.fda.gov/ICECI/EnforcementActions/
4. http://www.fda.gov/AboutFDA/ContactFDA/Stay
5. http://www.fda.gov/AboutFDA/ContactFDA/Stay

U.S. Food and Drug Administration

Home > News & Events > Speeches

News & Events

Margaret Hamburg, M.D. -- Food and Drug Law Institute

Remarks by:

Margaret Hamburg, M.D.
Commissioner of Food and Drugs

on

"Effective Enforcement and Benefits to Public Health"

August 6, 2009

Watch Video

Good afternoon. Thank you all for joining me today. I'd also like to thank FDLI for hosting this event.

This is my first presentation to FDLI as Commissioner… and I am looking forward to many more. I expect to discuss a wide range of important issues and efforts with you in the coming months and years.

I have just passed the eight-week mark for my time at the FDA. I can safely say that leading this vital agency is everything that I expected… and a lot more.

In my first weeks on the job, I have been especially impressed by FDA's career staff. I have met scores of public servants in our agency's headquarter and field offices who are subject matter experts… committed to their work… and devoted to advancing the health of our country. It is an honor to serv with them.

I have also appreciated the broad external support that exists for the FDA. In a series of listening sessions, I heard from representatives of more than 150 medical, industry, consumer, and patient organizations… including everyone from the Flavor Extract Manufacturers Association to "NAPNAP," the National Association of Pediatric Nurse Practitioners.

During these sessions, I have heard many different ideas and recommendations on a wide range of important issues. But I have also heard a common theme.

Again and again, from all sides of various questions, I heard support for a **strong FDA**… an agency that **protects** the safety of the food supply… an agency that facilitates access to **safe and effective** medical products… an agency for the American public to **count on**.

A strong FDA has credibility with the public.

A strong FDA is transparent in explaining its decisions.

A strong FDA pursues creative solutions to longstanding problems and is always looking for novel ways to prevent illness and promote health.

And a strong FDA enforces the law.

Every company with products or activities under FDA's jurisdiction has a duty to comply with the law… to meet the standards that the FDA has set to protect the public. I have been impressed by the commitment to compliance that many companies have made – both in terms of their corporate culture and their investment in compliance systems.

Our goal is for all companies to make and implement such a commitment in order to prevent harm to the American people. We have a responsibility to clearly articulate and explain our rules and regulations, but a key part of the strategy to support private sector compliance is effective enforcement against violations of the law.

Effective enforcement has many clear benefits to public health.

It enables FDA to intercept unsafe or fraudulent products promptly… and prevent additional harm.

By holding violators accountable, enforcement deters others who would put the public at risk or prey upon vulnerable consumers.

Visible and clearly explained enforcement actions inform members of the public about potential dangers.

And enforcement helps industry too – by maintaining a level playing field for safe products. Making sure that offenders are held legally accountable prevents companies from having to choose between doing the right thing and staying competitive.

Ultimately, an effective enforcement strategy creates public confidence in FDA oversight… which in turn keeps trust in the safety of FDA-regulated products from eroding. Such confidence is critical to the long-term interest of both consumers and industry.

I appreciate the opportunity today to provide my perspective on enforcement at the FDA. I will start by describing the elements of effective enforcement. I will then announce six initial steps to strengthen enforcement at the FDA… and discuss two examples of recent enforcement actions taken by the agency. Finally, I will conclude by explaining what the FDA's evolving approach to enforcement means for regulated industry.

An effective enforcement strategy depends on several key elements.

The FDA must be **vigilant**. Through regular inspections and follow-up on signals indicating problems, the FDA must work to identify and resolve problems early. Sometimes problems can arise despite the best of intentions and efforts to adhere to best practices. When this is the case, our expectation is that companies will work to quickly and thoroughly correct deficiencies and ensure safety. Companies must have a realistic expectation that if they are crossing the line, they will be caught, and that if they fail to act… we will.

The FDA must be **strategic**. The agency must place greater emphasis on significant risks and violations, and use meaningful penalties to send a stron message to discourage future offenses.

The FDA must be **quick**. The agency must be able to respond rapidly to egregious violations or violations that jeopardize public health.

And the FDA must be **visible**. The agency must show industry and consumers that we are on the job. We must publicize our enforcement actions – an the rationale for those actions – widely and effectively. This will increase public confidence, encourage compliance, and educate patients and consumers about potential risks.

In recent years, the Government Accountability Office and others have suggested that the FDA's enforcement efforts may not have always lived up to these principles.

Recent Developments/On the Horizon

- Electronic Records and Signatures
  - Announcement of intent to address Part 11 compliance in future inspections
  - Release of DRAFT guidance (comments due 4/7/2011) on electronic source documentation in clinical trials
- NPRM on Falsification
  - Sponsors who "become aware of" potential falsification (broadly defined) 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
  - No coordination with other federal misconduct regulations
- Sponsor Monitoring/Oversight of Investigators
  - FDA routinely holds sponsors accountable for investigators and investigators accountable for research staff (monitoring guidance is under revision)
  - Industry sponsors are beginning to track site performance on monitoring visits and FDA inspections (IRB and investigator) among other indicators and will likely use in selecting future sites
  - Orthocon recently permanently disqualified a site in response to an FDA warning letter
- And more!

The Role of Data Audits in Detecting Scientific Misconduct

(M.F. Shapiro, R.C. Charrow – JAMA 1989;261:2505-2511)

Results of Routine Data Audits by the Food and Drug Administration

	Period I, June 1977 to June 1981, No. (%)	Period II, July 1981 to September 1983, No. (%)	Period III, October 1983 to September 1985, No. (%)	Period IV, October 1985 to April 1988, No. (%)	Total, No. (%)
Routine data audits	549 (100)	415 (100)	422 (100)	569 (100)	**1955** (100)
Serious deficiencies found	57 (10)	54 (13)	55 (13)	45 (8)*	**211** (11)
Written response required to demonstrate solution to problems	24 (4)	37 (9)	39 (9)†	37 (6)	**137** (7)
For-cause investigation launched†	33 (6)	17 (4)	16 (4)	8 (1)*	**74** (4)
Specific deficiencies‡					
Problems with patient consent	212 (39)	253 (61)	246 (58)	291 (51)	**1002** (51)
Inadequate drug accountability	182 (33)	143 (34)	91 (22)	88 (15)	**504** (26)
Protocol nonadherence	106 (19)	114 (27)	132 (31)	155 (27)	**507** (26)
Inaccurate records	85 (15)	91 (22)	96 (23)	131 (23)	**403** (21)
Records not available	21 (4)	17 (4)	8 (2)	14 (2)	**60** (3)
Miscellaneous deficiencies	59 (11)	93 (22)	153 (36)	168 (30)	**473** (24)

*$P<.01$, comparing audits in period IV to periods I, II, and III.
†An additional 321 for-cause investigations were generated outside of the routine data audit process.
‡Some investigators had more than one deficiency. Percentages in the October 1985 to April 1988 period and totals for specific deficiencies are based on 1953 cases for which these analyses were completed.

- Recommendations
  - Certify clinical investigators (may help avoid honest error but not intentional misconduct)
  - Competition for right to conduct studies (peer review)
  - Reduce over-commitment via regulation (limit per-site recruitment opportunities)
  - Penalize manufacturers
  - Pre-hearing suspensions

Challenges and Opportunities

- Challenges
  - Resources
  - Education and training of IRBs, investigators and research staff
  - Identifying what studies are regulated
  - Maintaining focus on basic GCP requirements (and avoiding getting lost in the weeds of esoteric questions)
  - Assuring compliance with non-intuitive requirements
  - Adequately staffing and responding to inspections
  - Confusion re: accountability
  - Resources

- Opportunities
  - "Clean" studies avoid legal/regulatory risk
  - Sponsors' focus on site quality will give high-performing sites a competitive advantage
  - Good study management practices can actually produce efficiencies, for example by avoiding missing the forest for the trees
  - Better protection for research participants and, ultimately, patients who will be exposed to products

Resources

- FDA: http://www.fda.gov
- CDPH: http://www.cdph.ca.gov/programs/Pages/FoodDrugandRadiationSafetyDivision.aspx
- ICH cGCP Consolidated Guidance: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf

Fraud and Abuse

Basics

- Federal and state laws prohibit, discourage, or otherwise regulate payments between referral sources and providers of healthcare items (manufacturers) and services (hospitals, physicians) – for example:
  - Anti-kickback statute
  - False claims act
  - HIPAA (!)
- These impact many aspects of clinical research, including:
  - Grant applications and reports
  - Agreements with clinical trial sponsors (CTAs, consulting, etc.)
  - Patient/participant payments
  - Billing for clinical services performed in connection with research studies
- Enforcement may be initiated by
  - Federal or state prosecutors or civil litigators; whistleblowers
  - Public disclosures

Basics (cont'd)

- Common Problems in Research/Clinical Trials
  - Billing errors
  - Documentation deficiencies
  - Inaccurate or incomplete data
  - Unnecessary services
  - Excessive compensation for services

- Intent Matters – to Some Degree
  - Honest error
  - Reckless disregard/deliberate indifference
  - Intentional wrongdoing

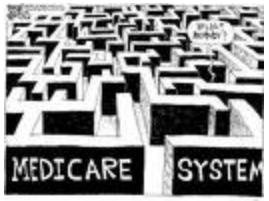
Recent Developments/On the Horizon

Recent Developments/On the Horizon

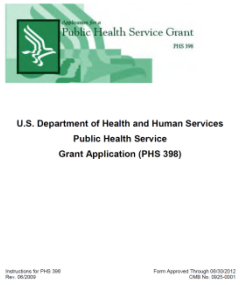
- Enforcement Environment Generally
  - Recovery initiative ABCs: FERA, PPACA, IPERA, MMSEA, etc.
- Enforcement Against Off-Label Promotion
  - Federal civil and criminal investigations
  - Allegations focus in part on alleged kickbacks to prescribers:
    - "Sham" clinical trials
    - Excessive payments for services
    - Lew Morris (DHHS OIG) emphasized repeatedly at a recent conference that there are two sides to every "kickback," seeming to imply planned enforcement efforts against individual recipients
- Executive Accountability
  - "Park Doctrine" prosecutions
  - OIG exclusions

Recent Developments/On the Horizon

- Clinical Research Billing
  - Recovery contractors in some regions have begun to demand substantial documentation
  - Enforcement includes at least two instances of significant penalties for self-disclosed lapses



- Medicare Secondary Payer/MMSEA
  - CMS interprets MSP to prohibit billing and reimbursement of services when a sponsor gratuitously agrees to pay
  - New rules require "liability insurers" – including sponsors – to report on payments proactively … intended to prevent "pay and chase" problems



- Grants
  - Multiple recent fraud and false claims cases
  - Fraud and abuse laws provide a secondary mechanism to punish/deter misconduct and other noncompliance
    - Application fabrication/falsification to secure awards
    - Progress report data fabrication/falsification to secure continuing funds
    - Inappropriate cost transfers, effort reporting deficiencies, etc.

OIG Workplan (2011)

- College and university compliance with A-21 cost principles
- FDA's process for reviewing investigational new drug ("IND") applications
- Use of data and safety monitoring boards ("DSMBs") in clinical trials and institutional compliance with NIH guidelines on data safety monitoring (see, e.g., here and here; see also here)
- Medicare payments for beneficiaries with other insurance, with particular emphasis on handling of credit balances when providers receive payments from Medicare and other insurers in excess of their charges
- Off-label promotion and off-label prescription of various drugs, including a review of Medicare payment for drugs and biologicals prescribed off-label for treatment of cancer that will determine whether approved therapies were attempted first in patients eventually prescribed medications off label, whether those patients' conditions improved, and how much money Medicare might have saved if only approved therapies were utilized
- NCRR oversight of CTSAs (with particular attention to awardee goals and milestones); and NIAID oversight of Project BioShield grants
- Subrecipient monitoring in the Public Health Emergency Preparedness program
- Etc.

Challenges and Opportunities

- Challenges
  - Rules are complex
  - Many are non-obvious, counter-intuitive, or even inconsistent
  - Financial pressures encourage pursuit of novel arrangements that may not yet have been fully vetted
  - No real end in sight
- Opportunities
  - Financial pressures encourage creative thinking about new approaches to encourage and facilitate external support of our academic mission
  - Careful planning can help avoid or substantially reduce risks inherent in these relationships
  - Increased oversight requires more rigorous budgeting and expenditure practices, and thus (it is hoped) more complete funding
  - Systems automation and other steps taken to increase administrative efficiencies can be leveraged to facilitate compliance

Resources

- Internal
  - ECAS Website: http://www.universityofcalifornia.edu/compaudit/welcome.html
  - ECAS Compliance Briefing for Researchers: http://www.universityofcalifornia.edu/compaudit/documents/compliance_briefiing_researchers.ppt
- External
  - DHHS OIG: http://oig.hhs.gov/
  - OIG Guidance on Permissive Exclusions: http://oig.hhs.gov/fraud/exclusions/files/permissive_excl_under_1128b15_10192010.pdf
  - FDA Guidance on Park Doctrine Prosecutions: http://www.fda.gov/ICECI/ComplianceManuals/RegulatoryProceduresManual/ucm176738.htm#SUB6-5-3
  - NIH Manual: http://oma.od.nih.gov/manualchapters/management/1754
  - (Withdrawn) OIG Draft Guidance for PHS Grantees: http://oig.hhs.gov/fraud/docs/complianceguidance/PHS%20Research%20Awards%20Draft%20CPG.pdf
  - StopMedicareFraud.gov: http://www.stopmedicarefraud.gov/

Insider Trading

Basics

- Federal and state securities laws are aimed at achieving a fair and honest securities market by preventing those in possession of material inside information from using that information to their own advantage
  - "Insider trading" is among the prohibited activities
- Enforcement
  - Civil (up to treble profits realized/losses avoided)
  - Criminal (up to 20 years/$5 million)
  - Other laws also potentially implicated (e.g., mail, wire fraud)

Basics (cont'd)

- Traditional theory of liability
  - Violation occurs where a corporate insider (someone who owes a fiduciary relationship to the corporation) trades in the securities of the corporation on the basis of material, non-public information
  - Enforcers must establish that the insider or "tipper" breached his or her fiduciary duty to the shareholders of the corporation by disclosing the information to a "tippee," and that the tipper directly or indirectly benefited from the disclosure
  - Whether or not the tipper trades, the tipper has the same liability as an insider who trades

Basics (cont'd)

- Misappropriation theory
  - Violation occurs where a person misuses information that properly belongs to another person
  - A fiduciary relationship between the trader or tipper and the corporation is not required
  - Liability attaches from the trader's use of someone else's information or the tipper's duty to not disclose the information of another
  - No showing of a personal benefit to the tipper is required

Recent Developments/On the Horizon

Recent Developments/On the Horizon

- Example: Yves Benhamou (2010)
  - Member of steering committee for Albuferon (Human Genome Sciences, Inc.) trial
    - Had a legal obligation to maintain confidentiality of data received
  - Accused of tipping a hedge fund manager of negative results
    - Six funds divested 6 million shares between 12/2007 and 1/2008
  - Parallel SEC (civil) and DOJ (criminal) investigations
  - Government need not prove that Benhamou directly profited
- Other Activities
  - SEC is in the midst of a sweeping investigation of potential insider trading via "expert networks"
  - Many physicians provide consulting services for individual hedge funds and for these networks
  - Dodd-Frank law contains new whistleblower provisions

Information Privacy and Security

Basics

- Sources of Rules and Enforcement
  - **H**ealth **I**nsurance **P**ortability and **A**ccountability **A**ct of 1996, **G**enetic **I**nformation **N**ondiscrimination **A**ct, **F**amily **E**ducational **R**ights and **P**rivacy **A**ct (and other federal laws and regulations)
  - NIH Grants Policy Statement
  - **C**onfidentiality of **M**edical **I**nformation **A**ct, **I**nformation **P**ractices **A**ct (and other state laws and regulations)
  - Common Rule/FDA Regulations/AAHRPP Standards
  - Joint Commission
  - Sponsors/CROs (via research and clinical trial agreements)
  - Private Citizens

Basics (cont'd)

- Individuals have a privacy interest in their identifiable health (and research) information
- Interest is recognized to varying degrees in federal and state laws and regulations and in the "common law" (court decisions)
- "Fair Information Practices" principles developed in the 1970s are incorporated into many modern laws and regulations, including IPA and HIPAA

Fair Information Practices

are commonly accepted responsibilities governing collection, access to, and control over personal information. They include:

- **Collection Limitation**: requires lawful, fair, and legitimate data collection.
- **Data Quality**: requires accuracy, completeness, and timeliness of data.
- **Purpose Specification**: requires entities to articulate why data is being requested and prohibits its use for other purposes.
- **Use Limitation**: requires consent for use of information inconsistent with the purpose of which it was collected.
- **Security Safeguards**: requires procedures to stop unauthorized access, use, modification, or disclosure of data.
- **Openness**: requires transparency of personal data practices, including notice of databases and the identity and location of the data controller.
- **Individual Participation**: requires access to, correction of, and sometimes destruction of personal information.
- **Accountability**: requires legal rights to ensure compliance.

From http://www.epic.org (2/20/2011)

Recent Developments/On the Horizon

Recent Developments/On the Horizon

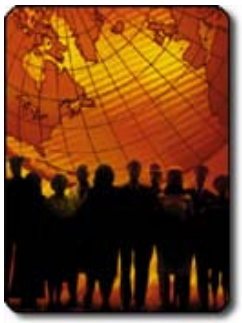
- HITECH Act
  - Statute
    - Imposes federal breach notification mandate
    - Prohibits sale of PHI, with limited exception for research and public health activities … subject to additional rulemaking
    - Substantially enhances penalties for non-compliance with privacy and security rules; provides for state attorney general enforcement
  - NPRM implementing HITECH offers some promise for improvement
    - Compound authorization for correlative specimen banks
    - Comment requested on "unspecified future use"
  - Other new regulations in development will require tracking of TPO disclosures, address minimum necessary standard, and more
- Oversight
  - Security Rule enforcement transferred from CMS to OCR
  - Continued breaches are driving more investigations and enforcement activities

Recent Developments/On the Horizon

- OCR Investigations (HIPAA Compliance/Research)
  - Example 1
    - Recruitment disclosures without authorization or IRB/Privacy Board waiver
    - OCR mandated
      - Revision of written policies and procedures regarding disclosures of PHI for research recruitment purposes to require valid written authorizations
      - Retraining of all staff on the new policies and procedures
      - Log the disclosure of the patient's PHI for accounting purposes
      - Send the patient a letter apologizing for the impermissible disclosure.
  - Example 2
    - Private practice physician/PI disclosed list of patients to CRO for recruitment purposes
    - Thought "review preparatory to research" exception applied
    - OCR concluded that: "[c]ontacting individuals to participate in a research study is a use or disclosure of protected health information (PHI) for recruitment, as it is part of the research and is not an activity preparatory to research."

Recent Developments/On the Horizon

- Research Participant Complaints to OHRP (Common Rule Compliance)
  - Rhode Island Hospital
    - When medical records are accessed for research purposes by members of the research team, the activity is human subjects research requiring informed consent (or waiver) … not so if HIM strips identifiers before turning over to researchers
  - [Not Yet Released]
    - Protocol/consent promised that only coded data would be sent to labs with specimens but identifiable specimens were sent … all without amendment/approval by IRB
- Academic/ELSI
  - Continuing debate on the extent of rights of individuals to opt in or opt out of research
  - Increased scrutiny of adequacy of "deidentification" processes currently permitted under HIPAA
  - SACHRP Activities



Recent Developments/On the Horizon

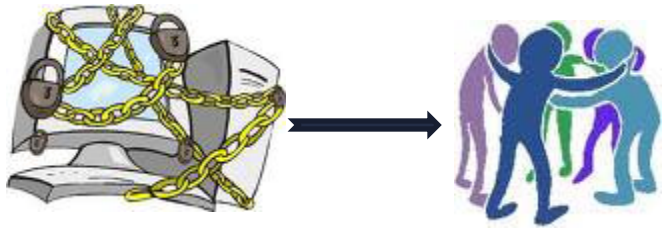
- University Professor Sanctioned (UNC)
  - Significant database breach occurred
  - Administrators found database was not securely maintained and that PI was accountable; recommended termination
  - PI demoted and is fighting the sanction; cites to inadequate training, reliance on technical staff

- VHA Handbook 1200.5 Revisions
  - New privacy and security mandates/protections, including expanded PO/ISO responsibilities
  - Special requirements for voice/video/photo consent
  - Investigator obligations include:
    - Assuring consistency among consent, authorization, protocol
    - No initial phone contact (always in person or by mail)
    - **Maintain master list of subjects after informed consent is obtained**
    - **Include in protocol: privacy/confidentiality section, information security plan, reuse of data**
    - **Consent must address, as applicable, future use of specimens/data, recontact, results disclosure; stand-alone authorization is mandatory**
  - International research complies with laws of both countries (includes sending data/specimens abroad)

VA PRIDE Program for Research Integrity Development & Education

Challenges and Opportunities

- Challenges
  - Administrative burden
  - Confusion re: implementation of research carve-out
  - Increased need for intra- and inter-institutional collaboration (and associated data transfer) in response to funding agency demands and scientific advances; policy incoherence (protection vs. sharing)
- Opportunities
  - Identification and implementation of sound practices for information security can efficiently facilitate compliance with current and future rules and better protect research participants
  - Steady commitment to strong privacy/security practices can not only reduce regulatory risk but also increase trust and, hopefully, participation in research
  - Broad data sharing can help drive discovery and advances in medical care while reducing the incidence of duplicative work



Resources

- Health Insurance Portability and Accountability Act of 1996: http://www.hhs.gov/ocr/privacy/hipaa/administrative/statute/index.html
- Health Information Technology for Economic and Clinical Health Act of 2009 (part of American Recovery and Reinvestment Act): http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111_cong_bills&docid=f:h1enr.pdf
- OCR Website: http://www.hhs.gov/ocr/privacy
- Regulations: 45 C.F.R. parts 160, 164 (subject to amendment)
  - Privacy Rule: http://www.hhs.gov/ocr/privacy/hipaa/administrative/privacyrule/index.html
  - Security Rule: http://www.hhs.gov/ocr/privacy/hipaa/administrative/securityrule/index.html
  - Breach Notification Rule: http://www.hhs.gov/ocr/privacy/hipaa/administrative/breachnotificationrule/index.html
  - Enforcement Rule: http://www.hhs.gov/ocr/privacy/hipaa/administrative/enforcementrule/index.html
- NIH Guidance: http://privacyruleandresearch.nih.gov
- NCI caBIG® Data Sharing & Intellectual Capital Knowledge Center: https://cabig-kc.nci.nih.gov/DSIC/KC
- List of Higher Ed Breaches: http://www.adamdodge.com/esi/

Clinical Laboratory Improvements Act

Basics

- Federal
  - **C**linical **L**aboratory **I**mprovements **A**mendments of 1988 (Pub. L. 100-578)
    - Triggered by revelations of poor quality control in Pap smear testing, with deadly results
      - Inadequately educated personnel read tests
      - Significant workload problems
      - Proliferation of unregulated laboratories
    - Purpose: assure the accuracy, reliability, and timeliness of patient test results
  - Regulations promulgated in 1992
- California
  - Cal Bus. & Prof. Code
  - Rules generally consistent with CLIA

Basics (cont'd)

- A clinical laboratory test must be ordered by a physician (or other specified licensed health professional)
  - 42 CFR § 493.1241 (an individual authorized under State law to order tests and receive results)
  - Cal. Bus. & Prof. Code § 1288
- A clinical laboratory test may be performed only at a certified facility (or a facility that has secured a certificate of waiver)
  - 42 USC § 263a(b)
  - Cal. Bus. & Prof. Code §§ 1241, 1281, 1288.5
- Results of a clinical laboratory test may be reported only to a physician (or other specified health professional) – generally only to the person who ordered the test
  - 42 CFR § 493.1291(f)
  - Cal. Bus. & Prof. Code § 1288

Recent Developments/On the Horizon

Recent Developments/On the Horizon

- Academic Exemption
  - "This chapter shall not apply to … clinical laboratories, or to persons performing clinical laboratory tests or examinations … [if they perform the tests] for research and teaching purposes only and do not report or use subject-specific results for the diagnosis, prevention, or treatment of any disease or impairment of, or for the assessment of the health of, an individual."

CLIA Does Not Apply	CLIA May Apply
A laboratory is conducting research to evaluate a new diagnostic test. Specimens are collected and tested in the laboratory. Only summary results are provided by the laboratory to the principal investigator.	A laboratory is conducting research to evaluate a new diagnostic test. Specimens are collected and tested in the laboratory. The laboratory reports results to the study coordinator, who uses the results to assign participants to a treatment arm of the study.
Community-based longitudinal research project collects data and specimens from individual participants. Individual results are not reported but community leaders (through a study advisory board) and all study participants are informed of group results and of publications resulting from the project.	Community-based longitudinal research project collects data and specimens from individual participants. Community advisory board requests that individual results be returned to participants upon request and the protocol and consent form are revised accordingly and approved by the IRB. Those who request results receive the information from genetic counselors.
Participant biopsy specimens are collected upon enrollment and after receiving study drug. The samples are assayed for biomarkers relevant to treatment or drug development. However, they are not used to determine what intervention (e.g., drug administered or dosage) the participant will receive. Results are not shared with the participant or study doctors, but are compiled and reported in the study results of a scientific publication.	A drug's toxicity or efficacy is found to be associated with a certain biomarker. Study participants are tested for presence of the biomarker and that information is used to assign participants to various arms of the study (e.g., treatment or no treatment or different dosages). The information is not shared with study doctors, study participants, or the participants' regular treating providers.
Study compares standard-of-care and new tests. Only SOC test will be used to make clinical decisions. Results are returned to the principal investigator for analysis only.	FDA-approved qualitative test is available on the market. Study will evaluate a new quantitative test that if accurate may help inform treatment decisions. Physician-researchers will receive individual results during the study but are informed the results may not be meaningful and retain full discretion to prescribe treatment during study consistent with the results of the qualitative test and their own medical judgment (protocol does not direct treatment options based on test results).

Challenges

- Federal and state regulators of clinical laboratories interpret current law to extend to academic laboratories in some cases.
- Some research activities previously presumed to be exempt from CLIA may in fact be subject to the law, including:
  - Virtually any study that involves the return of laboratory results to participants
  - Use of results to determine assignment of research interventions
- When CLIA applies, genetic analyses and other laboratory tests – even if performed solely for research purposes – must be:
  - Ordered by a physician (or other licensed health professional)
  - Performed in a licensed laboratory (unless the testing is "waived," in which case it may be performed in a facility that has procured a Certificate of Waiver
- Non-compliance may result in the issuance of "cease and desist" orders or, in some cases, in civil or criminal penalties.

Resources

- Federal
  - Centers for Medicare and Medicaid Services ("CMS"): http://www.cms.gov/CLIA/
  - Food and Drug Administration: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124105.htm
- California
  - California Department of Public Health
  - See http://www.cdph.ca.gov/programs/lfs/Pages/default.aspx and http://www.cdph.ca.gov/programs/lfs/Pages/ClinicalLaboratoryfacilities.aspx
- Other States
  - Some states regulate testing performed on their residents regardless of location of specimen collection, processing, or analysis
  - Example: New York Public Health Law, Sections 572 and 574: http://www.wadsworth.org/labcert/regaffairs/clinical/title5.pdf
- Accreditation
  - Multiple Organizations: http://www.cms.gov/CLIA/13_Accreditation_Organizations_and_Exempt_States.asp#TopOfPage
  - The Joint Commission: http://www.jointcommission.org

Open Q&A

- **How Can We Help?**
  - Keep you updated on new legal/regulatory developments
  - Provide advice on planned activities
  - Assist in review or investigation of potential problems
  - Defend UC conduct in government investigations

- **How Can You Find Us?**
  - http://www.ucop.edu/ogc/practgrps.html#health

Questions

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