

# Research Compliance: A Year in Review 2008/2009

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## Agenda

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- **A Quick Look Back**
  - Last Years Research Compliance Institute
  - 2009 OIG Work Plan
- **A Year-in-Review and Special Topics**
- **Building an Effective Compliance Program**
- **Closing Remarks / Q&A**
- **Appendix / Supplemental Materials**

## Why is a Year-in-Review Important?

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- Administration change
- New Legislation
- American Recovery and Reinvestment Act (ARRA) - A Major Influx of Federal Dollars Toward Research
- Increasing Funding for Federal Oversight and Investigations
- Landmark Settlements

## Research Compliance in 2008

*Major topics from the 2008 HCCA Research Compliance Conference*

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### What Were We Talking About Last Year?

- Clinical Trials Billing Compliance
- Research / Scientific Misconduct
- Compliance Program Management
- Quality Improvement in Research
- Human Subjects Protection / Oversight
- CTMS / IT-aided Research Compliance Infrastructure
- Conflict of Interest / Anti-Kickback

## DHHS OIG FY 2009 Work Plan Initiatives

### *Research Specific*

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- **Financial Conflicts of Interest in Research Funded by the National Institutes of Health**
  - Review NIH's oversight of grantees' compliance with financial **conflicts-of-interest** requirements.
    - Federal regulations at 42 CFR pt. 50, subpart F
  - Review NIH's processes for reviewing the nature and management of financial conflicts of interest reported by grantee institutions during FY 2006.
- **Colleges' and Universities' Compliance With Cost Principles**
  - Review colleges' and universities' compliance with *selected* cost principles governed by OMB Circular A-21, Cost Principles for Educational Institutions.
  - Conduct reviews at selected schools based on the dollar value of Federal grants received and on input from:
    - HHS' operating divisions,
    - Office of the Assistant Secretary for Budget, Technology, and Finance, and
    - Office of the Assistant Secretary for Administration and Management.

<http://oig.hhs.gov/publications/docs/workplan/2009/WorkPlanFY2009.pdf>

## DHHS OIG FY 2009 Work Plan Initiatives

### *Research Specific*

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- **National Institute of Environmental Health Science's Grant Process**
  - Review issues related to grants made by NIEHS to determine compliance with the HHS "Grants Administration Manual" and whether FY 2005 to 2007 expenses incurred by its Director's office were in accordance with NIH policies.
  - This review is being conducted in response to a congressional request.
- **Use of Data and Safety Monitoring Boards in Clinical Trials**
  - Review the extent to which Data and Safety Monitoring Boards (DSMB) monitor data in clinical trials.
  - Determine how and to what extent NIH is ensuring that grantees comply with the NIH policy for DSMBs in multi-site clinical trials.

<http://oig.hhs.gov/publications/docs/workplan/2009/WorkPlanFY2009.pdf>

## DHHS OIG FY 2009 Work Plan Initiatives

### *Research Specific*

#### ➤ **Clinical and Translational Science Awards**

- Review the National Center for Research Resources' (NCRR) process for overseeing Clinical and Translational Science Award (CTSA) grantees.
  - NCRR oversees this program and its milestones for compliance with CTSA program objectives and HHS grant administration requirements at 45 CFR pt. 74.
- Examine the types of innovative information sharing techniques developed through the CTSA program.

#### ➤ **Select Agent Regulations**

- Continue previous work at university, State, and private laboratories to strengthen control of select agents (biological agents or toxins with potential to pose a severe threat to public health or safety).

#### **Review of implementation of:**

- Centers for Disease Control and Prevention (CDC) regulations
- Food and Drug Administration (FDA) regulations

<http://oig.hhs.gov/publications/docs/workplan/2009/WorkPlanFY2009.pdf>

## DHHS OIG FY 2009 Work Plan Initiatives

### *Research Specific*

#### ➤ **FDA's Oversight of Post-marketing Surveillance Studies of Medical Devices**

- "FDA may require sponsors of medical devices to complete post-marketing surveillance for any moderate to high-risk medical device (Class II or III) that has a reasonable likelihood of serious adverse health outcomes."

#### ➤ **A 2006 OIG study found that the FDA "could not readily identify whether or how timely such post-marketing study commitments were progressing toward completion, in part because some information submitted by drug applicants was missing and incomplete."**

- OIG will examine the level of compliance among sponsors and "identify trends and challenges associated with post-marketing surveillance studies."

<http://oig.hhs.gov/publications/docs/workplan/2009/WorkPlanFY2009.pdf>  
<http://oig.hhs.gov/oei/reports/oei-01-04-00390.pdf>

## DHHS OIG FY 2009 Work Plan Initiatives

### *Research Specific*

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#### ➤ Foreign Clinical Trials

- OIG will “review the extent to which drug manufacturers use foreign clinical trials to support new drug applications (NDA) submitted to FDA” and specifically, “trends associated with use of foreign clinical trial data in the past 5 years and the number of NDAs supported solely by foreign trial data.”
  - FDA must not disqualify data gathered in accordance with world ethical principles.
  - 2007 OIG Report indicated 20-30% of data submitted in NDAs come from foreign trials, and “the FDA is often unaware that foreign trials have been conducted until after the results are submitted in NDAs.”

<http://oig.hhs.gov/publications/docs/workplan/2009/WorkPlanFY2009.pdf>

## Advisory Opinions, Updates and Rulings

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#### ➤ DHHS OIG Advisory Opinions

- <http://oig.hhs.gov/fraud/advisoryopinions/opinions.asp>

#### ➤ CMS Legislative Updates

- “The purpose of the Legislative Update is to provide the public and other interested parties with up-to-date information on CMS’ efforts to implement new legislation.
- It will contain information on published regulations, policy instructions, key implementation dates, and other accomplishments that relate to new legislation.”
- <http://www.cms.hhs.gov/LegislativeUpdate/>

#### ➤ CMS Rulings

- “CMS Rulings are decisions of the Administrator that serve as precedent final opinions and orders and statements of policy and interpretation.
- They provide clarification and interpretation of complex or ambiguous provisions of the law or regulations relating to Medicare, Medicaid, Utilization and Quality Control Peer Review, private health insurance, and related matters.

# A Year-in-Review & Special Topics

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## Issues and Events That Were Center Stage

Oct 2008  Sept 2009

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- The Obama Administration
- Human Subjects Research Protections
- Data Safety Monitoring Boards
- HIPAA
- Research Integrity and Researcher Misconduct
- Conflicts of Interest and Financial Disclosure
- Off-Label Marketing & Promotion
- Grants & Contracts Management
- Export Controls
- Animal Research
- Building an Effective Compliance Program

# The Obama Administration

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## Campaign Promises

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### ➤ Obama campaign promises to promote science and technology

- “We are committed to putting responsible science and technological innovation ahead of ideology when it comes to medical research.”<sup>1</sup>
- *In 2007, Mr. Obama voted in favor of the Stem Cell Research Enhancement Act.*
- Obama’s platform included:
  - Investing in biomedical research, as well as medical education and training in health-related fields
  - Providing more than \$1 billion in federal funding for autism research
  - Creating an independent institute to guide reviews and research on comparative effectiveness of treatments

### ➤ Comparative effectiveness reviews and research<sup>2</sup>

- “One of the keys to eliminating waste and missed opportunities is to increase our investment in comparative effectiveness reviews and research.”
- “Barack Obama and Joe Biden will establish an independent institute to guide reviews and research on comparative effectiveness...”

1. <http://www.barackobama.com/issues/healthcare/index.php>

2. <http://www.barackobama.com/pdf/issues/HealthCareFullPlan.pdf>

## Stem Cell Research

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- **March 9<sup>th</sup> 2009 – Obama signs executive order to reverse Bush policy on stem cell research: (EO) 13505—*Removing Barriers to Responsible Scientific Research Involving Human Stem Cells***
- **Subsequent Bills**
  - 111<sup>th</sup> Congress, House Bills
    - H.R. 110—Human Cloning Prohibition Act of 2009
    - H.R. 872—Stem Cell Research Improvement Act of 2009
    - H.R. 873—Stem Cell Research Enhancement Act of 2009
    - H.R. 877—Patients First Act of 2009
    - H.R. 1050—Human Cloning Prohibition Act of 2009
    - HR. 1654—Cures Can Be Found Act of 2009
    - HR. 2107—Cord Blood Education and Awareness Act of 2009
  - 111<sup>th</sup> Congress, Senate Bills
    - S. 99—Ethical Stem Cell Research Tax Credit Act of 2009
    - S. 487—Stem Cell Research Enhancement Act of 2009

<http://edocket.access.gpo.gov/2009/pdf/E9-5441.pdf>

## Stem Cell Research

### *Expectations for Research Institutions*

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- **The Guardian newspaper article titled “Obama overturns Bush policy on stem cell research,” published on March 9<sup>th</sup>, 2009, suggested:<sup>1</sup>**
  - “For Harvard University scientists, Obama’s repeal today of Bush’s restrictions on federal funding will have dramatic practical effects.”
    - ““This will mean the end of the quite onerous bookkeeping and segregation of supplies, equipment and people that were necessary under the Bush executive order,” said BD Colen, spokesman for the institute in Cambridge, Massachusetts.”
    - “Harvard stem cell institute co-director Doug Melton will apply for federal grants to research ways to turn stem cells into heart cells, pancreatic cells to treat diabetes, and neurons that could someday yield a cure for Parkinson’s and Alzheimer’s diseases.”
- **Glaxo Gives Harvard \$25 Million for Stem Cell Study<sup>2</sup>**
  - July 24 (Bloomberg) -- GlaxoSmithKline Plc, Europe’s largest drugmaker, will give the Harvard Stem Cell Institute at least \$25 million over five years to speed development of treatments using the technology.

1. <http://www.guardian.co.uk/world/2009/mar/09/obama-administration-stem-cell-funding>

2. <http://www.bloomberg.com/apps/news?pid=newsarchive&sid=aF15sOcXjDxo>

## Stem Cell Research

### *NIH Guidelines for Research Using Human Stem Cells*

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#### ➤ Principles:

- Responsible research with hESCs has the potential to improve our understanding of human health and illness and discover new ways to prevent and/or treat illness.
- Individuals donating embryos for research purposes should do so freely, with voluntary and informed consent.

#### ➤ Protection of Human Subjects:

- “*When research* involving human adult stem cells or induced pluripotent stem cells constitutes human subject research, Institutional Review Board review may be required and informed consent may need to be obtained per the requirements detailed in 45 C.F.R. 46, Subpart A. Applicants should consult <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>.”
- “...the HHS regulation, *Protection of Human Subjects*, 45 C.F.R. Part 46, Subpart A, may apply to certain research using hESCs. This regulation applies, among other things, to research involving individually identifiable private information about a living individual, 45 C.F.R. § 46.102(f).”

<http://stemcells.nih.gov/policy/2009guidelines.htm>

## Stem Cell Research

### *NIH Guidelines for Research Using Human Stem Cells*

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#### ➤ Use of NIH Funds

- “Prior to the use of NIH funds, funding recipients should provide assurances, when endorsing applications and progress reports submitted to NIH for projects using hESCs, that the hESCs are listed on the NIH registry.”

#### ➤ Research Using hESCs and/or Human Induced Pluripotent Stem Cells Ineligible for NIH Funding

- “Research in which hESCs (even if derived from embryos donated in accordance with these Guidelines) or human induced pluripotent stem cells are introduced into non-human primate blastocysts.”
- “Research involving the breeding of animals where the introduction of hESCs (even if derived from embryos donated in accordance with these Guidelines) or human induced pluripotent stem cells may contribute to the germ line.”

<http://stemcells.nih.gov/policy/2009guidelines.htm>

## American Recovery and Reinvestment Act

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- **February 13, 2009, the House of Representatives and Senate passed the American Recovery and Reinvestment Act of 2009.**
- **Some of the goals of the ARRA are to:**
  - Save and create more than 3.5 million jobs over the next two years;
  - Take a big step toward computerizing Americans' health records, reducing medical errors, and saving billions in health care costs;
  - Establish unprecedented levels of transparency, oversight, and accountability.

<http://www.recovery.gov/?q=content/act>

## American Recovery and Reinvestment Act

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- **Federal Coordinating Council for Comparative Effectiveness Research<sup>1</sup>**
  - ARRA created the Federal Coordinating Council for Comparative Effectiveness Research to coordinate comparative effectiveness research across the Federal government. \$1.1 billion has been appropriated for comparative effectiveness research.
- **National Institutes of Health<sup>2</sup>**
  - ARRA provides \$10.4 billion, available for two years through September 2010. Expectations to spend as much as possible in FY 2009.
    - Unprecedented \$8.2 billion in extramural funding (4,985 Grants as of 8/3/2009)
- **National Institute of Standards and Technology<sup>3</sup>**
  - ARRA provides \$610 million in funding to NIST
    - Covers lab research, measurements, competitive grants, research fellowships, and advanced measurement equipment, supplies and the expansion and development of EMR technology.

1. <http://www.hhs.gov/recovery/programs/os/cebios.html>  
 2. [http://www.nih.gov/about/director/02252009statement\\_arra.htm](http://www.nih.gov/about/director/02252009statement_arra.htm)  
 3. <http://www.nist.gov/recovery/>

## American Recovery and Reinvestment Act

### *Expectations for Research Institutions*

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- **NIH will invest in projects that will stimulate the economy, create or retain jobs, and have the potential for making scientific progress in 2 years.**
- **Research institutions can expect that NIH will:**
  - “Expand the pay line” and select recently peer-reviewed and approved, highly-meritorious research grant applications (\$5.7 Billion)
    - R01s and others that were not funded in FY 2008, as well as grant applications that would not otherwise likely be funded in FY 2009 or FY 2010.
  - Fund new research applications
  - Provide targeted supplements to current grants (approximately \$1 billion)
    - Competitive Revisions (NOT-OD-09-058) and Administrative Supplements (NOT-OD-09-056)
  - Support new types of activities such as the NIH Recovery Act Challenge Grant program to focus on health and science problems, including cancer and autism, where significant progress can be made in a two year time frame.
    - Challenge Grants (NOT-OD-09-058) (at least \$200 million / 200 grants)

[http://www.recovery.gov/?q=content/program-plan&program\\_id=7609](http://www.recovery.gov/?q=content/program-plan&program_id=7609)  
<http://grants.nih.gov/recovery/>

## American Recovery and Reinvestment Act

### *Expectations for Research Institutions*

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- **Research institutions can also expect that NIH will:**
  - Use other funding mechanisms as appropriate, including:
    - Grand Opportunity Program, or “GO grants” (RFA-OD-09-004) (at least \$200 million) to support high impact ideas requiring significant funding
    - New Faculty (RFA-OD-09-005) (approximately \$100 million) to support the recruitment of new faculty to conduct research at institutions across the country.
    - Summer Research Experiences for Students and Science Educators (NOT-OD-09-060) (approximately \$20 million) to provide summer jobs for high school/college students and teachers to work in science labs.
    - NIH Signature Initiatives to support exceptionally creative and innovative projects and programs, including: “nanotechnology, genome-wide association studies, health disparities, arthritis, diabetes, autism, the genetic risk for Alzheimer’s disease, regenerative medicine, oral fluids as biomarkers, and HIV vaccine research.”

[http://www.recovery.gov/?q=content/program-plan&program\\_id=7609](http://www.recovery.gov/?q=content/program-plan&program_id=7609)  
<http://grants.nih.gov/recovery/>

## American Recovery and Reinvestment Act

### *Guidelines for Research Institutions*

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- **Consistent with statutory and OMB guidance, NIH will be open and transparent in its spending of ARRA funding. Measures include:**
- Making public (on Recovery.gov) quarterly recipient reporting, as required by Section 1512 of the Recovery Act and OMB guidance.
  - Informing recipients of their reporting obligations, using standard terms and conditions, grant announcements, contract solicitations, and other program guidance.
  - Ensuring that appropriate processes by which an organization's resources are directed, monitored, and measured are in place throughout the entire funding cycle.
  - Providing more technical assistance to recipients.
  - Fully utilizing Project Officers to ensure compliance with reporting requirements.
  - Ensuring recipient cost and performance reporting requirements by issuing Recovery Act awards with special accounting numbers and codes to better track the funds and awards. **Reporting to begin October 1, 2009.**

**All Recovery Act funds must be awarded separately from the normal appropriation funds and all awards must comply with both existing NIH reporting requirements and the Recovery Act reporting requirements.**

[http://www.recovery.gov/?q=content/program-plan&program\\_id=7609](http://www.recovery.gov/?q=content/program-plan&program_id=7609)

## America's Affordable Health Choices Act

### *Proposed House Bill*

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- **Proposed changes to the Medicare program:**
- Comparative Effectiveness Research***
- Establish a Center for Comparative Effectiveness Research (Center) within the Agency for Healthcare Research and Quality (AHRQ) to conduct, support and synthesize research related to comparative effectiveness.
  - Establish a public/private stakeholder commission to oversee the Center, determine national priorities for research, identify research methods and standards of evidence, support forums to increase stakeholder feedback, appoint advisory panels on specific national priorities to advise on questions and methods, and make recommendations for the dissemination of findings.

[http://medicareupdate.typepad.com/medicare\\_update/2009/07/househealthcarereformlegislation.html](http://medicareupdate.typepad.com/medicare_update/2009/07/househealthcarereformlegislation.html)

## America's Affordable Health Choices Act

### *Proposed House Bill*

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#### ➤ **Proposed changes to the Medicare program:**

##### ***Enhanced Penalties and False Claims***

- Establish CMPs of \$50,000 per violation for the knowing submission of false statements or misrepresentation of material fact in information submitted to support a claim for payment.
- Terminology change of 'item or service' to mean "without limitation, any medical, social, management, administrative, or other item or service used in connection with or directly or indirectly related to a Federal health care program."

## America's Affordable Health Choices Act

### *Proposed House Bill*

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#### ➤ **Fraud, Waste and Abuse**

- "Sunshine" Provision: H.R. 3200 would require manufacturers or distributors of certain drugs, devices, biologicals or medical supplies to electronically report to HHS's Office of Inspector General (OIG) any payments or other transfers of value above a \$5 de minimis made to a "covered recipient" and require hospitals or entities that bill Medicare to report any ownership share by a physician.
- Failure to report would be subject to CMPs ranging from \$1,000 to \$10,000 per payment (with a \$150,000 maximum per year), transfer of value, or investment interest not disclosed.
- Penalties for a knowing failure to report would range from \$10,000 to \$100,000 per payment (not to exceed \$1,000,000 in 1 year or .1% of revenues for that year).
- Increased Funding: H.R. 3200 would provide an additional \$100 million in annual funding for the Health Care Fraud and Abuse Control Fund and provides for expanded use of the funds by the Centers for Medicare & Medicaid Services Medicare Integrity Program.

## America's Affordable Health Choices Act

### *Proposed House Bill*

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#### ➤ **Compliance Programs**

- H.R. 3200 would require all providers and suppliers (other than physicians) to adopt compliance programs and would authorize the Secretary to dis-enroll a supplier or impose CMPs or other intermediate sanctions for the failure to establish such a program.

[http://medicareupdate.typepad.com/medicare\\_update/2009/07/househealthcarereformlegislation.html](http://medicareupdate.typepad.com/medicare_update/2009/07/househealthcarereformlegislation.html)

## America's Affordable Health Choices Act

### *Expectations and Challenges for Research Institutions*

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- **More regulatory requirements**
- **More funding for research**
- **More health care quality measures**
- **Increased penalties for fraud and abuse**
- **Sunshine! and transparency**
- **Establishment of Compliance Programs**



# Human Subjects Research Protections

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## Human Subjects Research Protections *Laws, Regulations, & Responsibilities*

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### 21 CFR 56 Institutional Review Boards (FDA)

- **January 15, 2009** – The FDA issued a final rule (21 CFR 56.106) to require IRBs to register through a system maintained by the Department of Health and Human Services (HHS).
  - Registration information includes:
    - Contact information (such as addresses and telephone numbers),
    - The number of active protocols involving FDA-regulated products reviewed during the preceding 12 months, and
    - A description of the types of FDA-regulated products involved in the protocols reviewed.
  - The IRB registration requirements will make it easier for FDA to inspect IRBs and to convey information to IRBs.
  - **This rule was effective July 14, 2009.**
  - All IRBs must comply with the initial registration requirement and, if necessary, make required revisions to their registrations by September 14, 2009.

## Human Subjects Research Protections

### *Recent Headlines*

➤ **March 26, 2009 – GAO: Undercover Tests Show the Institutional Review Board System Is Vulnerable to Unethical Manipulation<sup>1</sup>**

- “The IRB system is vulnerable to unethical manipulation, which elevates the risk that experimental products are approved for human subject tests without full and appropriate review.”
- “GAO investigators created fictitious companies, used counterfeit documents, and invented a fictitious medical device to investigate three key aspects of the IRB system.”

**Results:**

- GAO succeeded in getting approval from an actual IRB to test a fictitious medical device (with fake specifications that matched several examples of “significant risk” devices from FDA guidance) on human subjects.
- The IRB did not verify the false information that FDA had already cleared GAO’s device for marketing.
- June 30, 2009 – Coast IRB closed its doors and ceased operations following GAO sting and FDA warning.<sup>2</sup>

1. <http://www.gao.gov/new.items/d09448t.pdf>
2. [http://www.coastirb.com/coastirb\\_fda](http://www.coastirb.com/coastirb_fda)

## Human Subjects Research Protections

### *Recent Headlines*

➤ **Dr. Jeffrey Wang, a top spine surgeon at UCLA, failed to disclose payment from medical companies while he was researching their products**

- As of July 22, 2009, Dr. Wang lost his position as executive director of UCLA’s spine center and faces an investigation by the school into his research due to an alleged failure to disclose he was being paid by several companies whose products he was studying.
- This discovery was noted in a correspondence from Senator Chuck Grassely (May 21, 2009).
- The school issued the following statement about the financial relationships (consulting payments, stock options and royalties) with five companies on whose products he was conducting research spanning from 2002 to 2008: “UCLA regrets that in the case of Dr. Jeffrey Wang, associate professor of orthopedic surgery, a pattern of non-disclosure could have persisted without our knowledge. We are committed to examining our processes to determine how, as an institution, we will prevent similar problems in the future.”

## Human Subjects Research Protections

### *Recent Headlines*

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➤ **Fifth Circuit Says Clinical Investigators Can Be Criminally Liable For Violating FDA Record-Keeping Requirements**

- In *United States v. Palazzo*, a licensed medical doctor specializing in psychiatry was a Medicare provider authorized to submit bills for reimbursement for certain medical services provided to eligible Medicare beneficiaries.
- Plaintiff-Appellant, the United States ("the Government"), brought charges against Dr. Palazzo for health care fraud and failure to maintain records of the clinical drug studies.
- In its appellate review of FDA Regulations and 21 C.F.R. § 312.62(b), the Fifth Circuit clinical investigators to be subjected to criminal liability for the failure to adhere to recording keeping and reporting requirements.

[http://www.circare.org/lex/palazzo\\_0731119.pdf](http://www.circare.org/lex/palazzo_0731119.pdf)

## Human Subjects Research Protections

### *Recent Headlines*

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➤ **On August 16, 2009, the FDA published two rules that seek to clarify the methods available to seriously ill patients interested in gaining access to investigational drugs and biologics when ineligible to participate in clinical trials and without satisfactory treatment options.**

- "Expanded Access to Investigational Drugs for Treatment Use," makes investigational drugs more widely available to patients by clarifying procedures and standards.
- "Charging for Investigational Drugs Under an Investigational New Drug Application." The latter describes the specific circumstances and types of costs for which manufacturers can charge patients for investigational drugs when used as part of a clinical trial or outside the scope of a clinical trial.
- "The final rules balance access to promising new therapies against the need to protect patient safety and seek to ensure that expanded access does not discourage participation in clinical trials or otherwise interfere with the drug development process," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research.

<http://www.medicalnewstoday.com/articles/160783.php>

## Human Subjects Research Protections

### *Policy, Guidance and Resources*

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- **The OHRP website [<http://www.hhs.gov/ohrp>] provides several resources on human subject protections.**
  - <http://www.hhs.gov/ohrp/education/>
  - <http://www.hhs.gov/ohrp/policy/index.html>
- **NIH Office of Human Subjects Research (OHSR)**
  - <http://ohsr.od.nih.gov/index.html>
- **The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (April 18, 1979)**
  - <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>
- **The World Medical Association (WMA) Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects**
  - <http://www.wma.net/e/policy/b3.htm>

## Human Subjects Research Protections

### *Policy, Guidance and Resources*

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- **The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)**
  - <http://www.ich.org>
- **NIH Regulations, Policy and Guidance for Research Involving Human Subjects**
  - [http://grants.nih.gov/grants/policy/hs/hs\\_policies.htm](http://grants.nih.gov/grants/policy/hs/hs_policies.htm)
- **NIH Resource for Ethical Guidelines & Regulations**
  - [http://grants.nih.gov/grants/policy/hs/ethical\\_guidelines.htm](http://grants.nih.gov/grants/policy/hs/ethical_guidelines.htm)
- **NIH Required Education in the Protection of Human Research Participants**
  - June 5, 2000 (Revised August 25, 2000)
  - Beginning on October 1, 2000, the NIH requires education on the protection of human research participants for all investigators submitting NIH applications for grants or proposals for contracts or receiving new or non-competing awards for research involving human subjects.
  - <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>

# Data Safety Monitoring Boards

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## Data Safety Monitoring Boards (DSMB)

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➤ **HHS OIG FY 2009 Work Plan (Recap)**

- Use of Data and Safety Monitoring Boards in Clinical Trials
  - Review the extent to which Data and Safety Monitoring Boards (DSMB) monitor data in clinical trials.
  - Determine how and to what extent NIH is ensuring that grantees comply with the NIH policy for DSMBs in multi-site clinical trials.

- **A DSMB is a group of individuals with pertinent expertise that regularly reviews accumulated data from one or more ongoing clinical trials to ensure the safety of participants in the trials and the validity and integrity of the scientific data generated.**

## **DSMBs**

### ***Policy, Guidance and Resources***

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- **Federal Register (January 15, 2009; Volume 74, Number 10)**
  - The FDA guidance entitled “**Guidance for Clinical Investigators, Sponsors, and IRBs Adverse Event Reporting to IRBs- Improving Human Subject Protection**” is intended to provide assistance to the research community in interpreting requirements for submitting reports of unanticipated problems, including certain adverse events reports, to the IRB.
- **FDA Science and Research Guidance, Information Sheets, and Notices**
  - <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/default.htm>
- **FDA Guidance, Regulation and Resources for Running Clinical Trials**
  - <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm>
- **CFR TITLE 21--FOOD AND DRUGS**
  - <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/cfrsearch.cfm>

**HIPAA**

## Health Insurance Portability & Accountability Act *Laws, Regulations, & Responsibilities*

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- **The HIPAA Privacy Rule was the first comprehensive Federal protection for the privacy of personal health information (PHI).**
  - Research institutions and investigators *may or may not* be covered by the HIPAA Privacy Rule.
  - <http://privacyruleandresearch.nih.gov/> provides all the information you need to know on the HIPAA Privacy Rule and its relationship to research.
- **Prior to HIPAA, investigators were already required to take measures to protect PHI from inappropriate use or disclosure.**
  - As we discussed, these measures are included in the HHS and FDA Protection of Human Subjects regulations 45 CFR part 46 or 21 CFR parts 50 and 56, respectively.

[http://privacyruleandresearch.nih.gov/clin\\_research.asp](http://privacyruleandresearch.nih.gov/clin_research.asp)

## HIPAA *Laws, Regulations, & Responsibilities*

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- **Authorization for Research Purposes**
  - Pertains only to a specific research study, not to future, unspecified projects.
  - An Authorization is different than Informed Consent
    - An Authorization is an individual's permission for a covered entity to use or disclose PHI for a certain purpose, such as a research study.
    - Informed Consent is the individual's permission to participate in the study.
  - An Authorization can be combined with an Informed Consent Form (ICF)
    - Must include the core elements and required statements. See <http://privacyruleandresearch.nih.gov/authorization.asp#samplelang>

[http://privacyruleandresearch.nih.gov/clin\\_research.asp](http://privacyruleandresearch.nih.gov/clin_research.asp)

## HIPAA

### *Laws, Regulations, & Responsibilities*

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- **Covered entities may permit researchers to review PHI in medical records or elsewhere during reviews preparatory to research, as long as the covered entity receives representations from the researcher that:**
  - The use or disclosure is sought solely to review PHI as necessary to prepare the research protocol or other similar preparatory purposes.
  - No PHI will be removed from the covered entity during the review.
  - The PHI that the researcher seeks to access is necessary for the research purposes.

[http://privacyruleandresearch.nih.gov/clin\\_research.asp](http://privacyruleandresearch.nih.gov/clin_research.asp)

## HIPAA

### *Recent Headlines*

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#### **Institute of Medicine**

- **February 2009 – IOM: “Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health Research”**
  - IOM committee concludes that the HIPAA Privacy Rule does not protect privacy as well as it should, and that, as currently implemented, it impedes health research.
  - Recommended that federal policymakers develop a new privacy framework apart from HIPAA for health research that standardizes ethical oversight and emphasizes strong security protections.
  - Recommended extending the Common Rule to all interventional research regardless of funding source.

<http://www.iom.edu/Object.File/Master/61/836/HIPAA%20report%20brief%20FINAL.pdf>

## **HIPAA**

### ***Policy, Guidance and Resources***

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➤ **For more on the HIPAA Privacy Rule:**

- <http://www.hhs.gov/ocr/privacy/hipaa/administrative/privacyrule/index.html>
- 45 CFR Parts 160, 162, and 164

➤ **Additional information about the Privacy Rule's potential impact on other research activities:**

- Research Repositories and Databases
  - [http://privacyruleandresearch.nih.gov/research\\_repositories.asp](http://privacyruleandresearch.nih.gov/research_repositories.asp)
- Health services research
  - <http://privacyruleandresearch.nih.gov/healthservicesprivacy.asp>
- Institutional Review Boards (IRBs)
  - <http://privacyruleandresearch.nih.gov/irbandprivacyrule.asp>
- Privacy Boards
  - [http://privacyruleandresearch.nih.gov/privacy\\_boards\\_hipaa\\_privacy\\_rule.asp](http://privacyruleandresearch.nih.gov/privacy_boards_hipaa_privacy_rule.asp)

## **Research Integrity & Researcher Misconduct**

## Research Integrity & Researcher Misconduct

### *Laws, Regulations, & Responsibilities*

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- **"The public will support science only if it can trust the scientists and institutions that conduct research."**
  - Institute of Medicine and National Research Council, Integrity in Scientific Research: Creating an Environment That Promotes Responsible Conduct, 2002.
- **Research misconduct policies provide guidance on responsible conduct in three main areas. They:**
  1. Establish definitions for misconduct in research,
  2. Outline procedures for reporting and investigating misconduct, and
  3. Provide protection for whistleblowers (persons who report misconduct) and persons accused of misconduct.
- **What are the laws?**
  - 42 CFR Parts 50 and 93: Public Health Service Policies on Research Misconduct
    - Effective since June 16, 2005

<http://ori.dhhs.gov/documents/rcrintro.pdf>

## Research Integrity & Researcher Misconduct

### *Recent Headlines*

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- **Ryan M. Wolfort, M.D., Ph.D., Louisiana State University Health Sciences Center--Shreveport**
  - [Federal Register: August 18, 2009 (Volume 74, Number 158)]
  - Research misconduct related to his dissertation research as a graduate student
  - PHS found that Dr. Wolfort engaged in research misconduct by falsifying and fabricating data reported in three publications and one manuscript that had been submitted for publication, reviewed, and returned for revision.
  - Dr. Wolfort entered into a **Voluntary Exclusion Agreement** in which he has voluntarily agreed, for a period of two (2) years, beginning on July 13, 2009:
    1. To exclude himself from any contracting or subcontracting with any agency of the government and from eligibility or involvement in non-procurement programs of the US pursuant to HHS' Implementation (2 CFR part 276 et seq.) of OMB Guidelines to Agencies on Government wide Debarment & Suspension (2 CFR, part 180); and
    2. To exclude himself from serving in any advisory capacity to PHS, including but not limited to service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

[http://ori.dhhs.gov/misconduct/cases/Wolfort\\_Ryan.shtml](http://ori.dhhs.gov/misconduct/cases/Wolfort_Ryan.shtml)

## **Research Integrity & Researcher Misconduct**

### ***Policy, Guidance, & Resources***

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- **OSTP Federal Research Misconduct Policy**
  - [http://ori.dhhs.gov/policies/fed\\_research\\_misconduct.shtml](http://ori.dhhs.gov/policies/fed_research_misconduct.shtml)
- **Department of Health and Human Services (HHS) Office of Research Integrity (ORI) Research Misconduct Policy**
  - [http://ori.dhhs.gov/documents/42\\_cfr\\_parts\\_50\\_and\\_93\\_2005.pdf](http://ori.dhhs.gov/documents/42_cfr_parts_50_and_93_2005.pdf)
- **National Science Foundation Research Misconduct Policy**
  - <http://www.nsf.gov/oig/resmisreg.pdf>
- **Requirements for Institutional Policies and Procedures on Research Misconduct under the PHS Policies on Research Misconduct, 42 CFR 93**
  - <http://ori.dhhs.gov/documents/requirmnts.pdf>
- **Model Policy and Procedures for Responding to Allegations of Scientific Misconduct**
  - This model policy is intended to provide guidance to research institutions on handling allegations of research misconduct, and does not impose binding requirements.
  - [http://ori.dhhs.gov/policies/documents/Model\\_Policy\\_rev10-20-06.pdf](http://ori.dhhs.gov/policies/documents/Model_Policy_rev10-20-06.pdf)

## **Conflicts of Interest & Financial Disclosure**

## Conflicts of Interest & Financial Disclosure

### Context

- **OIG FY 2009 Work Plan Initiative (Recap):**
  - Financial Conflicts of Interest in Research Funded by the National Institutes of Health
    - Review NIH's oversight of grantees' compliance with financial conflict-of-interest requirements.
  - Federal regulations at 42 CFR pt. 50, subpart F
  - Review NIH's processes for reviewing the nature and management of financial conflict of interest reported by grantee institutions during FY 2006.

<http://oig.hhs.gov/publications/docs/workplan/2009/WorkPlanFY2009.pdf>

## Conflicts of Interest & Financial Disclosure

### General Definition

- **A conflict of interest involves the abuse -- actual, apparent, or potential -- of the trust that people have in professionals.**
- **Simple Working Definition:**
  - "An **actual conflict of interest** is a situation in which financial or other personal considerations have the potential to compromise or bias professional judgment and objectivity."
  - An **apparent conflict of interest** is one in which a reasonable person would think that the professional's judgment is likely to be compromised.
  - A **potential conflict of interest** involves a situation that may develop into an actual conflict of interest.
- **Note:**
  - A conflict of interest exists whether or not decisions are affected by a personal interest.
  - A conflict of interest implies only the potential for bias, not a likelihood.
  - Conflicts may involve both individuals and institutions

[http://cnmtf.columbia.edu/projects/rcr/rcr\\_conflicts/foundation/index.html](http://cnmtf.columbia.edu/projects/rcr/rcr_conflicts/foundation/index.html)

## Conflicts of Interest & Financial Disclosure

### *Proposed PHS Legislation*

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- **On May 8, 2009, The National Institutes of Health (NIH) issued an Advance Notice of Proposed Rulemaking (ANPRM) in the Federal Register.**
  - The purpose was to gain public input on whether modifications are needed to the PHS regulations on the Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought (42 C.F.R. Part 50, Subpart F) and Responsible Prospective Contractors (45 C.F.R. Part 94).
- The NIH is specifically interested in comments regarding the:
  - Expansion of the scope of the regulation and disclosure of interests;
  - Definition of “significant financial interest”;
  - Identification and management of conflicts by institutions;
  - Assurance of institutional compliance;
  - Provision of additional information to federal officials by research institutions; and
  - Broadening of the regulations to address institutional conflicts of interest.

## Conflicts of Interest & Financial Disclosure

### *Industry Trends*

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- **Increased transparency and plans for public disclosure of payments to physicians**
  - Eli Lilly & Company to post in an online database all its payments to doctors for speaking and consulting services in 2009.<sup>1</sup>
    - July 31, 2009 – New “faculty registry” lists payments to all the doctors who served as consultants in the first quarter of this year<sup>3</sup>
  - Merck & Company also said that it would disclose speaking fees it pays to doctors, beginning in 2009.<sup>1</sup>
  - Johnson & Johnson said that the company supported a “revised version” of the Physician Payments Sunshine Act, and is committed to disclosing payments for educational grants and to patient-advocacy organizations by early 2009.<sup>1</sup>

<sup>1</sup>.<http://www.nytimes.com/2008/09/25/health/policy/25drug.html>

## Conflicts of Interest & Financial Disclosure

### *Industry Trends*

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- **February 9, 2009 – Pfizer Inc. announced that it will publicly disclose online payments made to healthcare providers, principal investigators, major academic institutions, and clinical research sites. This will include payments made for consulting services, speaking engagements, and conducting clinical trials.<sup>1</sup>**
  - Plans to first publish on its website in 2010, but will include all payments made after July 1, 2009.
  - Pfizer also supports the Physician Payments Sunshine Act.

1. <http://www.healthlawyers.org/News/HLWArchive/Pages/2009/February%202009/February%2013%202009/PfizerAnnouncesPhysicianPaymentDisclosureProgram.aspx>  
 2. <http://blogs.wsj.com/health/2009/07/31/eli-lillys-payments-to-doctors-revealed/>

## Conflicts of Interest & Financial Disclosure

### *Industry Trends*

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- **Strengthening ethical standards governing vendor gift-giving and marketing practices through adoption of voluntary codes and policies**
  - April 28, 2009 – Institute of Medicine (IOM) issues a report called “Conflict of Interest in Medical Research, Education, and Practice. “
    - Argues for voluntary and regulatory measures to be take to reduce conflicts of interest.
    - Stresses the importance of preventing bias and mistrust
    - Focuses specifically on financial conflicts of interest involving pharmaceutical, medical device, and biotechnology companies, and
    - Recommends the implementation of policies and procedures to reduce the risk of conflicts of interest that can jeopardize research integrity, objective medical education, quality of care, and public trust.

<http://www.iom.edu/CMS/3740/47464/65721.aspx>

## Conflicts of Interest & Financial Disclosure

### *Clinical Investigator Responsibilities -FDA*

#### ➤ 42 CFR Part 54, Financial Disclosure by Clinical Investigators

- This federal regulation affects clinical investigators linked to clinical data submitted to the FDA in marketing applications for drugs, biological products, and devices.
- Applicants must disclose or certify information concerning the financial interests of all of all clinical investigators who conducted covered clinical studies:
  - (a) Attestation to the absence of financial interest and arrangements (completed FDA Form 3454)
  - (b) Disclosure (FDA Form 3455) of:
    - financial arrangements between sponsor and investigator,
    - significant payments from sponsor to investigator
    - proprietary interest (patent, trademark) in the test product held by the i
    - significant equity interest held by investigator
  - (c) PIs must provide the sponsor with accurate financial information during disclosure process.
  - (d) FDA may refuse to file a marketing application if there was no certification or disclosure of financial information.

**Significant payments are more than \$25,000. Significant equity interest is any ownership interest, stock options, or other financial interest in a public corporation that exceeds \$50,000. These thresholds are applicable during the time project and for 1 year after completion of the study.**

## Conflicts of Interest & Financial Disclosure

### *Industry Trends – Interactions with Healthcare Providers*

#### ➤ July 10, 2008 – Pharmaceutical Research and Manufacturers of America (PhRMA) revised Code on Interactions with Healthcare Professionals (Effective January 2009)

- New Provisions & Revisions
  - Prohibit giving non-educational items (e.g. pens, mugs and other “reminder” objects adorned with a company or product logo) to healthcare providers and their staff.
  - Prohibit sales representatives from “wining and dining” (providing restaurant meals to healthcare professionals).
  - Require companies ensure that their sales reps are sufficiently trained about applicable laws, regulations, and industry codes of practice that govern interactions with healthcare professionals.

## Conflicts of Interest & Financial Disclosure

### *Industry Trends – Interactions with Healthcare Providers*

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#### ➤ **PhRMA Code (continued)**

- Recommends that companies assess compliance with relevant standards of conduct.
- Requires yearly certification by company CEOs and CCOs that they have processes in place to comply with the revised Code.
  - Disclosure requirements for healthcare providers who help set formularies or develop clinical practice guidelines and who serve as speakers or consultants for a pharmaceutical company.
- More comprehensive guidance regarding speaking and consulting arrangements with healthcare professionals.
- Accordance with the revised Physician Payments Sunshine Act (S. 2029).

<http://www.phrma.org/files/PhRMA%20Marketing%20Code%202008.pdf>

## Conflicts of Interest & Financial Disclosure

### *Industry Trends – Interactions with Healthcare Providers*

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#### ➤ **December 18, 2008 – Advanced Medical Technology Association (AdvaMed), a national trade association of medical technology manufacturers, issued a revised Code of Ethics on Interactions with Healthcare Professionals. (Effective July 2009)**

- Contains changes that will impact the AdvaMed members in the medical device industry, as well as non-members who may chose to adopt the ethical standards. Changes include:
  - AdvaMed's public website will list companies that certify their adoption of the Code.
  - A ban on providing restaurant meals, entertainment or recreation, and gifts of *any* type to Healthcare professionals (HCPs).
  - Additional guidelines for royalty payments to Healthcare Professionals in exchange for substantial contributions that improve medical technologies.
  - A new section addressing Evaluation and Demonstration Products that sets forth appropriate parameters under which companies may provide no-charge products intended to educate both HCPs and patients on newer or improved medical technologies.

<http://www.advamed.org/MemberPortal/About/code/>

## Conflicts of Interest & Financial Disclosure

### DHHS Guidance

Financial Interests and the Safety/Welfare of Human Subjects Points of Consideration		
Institutions	IRBs	Investigators
Establish a Conflicts of Interest Committee and Policies/Procedures on its Operation and Communication with the IRB	Determine If Methods to Manage Conflicts Adequately Protects Human Subjects or Whether Additional Actions are Necessary	Modify the informed consent process when a potential or actual financial conflict exists, by either <ul style="list-style-type: none"> <li>• Having a another individual involved in the consent process or,</li> <li>• Using independent monitoring of the research.</li> </ul>
Determine What Constitutes an Institutional Conflict of Interest	Determine the kind, amount, and level of detail of information to be provided to research subjects regarding the source of funding, funding arrangements, financial interests of parties involved in the research, and any financial interest management techniques applied.	
Develop Policies/Procedures on the Financial Relationships that may/may not be held by those involved in research		

## Conflicts of Interest & Financial Disclosure

### DHHS Guidance (continued)

- **Research institutions and academic medical centers must adopt and enforce conflict of interest policies that counterbalance often competing priorities and anticipate difficult deliberations. Examples:**
  - An individual has significant financial interest (e.g. a consulting relationship or intellectual property) but may be essential to the conduct of the forecasted research.
- **Entities such as conflict of interest committees (COIC) – made up of ex-officio members (Compliance, General Counsel) and voting members (department heads, community members, faculty researchers) – are well situated to determine how best to manage the conflict and protect the integrity of the research.**

## **Conflicts of Interest & Financial Disclosure**

### ***DHHS Guidance (continued)***

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- **Every institution or organization should first assess whether it encounters conflicts of interest and the appropriate infrastructure to cope with assessing and managing them.**
- **Policies, procedures and process flows need to be developed, vetted and disseminated organization wide**
- **Prioritize federally regulated areas such mechanisms to ensure as research contributors are disclosing “significant financial interests” on an annual basis.**
- **If such policies, procedures and process flows do already exist, it is advisable to review and update them periodically to ensure they remain operationally relevant.**

## **Conflicts of Interest & Financial Disclosure**

### ***DHHS Guidance (continued)***

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- **Institutions should prioritize implementing a reporting, evaluation and management process reliant on review by either:**
  - An internal conflict of interest committee (COIC) or, if a smaller entity with limited resources, an external reviewer.
  - COIC should ideally have an administrative arm that assists with tasks such as documenting minutes, collection of annual disclosures, maintenance of records (e.g. issued management plans) and coordinates meeting with Principal Investigators.
  - Reporting of conflicts of interests can be effectuated by use of either a manual or electronic/automated solution.

# Off Label Marketing & Promotion

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## Off-Label Marketing and Promotion

### *Context*

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➤ **Increasing Trends:**

- More state False Claim Acts enacted over recent years
- More off-label use and promotion by physicians
- More investigations and litigation
- More legal uncertainty and risk for the pharmaceutical industry

➤ **While the number of post-marketing studies are increasing, there still remains a need for clarifying the laws and regulations that apply to “non-registrational” (i.e. non-IND/IDE) vs. “registrational” studies (i.e. studies with IND/IDE).**

- “Use of a marketed product... when the intent is the “practice of medicine” does not require the submission of an Investigational New Drug Application (IND), Investigational Device Exemption (IDE) or review by an IRB”
- Thus, different rules apply when investigators prescribe drugs for off-label use not covered under an IND, but receive payment from pharmaceutical companies for participating in the post-marketing study of the drug.

## Off-Label Marketing and Promotion

### *Laws, Regulations, & Responsibilities*

- **The two major laws that generally apply to allegations of improper, off-label promotion of approved drugs are:**
  - The Anti-kickback Statute, and the False Claims Act (both Federal and State laws)
- **In some cases, other applicable laws and regulations that can apply are:**
  - HIPAA
  - The Common Rule
  - Food and Drug Administration Modernization Act (FDMA)
  - Generic Drug Enforcement Act (for investigators on the FDA's Debarment List)
  - Reporting Post-marketing Adverse Drug Experiences and Unanticipated Side Effects (21 CFR 314.80)
- **Laws that do not generally apply to off-label ("non-registrational"), post-marketing studies:**
  - 21 CFR 54 (Financial Disclosure)
  - 21 CFR 312 (IND Requirements)
  - Physician Self-referral ("Stark")

## Off-Label Marketing and Promotion

### *New State Laws*

- **August 10, 2008 – Gov. Patrick of Massachusetts signs into law the Pharmaceutical and Medical Device Manufacturer Conduct statute (Mass. Gen. L. c. 111N)<sup>1</sup>**
  - *Effective July 1, 2009*, the Massachusetts Code prohibits payment for outside meals, entertainment or recreational items of value (i.e., theater tickets, sporting events, concerts, etc.) or non-educational gifts, including complimentary items such as pens and coffee mugs.
  - *Effective by July 1, 2010*, the Massachusetts Code requires companies to disclose of payments to providers for each individual payment of at least \$50
- **June 8, 2009 – Gov. Douglas of Vermont signs into law the an act relating to the marketing of prescribed products (Act No. 59)**
  - Similar to the Massachusetts law
  - *Effective July 1, 2009*, the Vermont Act companies from paying for any food, entertainment, travel, subscription, advance, service, or anything else of value provided to a health care provider.
  - Annually required disclosure of all payments by companies to providers with prescribing authority

1. [http://www.nixonpeabody.com/publications\\_detail3.asp?ID=2799](http://www.nixonpeabody.com/publications_detail3.asp?ID=2799)  
 2. <http://www.leg.state.vt.us/DOCS/2010/ACTS/ACT059.PDF>

## Off-Label Marketing and Promotion

### *Proposed Federal Legislation*

- **January 22, 2009 – Senators Grassley (R-IA) and Kohl (D-WI) introduce The Physician Payments Sunshine Act of 2009, to require drug and device manufacturers to publicly report payments (over \$100) to physicians every year.**
  - Companies will be required to report items, such as:
 

– Consulting Fees	– Food
– Compensation for services other than consulting	– Gifts
– <i>Honoraria</i>	– Entertainment
– Current or prospective ownership or investment interests	– Travel
– Compensation for serving as a faculty member / speaker for CME program	– Education
– Grants	– Research
– Any other payment or transfer of value as defined by the secretary	– Charitable Contributions
	– Royalties or licenses

<http://www.policymed.com/2009/01/physician-payment-sunshine-act-2009-introduced.html>

## Off-Label Marketing and Promotion

### *Proposed Federal Legislation*

- **The Physician Payments Sunshine Act of 2009 also includes:**
  - Required reporting of research payments
  - Required reporting of physician ownership interests in private companies
  - Unintentional failure to report: penalties to include fines from \$1,000 - \$10,000 for each payment not reported with a cap of \$150,000/year
  - Intentional failure to report: penalties to include fines from \$10,000 - \$100,000 for each payment not reported with a cap of \$1 million/year
- **March 11, 2009 – Promoting Innovation and Access to Life-Saving Medicine Act<sup>2</sup>**
  - Provide for the licensing of biosimilar and interchangeable biological products
  - Allows any person to file an abbreviated biological product application with the Secretary of HHS
  - Requires applications to demonstrate a high degree of similarity or interchangeability between the biological product and the licensed biological product (reference product)

1. <http://www.policymed.com/2009/01/physician-payment-sunshine-act-2009-introduced.html>  
 2. <http://www.opencongress.org/bill/111-h1427/show>

## Off-Label Marketing and Promotion

### *Recent Headlines*

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- **September 29, 2008 – Cephalon Inc. settles for \$425 million to resolve allegations of off-label marketing<sup>1</sup>**
  - Entered a criminal plea that it marketed three drugs for uses not approved by the FDA
  - Enters into a 5 year CIA
  - The lawsuits were brought by former Cephalon employees and filed under the *qui tam* provisions of the False Claims Act.
- **September 2, 2009 – Pfizer to Pay \$2.3 Billion for Fraudulent Marketing<sup>2</sup>**
  - To settle a federal investigation into its alleged off-label marketing of the now-withdrawn painkiller Bextra.
  - Largest settlement of improper off-label marketing practices
  - ***Largest health care fraud settlement in the history of the Department of Justice***
  - Already in a 5 year CIA from 2004 for off-label promotion of Neurontin<sup>3,4</sup>

1. <http://www.usdoj.gov/opa/pr/2008/September/08-civ-860.html>
2. <http://www.usdoj.gov/opa/pr/2009/September/09-aag-900.html>
3. [http://oig.hhs.gov/fraud/cia/agreements/pfizer\\_5\\_11\\_2004.pdf](http://oig.hhs.gov/fraud/cia/agreements/pfizer_5_11_2004.pdf)
4. [http://www.usdoj.gov/opa/pr/2004/May/04\\_civ\\_322.htm](http://www.usdoj.gov/opa/pr/2004/May/04_civ_322.htm)

## Off-Label Marketing and Promotion

### *Recent Headlines*

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- **July 14, 2009 – Endoscopic Technologies Inc. (Estech) agrees to pay U.S. \$1.4 million to resolve allegations of Medicare fraud, including:<sup>1</sup>**
  - Off-label marketing its medical devices to treat atrial fibrillation, a use that is not approved by the FDA.
  - Promoting expensive heart surgeries using the company's devices when less invasive alternatives were appropriate,
  - Advising hospitals to up-code surgical procedures using the company's devices to inflate Medicare reimbursements, and
  - Paying kickbacks to healthcare providers to use its devices.
- **November 14, 2008 – U.S. Files Suit Against New Jersey Generic Drug Manufacturer That Distributed Adulterated and Misbranded Products<sup>2</sup>**

1. <http://www.usdoj.gov/opa/pr/2009/July/09-civ-681.html>
2. <http://www.usdoj.gov/opa/pr/2008/November/08-civ-1012.html>

## Off-Label Marketing and Promotion

### Recent Headlines

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- **January 15, 2009 – Eli Lilly Agrees to Pay \$1.415 Billion to Resolve Allegations of Off-label Promotion of Zyprexa –Total Tab tops \$2 Billion<sup>1</sup>**
  - Lilly admitted guilt to the criminal charge of misbranding
    - Between Sept. 1999 and March 31, 2001, the company promoted Zyprexa in elderly populations to treat dementia, including Alzheimer’s dementia.
  - **\$515 Million Criminal Fine; Civil Settlement up to \$800 Million**
- **\$800 million civil settlement with the federal government (\$438 million) and various states (\$362 million) to resolve False Claims Act claims and related state claims by Medicaid and other federal programs and agencies.**
- **\$78 million will go to the qui tam whistleblowers.**
- **\$62 million to settle prior consumer protection lawsuits brought by 33 states in 2008.**
- **5 Year Corporate Integrity Agreement (CIA)**

<http://www.usdoj.gov/opa/pr/2009/January/09-civ-038.html>

## Off-Label Marketing and Promotion

### Guidance

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- **Pay investigators reasonable compensation and for study services only.**
- **Keep payments consistent among sites**
- **Conduct the study with a clear scientific purpose with a well designed protocol**
  - Studies designed and funded by a company’s marketing department raises a big red flag for the OIG
  - Extremely large sample sizes and enrolled sites may be viewed by the OIG as a “seeding study” or “unnecessarily duplicative” to generate business.
- **Although IRB review is not federally required for post-marketing, non-registrational studies, obtaining IRB approval and giving informed consent is a good idea.**
- **Guide investigators into a “safe harbor”**
  - Sign written investigator agreements for one-year terms that cover all services provided, and pre-set the payments.

## Off-Label Marketing and Promotion

### Guidance (Continued)

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- **Make sure investigators understand the laws when becoming involved in post-marketing, off-label use studies.**
- **Interesting FDA Guidance published on January 13, 2009, entitled: “*Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices*”<sup>1</sup>**
  - This guidance provides drug, biologics, and device manufacturers with the agency's views on the distribution of medical journal articles and scientific or medical reference publications that discuss unapproved new uses for FDA-approved drugs or biologics or FDA-approved or cleared medical devices to healthcare professionals and healthcare entities.
- **FDA Inspections, Compliance, Enforcement, and Criminal Investigations<sup>2</sup>**
  - <http://www.fda.gov/ICECI/EnforcementActions/BioresearchMonitoring/default.htm>

1. <http://edocket.access.gpo.gov/2009/E9-452.htm>  
2. <http://www.fda.gov/ICECI/default.htm>

## Grants & Contracts Management

## Grants & Contracts Management

### *Context*

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- **Many colleges and universities are not well prepared to comply with post-award responsibilities.**
- **Large grants bring additional scrutiny**
  - More public demand for accountability
- **There have been an increasing number of federal fraud cases associated with university research grants.**
  - Increasing use of qui tam provisions of FCA
- **An HHS OIG FY 2009 Work Plan Initiative (*Recap*):**
  - Colleges' and Universities' Compliance With Cost Principles
    - Review colleges' and universities' compliance with *selected* cost principles governed by OMB Circular A-21, Cost Principles for Educational Institutions.
    - Conduct reviews at selected schools based on the dollar value of Federal grants received and on input from:
      - HHS' operating divisions,
      - Office of the Assistant Secretary for Budget, Technology, and Finance, and
      - Office of the Assistant Secretary for Administration and Management

## Grants & Contracts Management

### *The Issues*

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- **Unallowable costs, misallocation of costs**
- **Direct-Charging of Administrative and Clerical Costs (F&A)**
- **Effort Reporting**
- **Cost Transfers**
- **Inadequate sub-recipient monitoring**
- **Non-compliance with Assurances and special terms and conditions of award**
- **Double Billing / Overlap with Medicare billing for clinical research**
- **Delinquent closeout reporting**
- **Incomplete forms describing existing support on applications**
- **Inadequate institutional oversight**

## Grants & Contracts Management

### *Result of Non-compliance*

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- **Loss of grant funding**
- **Audits, investigations**
- **Lawsuits, settlements/fines and corrective actions**
- **Administrative sanctions**
- **Bad Press!**

## Grants & Contracts Management

### *Recent Headlines – False Claims*

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- **December 23, 2008 – Yale University to pay \$7.6 Million to Resolve False Claims Act and Common Law Allegations**
  - YALE UNIVERSITY has entered into a civil settlement agreement with the Government in which it will pay \$7.6 million to resolve allegations that it violated the False Claims Act and the common law in the management of federally-funded research grants awarded to the university between January 2000 and December 2006.

## Grants & Contracts Management

### *Recent Headlines – Billing Fraud*

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- **February 6, 2009 - Neurometrix, Inc. enters in 5 year CIA<sup>1</sup>**
  - Per a Deferred Prosecution Agreement, the Company agreed to a \$1.2 million
  - February 9, 2009 – Civil Settlement Agreement with the DOJ and OIG
    - Involved improper reimbursement when investigators used the wrong CPT codes for a procedure done in a nerve conduction study, where a certain component of the procedure justifying the use of that CPT code was not performed<sup>2</sup>

1. [http://oig.hhs.gov/fraud/cia/cia\\_list.asp](http://oig.hhs.gov/fraud/cia/cia_list.asp)

2. [http://edgar.brand.edgar-online.com/EFX\\_dll/EDGARpro.dll?FetchFilingHTML1?ID=6395125&SessionID=hdNjWSPZzEjcaz7](http://edgar.brand.edgar-online.com/EFX_dll/EDGARpro.dll?FetchFilingHTML1?ID=6395125&SessionID=hdNjWSPZzEjcaz7)

## Grants & Contracts Management

### *Recent Headlines – Anti-Kickback Scheme*

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- **November 25, 2008 – Bayer HealthCare LLC (Bayer) settles for \$97.5 million**
  - Bayer paid kickbacks to a number of diabetic suppliers to convert their patients to Bayer's products from supplies manufactured by its competitors, and caused those suppliers to submit false claims to Medicare.
  - Enters into a 5 year CIA.

## Grants & Contracts Management

### *Recent Headlines – Anti-Kickback Scheme*

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➤ **May 31, 2009 – Medtronic, Inc. and Medtronic Sofamor Danek U.S.A., Inc.<sup>1</sup>**

- Medtronic enters into a 5 year CIA stemming from a 2006 settlement with the U.S. for \$40 million to settle civil allegations that its Medtronic Sofamor Danek division (“MSD”) paid kickbacks to doctors to induce them to use MSD’s spinal products.<sup>2</sup>
  - The investigation by the DOJ began with a whistleblower (*qui tam*) action filed by a former MSD employee in their Medtronic’s Travel department.
  - “payments and other remuneration for physicians’ attendance and expenses at medical education events, think tanks, VIP/MVP events, and meetings at resort locations,” and
  - “payments made pursuant to consulting, royalty, fellowship and research agreements with physicians and entities.”
- Initiated a voluntary compliance program

1. [http://oig.hhs.gov/fraud/cia/cia\\_list.asp](http://oig.hhs.gov/fraud/cia/cia_list.asp)

2. <http://www.kslaw.com/library/clientalert/ca072606.pdf>

## Export Controls

## Export Controls

### *Laws, Regulations, & Responsibilities*

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➤ **What are Export Control Regulations?**

- Federal laws and regulations devised to prohibit the unauthorized “export” or transfer of strategically important products, services or technologies and sensitive information (e.g. technical data or research findings) to “foreign persons” in the U.S. or abroad.

➤ **What constitutes an “export”?**

- Verbal and/or visual release or disclosure of any controlled technology, software or technical data either in the U.S. (“deemed export”) or abroad.
- Electronic and/or digital transmission of controlled items, information, software or related to controlled items and technology.
- Shipment of tangible, controlled (subject to export regulations) items or goods outside of the U.S.
- Use or application of controlled technology for the benefit or on behalf of “foreign persons” either in U.S. or abroad.

## Export Controls

### *Laws, Regulations, & Responsibilities (continued)*

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➤ **What constitutes a “deemed export”?**

- The transfer of technology to a foreign person in the United States is “deemed” to be an export.
- A “deemed export” can be information in the form of technical data or assistance.
- Controlled technologies such as software, if released or disclosed to foreign students, foreign researchers from abroad and on site visits or foreign laboratory staff, could not only be a deemed export, but also raise licensing issues.

➤ **Foreign persons include:**

- Foreign governments
- Foreign entities or corporations neither incorporated in nor organized to conduct business in the United States
- An individual who is neither a U.S. Citizen nor Lawful Permanent Resident (Green card holder) of the United States.

## Export Controls Oversight

- **Export Control Laws cover specific domain and different federal agencies are charged with enforcing them:**

<i>Export Control Law</i>	<i>Federal Oversight Authority</i>	<i>Administering Agency</i>	<i>Domain/Scope</i>
International Traffic in Arms Regulations (ITAR) <i>22 CFR §§ 120-130</i>	State Department	Directorate of Defense Trade Controls (DDTC)	Military technologies
Export Administration Regulations (EAR) <i>15 CFR §§ 730-774</i>	Commerce Department	Bureau of Industry and Security (BIS)	"Dual use" (civilian and military) technologies
Economic and Trade Sanction Regulations <i>(referred to as OFAC in this deck - Statutes, Executive Order)</i>	Treasury Department	Office of Foreign Assets Control (OFAC) –	Regulates transactions with countries subject to trade sanctions, embargoes and/or boycotts

## Export Controls Recent Headlines

- **August 6, 2009: DHL Settles Iranian Transactions Regulations, Sudanese Sanctions Regulations, Reporting, Procedures and Penalties Regulations, and Export Administration Regulations Allegations with OFAC and the Department of Commerce's Bureau of Industry and Security (BIS):**
- DPWN Holdings (USA), Inc. and DHL Express (USA), Inc. (collectively "DHL") have agreed to remit \$9,444,744 to settle allegations of violations of the Iranian Transactions Regulations, the Sudanese Sanctions Regulations, the Reporting, Procedures and Penalties Regulations (collectively, the "OFAC Regulations") and the Export Administration Regulations ("EAR").
  - OFAC alleged that, between August 2002 and March 2007, DHL made numerous shipments to Iran and Sudan in violation of the OFAC Regulations and that the company failed to maintain records with respect to other shipments to those countries.
  - BIS alleged that between June 2004 and September 2004, DHL made certain unlicensed exports to Syria in violation of the EAR and in connection with a number of other exports to Syria failed to retain airway bills and other export control documents in violation of the EAR.
  - DHL did not voluntarily disclose this matter to OFAC or BIS. It was resolved according to the prior enforcement guidelines published by OFAC at 68 Fed. Reg. 4422.

## **Export Controls**

### ***What You Need to Know***

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- **Export control regulations are intended to protect national security and to secure both domestic and foreign policy initiatives.**
- **Each of academic medical center, hospital, pharmaceutical or device maker should be able to satisfactorily answer the following questions:**
  - *Who works here and collaboratively with our employees?*
  - *What is in my research portfolio/ under development?*
  - *Where will the devices, technologies, drugs, etc. head next?*
  - *What types of technical data or items in-coming to our laboratories?*
- **As industries – including health care – become increasingly enmeshed in a global economy, planning and developing an infrastructure to mindfully accommodate and compliantly manage research initiatives and the exchange of information and technologies is critical.**
- **Such an approach not only protects an organization from onerous civil and criminal penalties, but, ultimately, for long term success.**

## **Animal Research**

## Animal Research

### *Laws, Regulations, & Responsibilities*

- Provided below are two of the main regulatory frameworks that inform all animal research conducted in the United States along with a brief description and the government agencies charged with their enforcement:

<i>Government Agency</i>	<i>Role/Responsibility</i>	<i>Scope of Regulation</i>
U.S. Department of Agriculture (USDA)	Oversee the Animal Welfare Act (AWA) via the Animal and Plant Inspection Service (APHIS)	Performs annual inspections of registered research facilities
Office of Laboratory Welfare (OLAW) – an arm of the U.S. Public Health Service (PHS) National Institutes of Health (NIH) Office of Extramural Research	Implement and enforce PHS Policy on <i>Humane Care and Use of Laboratory Animals</i>	Applicable to any PHS funded animal research studies

## Animal Research

### *Recent Headlines*

- **The HSUS v. U.S. Department of Agriculture (Laboratory animal pain & distress)**
- The HSUS filed the case in federal court in January 2005 under the FOIA, alleging that the USDA violated the FOIA.
  - Pursuant to the settlement agreement signed by the Humane Society of the United States (HSUS) and the USDA, all of the annual reports, including pain and distress information, are to be made available to the public electronically and in a timely manner. USDA also agreed to indicate on its website which facilities did not submit annual reports, and therefore failed to abide by the Animal Welfare Act (AWA).
  - The goal of the settlement is to provide additional transparency about animal use and care at research facilities across the nation. The lawsuit assures public access to information tracking whether:
    - Research institutions are abiding by AWA and the USDA is enforcing regulations.

## **Animal Research**

### ***Recent Headlines (continued)***

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➤ **What triggered the HSUS' lawsuit against the USDA?**

➤ **Timeline\*:**

- 2001: The HSUS files a request with the USDA for certain documents related to pain and distress in laboratory animals.
- 2002: USDA removes key documents concerning the use of animals in research from its website.
- January 2005: The HSUS files suit against the USDA seeking to restore the reports.
- May 2005: USDA announces that in response to The HSUS's lawsuit, the agency will again start posting registered research facilities' annual reports to their website, as required by the FOIA.
- March 2008: USDA discloses to the HSUS that it never received mandatory annual reports from 81 animal research facilities over the course of five (5) years.

\* [http://www.hsus.org/press\\_and\\_publications/press\\_releases/hsus\\_and\\_usda\\_reach\\_settlement\\_to\\_improve\\_animal\\_research\\_monitoring\\_070109.html](http://www.hsus.org/press_and_publications/press_releases/hsus_and_usda_reach_settlement_to_improve_animal_research_monitoring_070109.html)

## **Building an Effective Compliance Program**

## Building an Effective Compliance Program

### *“Good Medicine” for Mitigating Risks in 2009 & Beyond*

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- Acknowledging that an effective compliance program can be mitigate reputational, regulatory, operational and financial risks might provide sufficient incentive for an organization to either implement or update one.
- However, this realization a compliance program could be a problem solver does not come with a road map or “how-to” guide.
- Luckily, however, the Office of Inspector General (OIG) decided to take the guesswork out of how where to start by issuing the Federal Sentencing Guidelines or the Seven Elements of an Effective Compliance Program.
- The OIG offers uses this guidance to assist pharmaceutical and device manufactures and hospitals in designing compliance programs effective in its view.

## Building an Effective Compliance Program

### *Laws, Regulations, & Responsibilities - The “Seven Elements”*

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- 1. Standards of Conduct/Policies and Procedures**
  - These documents are the fabric of the organization and the roadmap for how employees should be complying with laws and regulations
  - Tools to ensure consistent processes and practices
- 2. Compliance Officers and Committees**
  - Resource for legal and regulatory inquiries
  - Oversee Compliance Program and compliance committee operations
  - Respond to reported compliance questions and investigates issues of non-compliance
- 3. Education and Training**
  - Demonstrate the health systems commitment to Compliance/ethical behavior
  - Raise awareness of compliance and staff accountability
  - Inform an educate staff regarding high risk areas of compliance
- 4. Communication**
  - Promote open communication throughout the health system
  - Provide a process for reporting confidential complaints

## **Building an Effective Compliance Program**

### ***The “Seven Elements” (continued)***

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#### **5. Enforcement and Disciplinary Action**

- Disciplinary action must be consistent with the violations

#### **6. Auditing and Monitoring**

- Implement systems and controls to monitor organizations compliance risk
- Provide external audits
- Audit policies, procedures and Standards effectiveness

#### **7. Response and Reporting**

- Report and respond to concerns of non compliance
- Oversee internal and external investigations
- Create process and systems to correct and prevent errors

**Compliance programs that include a focus on each of the Seven Elements do not, in an of themselves, equate to effectiveness.**

## **Building an Effective Compliance Program**

### ***Laws, Regulations, & Responsibilities – Bio Tech Companies***

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#### **Pharmaceutical and Device Manufacturers:**

##### **➤ How does OIG guidance regarding compliance programs for pharmaceutical and device manufacturers differ?**

- The OIG identifies three major potential risks factors that are to be specifically addressed in written policies and procedures developed by manufacturers:
  1. Integrity of the data used by state and federal governments to establish payment;
  2. Kickbacks and other illegal remuneration; and
  3. Compliance with law regulating drug samples.

## Building an Effective Compliance Program

### *Bio Tech Companies (continued)*

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- **While some regulatory concerns are shared by manufacturers and health care providers, there are laws, regulations and guidance that are either unique to manufacturers or impact industry differently.**
- **Some of these include:**
  - PhRMA Code
  - AdvaMed Code
  - Medicare Best Price Law 42 U.S.C. § 1396r-8(c) and other pricing related regulations such as discount safe harbor
  - Off-label usage
  - Federal anti-kickback statute
  - Federal Food, Drug and Cosmetic Act (FDCA)
  - Prescription Drug Marketing Act (PDMA)
  - American Medical Association (AMA)
  - Guidelines on Gifts to Physicians from Industry and Accreditation Council for Continuing Medical Education (ACCME) Standards

## Building an Effective Compliance Program

### *Laws, Regulations, & Responsibilities - FCPA*

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#### **Foreign Corrupt Practices Act (FCPA) 15 U.S.C. §§ 78dd-1, et seq.**

- **Manufacturers must make decision as to whether their particular business enterprise warrants the development of additional policies and procedures requiring compliance.**

Example:

- An international pharmaceutical manufacturer with ties to Europe, India and China must develop a policy, procedure and infrastructure to fully comply with the FCPA.
- FCPA prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity as a foreign government official.
- Some countries such as India and China are viewed by the Department of Justice (DOJ) as “hot spots” from an enforcement perspective.
- Other countries (including virtually all European countries) have enacted legislation similar to the FCPA.
- In some cases, the local laws are even more stringent than the requirements of the FCPA.

## Building an Effective Compliance Program

### *Challenges for Research Compliance*

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- **Research Institutions**
  - Cost and Performance Reporting
  - Effort Reporting
  - Improper Payments
  - Increased Need for Institution Oversight
  - Sub-recipient Monitoring
- **Agencies, Institutes and Centers**
  - Transparency
    - Posting requirements
    - Spending Reporting
    - Program Compliance Risk Assessments
  - Government-wide Standard Terms and Conditions
- **Does anyone have the staff or IT infrastructure to keep up?**
- **TMI – “To Much Information”**

## Building an Effective Compliance Program

### *Creating a Culture of Compliance*

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- **A compliance program with a vast array of well drafted policies and procedures does little to ensure a pharmaceutical manufacturer or hospital have adequately addressed or managed regulatory or financial risks.**
- **An Annual Compliance Work Plan should guide the compliance department’s auditing and monitoring efforts. This document should be:**
  - The result of collaborative input from: the Board of Directors, senior leadership (operational, administrative and compliance) and clinical departments;
  - Mindful of regulatory trends and ‘hot’ topics; and
  - Realistic in scope, e.g. not overextend compliance staff or resources
- **Dedicated staff members and resources in a compliance department might be identified as an “investigatory arm”. Other organizations prefer to rely on the compliance program to identify and monitor issues and deploy Internal Audit for audit purposes.**

## Questions?

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## Appendix

## Key Players

### *Government Organizations and Their Roles*

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- **Department of Health and Human Services (HHS)**
  - Office of Inspector General (OIG)
  - Centers for Medicare & Medicaid Services (CMS)
    - State Medicaid Fraud Control Units
  - Food and Drug Administration (FDA)
  - Office for Human Research Protections (OHRP)
  - Office of Research Integrity (ORI)
  - National Institutes of Health (NIH)
- **Department of Justice (DOJ)**
  - U.S. Attorney Offices
  - State Attorney General Offices
  - Federal Bureau of Investigation (FBI)
- **HHS/DOJ Health Care Fraud and Abuse Control Program**
- **U.S. Department of Agriculture (USDA)**
- ***Departments that Govern Export Controls***
- **Government Accountability Office (GAO)**
- **Office of Management and Budget (OMB)**

## DHHS

### *Food and Drug Administration (FDA)*

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- **Mission:**
  - Assuring the safety, efficacy, and security of human and veterinary drugs, biologics, medical devices, our nation's food supply, cosmetics, and products that emit radiation
  - Hasten innovations that make drugs and foods safer, and more effective and affordable
  - Help the public get the accurate, science-based information they need to use medicines and foods to improve their health

## DHHS

### *Food and Drug Administration (FDA)*

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➤ **Regulatory Authority:**

- Among other regulatory responsibilities, the FDA has authority over the following:
  - Biologics**
    - Product and manufacturing establishment licensing
    - Safety of the nation's blood supply
    - Research to establish product standards and develop improved testing methods
  - Drugs**
    - Product approvals
    - OTC and prescription drug labeling
    - Drug manufacturing standards
  - Medical Devices**
    - Pre-market approval of new devices
    - Manufacturing and performance standards
    - Tracking reports of device malfunctioning and serious adverse reactions
- Regulatory References for Drugs and Devices**
  - Code of Federal Regulations: 21 Parts 312, 314, 600, 812, and 814

<http://www.fda.gov/AboutFDA/WhatWeDo/WhatFDARegulates/default.htm>

## DHHS

### *Office of Human Research Protections (OHRP)*

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- **OHRP's Division of Compliance Oversight (DCO) reviews institutional compliance with the federal regulations governing the protection of human subjects in HHS-sponsored research 45 CFR 46.<sup>1</sup>**
- Evaluates all written substantive allegations or indications of noncompliance with the HHS regulations, opens formal evaluations and, if necessary, requires corrective action by the institution.
  - DCO issues findings of noncompliance in the form of determination letters
  - Determination letters are available on:
    - <http://www.hhs.gov/ohrp/compliance/letters/index.html>
    - Determination letters are edited to remove those portions that relate to issues still under discussion with the institution.
  - Case materials from DCO evaluations are available, through a Freedom of Information Act (FOIA) request, once the investigation is complete.

1. <http://www.hhs.gov/ohrp/compliance/>

## DHHS

### *Office of Research Integrity (ORI)*

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➤ **The Office of Research Integrity (ORI) oversees and directs Public Health Service (PHS) research integrity activities on behalf of the Secretary of HHS.<sup>2</sup>**

- Exception: Regulatory research integrity activities of the FDA

➤ **ORI carries out its responsibility by:**

- Developing policies, procedures and regulations related to the detection, investigation, and prevention of research misconduct and the responsible conduct of research;
- Reviewing and monitoring research misconduct investigations conducted by applicant and awardee institutions, intramural research programs, and the Office of Inspector General in the Department of Health and Human Services (HHS);
- Recommending research misconduct findings and administrative actions to the Assistant Secretary for Health for decision, subject to appeal;
- Assisting the Office of the General Counsel (OGC) to present cases before the HHS Departmental Appeals Board;

1. <http://www.hhs.gov/ohrp/compliance/>  
2. <http://ori.dhhs.gov/about/index.shtml>

## DHHS

### *Office of Research Integrity (ORI)*

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➤ **ORI carries out its responsibility by (continued):**

- Providing technical assistance to institutions that respond to allegations of research misconduct;
- Implementing activities and programs to teach the responsible conduct of research, promote research integrity, prevent research misconduct, and improve the handling of allegations of research misconduct;
- Conducting policy analyses, evaluations and research to build the knowledge base in research misconduct, research integrity, and prevention and to improve HHS research integrity policies and procedures;
- Administering programs for: maintaining institutional assurances, responding to allegations of retaliation against whistleblowers, approving intramural and extramural policies and procedures, and responding to Freedom of Information Act and Privacy Act requests.

## DHHS

### National Institutes of Health (NIH)

#### ➤ Overview<sup>1</sup>:

- NIH is the primary Federal agency for conducting and supporting medical research.
- 27 Institutes and Centers (ICs)
- Annually invests over \$28 billion in medical research.
- Almost 50,000 extramural, competitive grants to more than 325,000 researchers at over 3,000 universities, medical schools, and other research institutions in every state and around the world.
  - 90% of total budget
  - 10% to over 6,000 NIH Intramural scientists

#### ➤ “Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.”<sup>2</sup>

1. <http://www.nih.gov/about/NIHOverview.html>
2. <http://www.nih.gov/about/index.html#mission>

## DHHS

### National Institutes of Health (NIH)

#### ➤ Federal administrative requirements, cost principles and audit requirements applicable to NIH grants

Compliance Requirements At A Glance			
Grantee Type	Admin Requirements	Cost Principles	Audit Requirements
State & Local Governments	<a href="#">A-102 (45CFR Part 92)</a>	<a href="#">A-87 (2 CFR Part 225 - PDF 362 KB)</a>	<a href="#">A-133</a>
College & Universities	<a href="#">A-110 (2 CFR Part 215)</a> Formerly at (45 CFR Part 74)	<a href="#">A-21 (2 CFR Part 220 - PDF 384 KB)</a>	
Non-Profits		<a href="#">A-122 (2 CFR Part 230 - PDF 362 KB)</a>	
Hospitals		45 CFR Part 74, App E	
For-Profits		<a href="#">FAR 31.2 (48 CFR Subpart 31.2)</a>	
Foreign		<a href="#">2 CFR Part 215</a> (formerly 45 CFR Part 74 or Part 92)	
			----- <a href="#">45 CFR Part 74.26</a> <a href="#">NIH GPS</a> (same as <a href="#">45 CFR Part 74.26</a> )

## DHHS

### *National Institutes of Health (NIH)*

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#### ➤ **NIH Compliance Oversight Activities<sup>1</sup>**

- The Office of Extramural Research Division of Grants Compliance & Oversight (DGCO) is the principal compliance office overseeing recipient institutions.
- Compliance is a “shared responsibility” between NIH and the recipient institutions

#### ***Proactive Compliance Site Visits (PCSVs)***

- DGCO site visits are NOT considered investigations or audits. They help:
  - assess institutional understanding of Federal policies and regulations
  - minimize or eliminate areas of non-compliance by nurturing partnerships between NIH and its grantee institutions

#### ***Targeted Site Reviews and Pilot Compliance Program<sup>2</sup>***

- NIH initiative that focuses specifically on compliance with Financial Conflict of Interest (FCOI) regulations (42 CFR Part 50 Subpart F)

#### ***Genetic Research Oversight***

- Office of Biotechnology Activities (OBA) –oversight for recombinant DNA research
- Recombinant DNA Advisors Committee (RAC) advises OBA

1. <http://grants.nih.gov/grants/compliance/compliance.htm>
2. <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-010.html>

## DHHS

### *National Institutes of Health (NIH)*

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#### ➤ **Compliance Resources**

<http://grants.nih.gov/grants/compliance/compliance.htm#resources>

#### ***Conflicts of Interest***

- <http://grants.nih.gov/grants/policy/coi/index.htm>
- <http://grants.nih.gov/grants/policy/coifaq.htm>
- [http://grants.nih.gov/grants/policy/coi/nih\\_review.htm](http://grants.nih.gov/grants/policy/coi/nih_review.htm)

#### ***Reporting Compliance Concerns***

- Compliance concerns should be addressed to your institution’s Office of Sponsored Research, the Chief Grants Management Officer (GMO) listed on the NoA, or the DGCO at [GrantsCompliance@nih.gov](mailto:GrantsCompliance@nih.gov)
- Formal allegations of fraud, waste and abuse should be made to the HHS OIG hotline: <http://oig.hhs.gov/hotline.html> or to the NIH Office of Management Assessment, directly. See <http://oma.od.nih.gov/pi/dpi.html> for contact information.

## Department of Justice (DOJ)

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- **The U.S. Department of Health and Human Services (HHS) and U.S. Department of Justice (DOJ) are working together to help eliminate fraud and investigate fraudulent Medicare and Medicaid operators who are cheating the system.**
  - Use Medicare Fraud Strike Force (MFSF) teams
  - Help State Medicaid offices conduct audits and monitor activities to detect fraud
  - Criminally prosecute to deter health care fraud
  - Help train providers on Medicare compliance and give them resources to help identify and prevent fraud

## Health Care Fraud and Abuse Control Program

### *Statutory Background*

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- **The Social Security Act Section 1128C(a), as established by the Health Insurance Portability and Accountability Act of 1996 (P.L. 104-191, HIPAA or the Act), created the Health Care Fraud and Abuse Control Program, a far-reaching program to combat fraud and abuse in health care, including both public and private health plans.**
- **Under the joint direction of the Attorney General and the Secretary, the Program's goals are:**
  - to coordinate federal, state and local law enforcement efforts relating to health care fraud and abuse with respect to health plans;
  - to conduct investigations, audits, inspections, and evaluations relating to the delivery of and payment for health care in the United States;
  - to facilitate enforcement of all applicable remedies for such fraud;
  - to provide guidance to the health care industry regarding fraudulent practices; and
  - to establish a national data bank to receive and report final adverse actions against health care providers, and suppliers.