

FRAUD IN CLINICAL TRIALS AND RESEARCH

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DISCLAIMERS

- 1. My personal opinions
- 2. Not official policy of Department of Justice.
- 3. A complaint or indictment is an allegation, and the defendant has a presumption of innocence and right to put government to its proof.

THE RESEARCH FRAUD PROBLEM

- It's not new
 - ◆ Sigmund Freud fabricated case studies
 - ◆ Isaac Newton altered records of lunar and solar sightings to fit his theories
 - ◆ Pasteur made false statements about the first public trial of his anthrax vaccine
 - ◆ Gregor Mendel's plant-breeding results are too good to be true

WHAT IS RESEARCH FRAUD

■ Intentional

◆ Scientific/research misconduct

- ◆ Fabricating or falsifying data

- ◆ Plagiarism

- ◆ Overstating, misreporting results

- ◆ Misrepresenting credentials

WHAT IS RESEARCH FRAUD(2)

■ FRAUD ON IRB

- ◆ Failure to submit and obtain approval
- ◆ Failure to identify changes
- ◆ Failure to comply with study protocol
- ◆ Failure to comply with subject disclosures and protections

EXAMPLES OF RESEARCH FRAUD-BIOCRYST'S BCX-34

- 1994 study - University of Alabama-Birmingham - psoriasis, lymphoma treatment
- “It wasn’t a school overly burdened with strictures or rules and regulations.” (UAB Director of gene therapy program)
- False records, false reports, inflated improvement rates

BIOCRYST'S BCX-34

- 1994-False reports to FDA
- False statements for company press release
- 1995 FDA investigation
- 2000 trial – Dr. Harry Snyder and Study coordinator Renee Peugeot-convicted
- 2000 sentencing/appeal
- 2002 appeal denied
- 2004-Snyder 34 months, Peugeot 28 months

EXAMPLES OF RESEARCH FRAUD-3/17/05

- Dr. Eric Poehlman, U. of Vermont Professor of Medicine
- Fabricated research data in “Longitudinal Menopause Study” and “Longitudinal Study of Aging”
- False grant applications and papers
- Guilty plea to 1001, related to NIH grant
- Permanent exclusion from all federal health programs

EXAMPLES OF RESEARCH FRAUD/SAFETY ISSUE-

University of Pennsylvania - 2/05

- Jesse Gelsinger - gene therapy research participant - died from research role
- Prof. James Wilson - barred until 2010 from research on humans
- Research team failed to halt study on learning of serious toxicities, and failed to disclose risks to participants

EXAMPLES OF RESEARCH FRAUD

- ◆ University of South Florida - testing of drug for fetal lung development on pregnant women
- ◆ Multiple amniocenteses
- ◆ Failure to disclose alternative approved drug
- ◆ Private civil action, no prosecution

EXAMPLES OF ALLEGED FRAUD

- BioCryst Pharmaceuticals/University of Alabama-Birmingham- RN Renee Peugeot and Harry Snyder, Ph.D.-false reporting of results of lymphoma study- nurse and scientist convicted- 291 F. 3d 1291 (111th Cir. 2002)
- Pat Palmer, University of Iowa-fabricated interviews with autism families, her degrees, and her publications 69 F.R. 7488
- Lajuane Woodward - U. of Md.- fabricated interview records for teen HIV prevention program 68 F.R. 67450

HOW EXTENSIVE IS RESEARCH FRAUD?

- Some studies suggest- 40% of researchers are aware of misconduct but have not reported it. (Nicholas Steneck, U. of Michigan)
- Office of Research Integrity (ORI) handles HHS research-receives 150-200 reports/year
- NSF-100 misconduct complaints/year
- How many clinical trials have same issues?
- FDA Clinical Investigator Inspections/IRB Inspections

FOCUS IN CLINICAL RESEARCH ENFORCEMENT

- MAKING INSTITUTIONS AND SPONSORS RESPONSIBLE FOR THEIR CONDUCT
- MAKING INDIVIDUAL RESEARCHERS ACCOUNTABLE FOR THEIR ACTS
- EMPOWERING PATIENTS, SUBJECTS, AND COMMUNITIES

RESPONSIBLE INSTITUTION

- Sponsor
- Institutional review board (“IRB”)
- Contract research organization
- Site management organization
- University

INDIVIDUALS

- INVESTIGATOR
- CLINICAL COORDINATOR
- IRB MEMBER
- TREATING PHYSICIAN

RELEVANT LAW (available at <http://ohsr.od.nih.gov/guidelines>)

- NUREMBERG CODE
- DECLARATION OF HELSINKI
- BELMONT REPORT
- COMMON RULE (PROTECTION OF HUMAN SUBJECTS) - 45 CFR 46
- FDA INFORMED CONSENT/PARTICIPANT PROTECTION RULES 21 CFR Part 50, 21 CFR Part 56 (IRBs)

AGENCY EXPERTISE

- Office for Human Research Protections (“OHRP”)-<http://www.hhs.gov/ohrp/>
- Office of Research Integrity (“ORI”) (<http://ori.dhhs.gov>)
- FDA (clinical trials, post-marketing studies)
- AAHRPP (PRIVATE ACCREDITER)
- AAU - GUIDELINES FOR RESEARCHERS’ CONDUCT
- AAMC

BAD ACTS

- MISLEAD/MISTREAT SUBJECTS
- MISLEAD/ CHEAT SPONSORS AND PAYORS
- FAKE SCIENCE
- FAKE SCIENTISTS

FRAUDULENT CONDUCT

- RECRUITMENT
- QUALIFYING
- GHOST SUBJECTS
- FORGED OR FALSE CONSENT FORMS
- THREATS TO PATIENTS
- IRB VIOLATIONS

FRAUDULENT CONDUCT

- FAILURE TO BLIND PLACEBO
- FRAUD IN CONDUCTING RESEARCH
- FAILURE TO DISCLOSE RELATIONSHIP, RISKS, AND BENEFITS
 - ◆ December 2003 - Los Angeles Times- hundreds of payments from drug and biomedical companies to NIH employees, including lab chiefs and institute directors
 - ◆ September 2004 NIH announces ban on all agency employees accepting payments from drug companies “for at least one year”-Los Angeles Times 9/24/04

Corporate Compliance and RESEARCH - The New World

- Effective reporting and compliance system?
- Who gets the reports? Who checks the reports?
- Who certifies that the system is effective?
- CEOs, auditors, attorneys
- Who knows where it is not effective?

COMPLIANCE AND RESEARCH-THE NEW WORLD

■ PROPOSED NEW REGULATIONS

“Responsibilities of Awardee and Applicant Institutions for Dealing with and Reporting Possible Misconduct in Science” 42 CFR 50 is to be replaced with new 42 CFR 93. See 69 F.R. 20778, April 16, 2004

- Institutional Review Boards registration requirements for human subject research conducted or supported by HHS, 45 C.F.R. new part 46, see 69 F.R. 40584, July 6, 2004 (similar rule proposed for FDA)

COMPLIANCE AND RESEARCH-NEW WORLD

■ PROPOSED NEW REGULATIONS

- ◆ FDA Foreign clinical trials - June 10, 2004
- ◆ FDA Additional Safeguards for Children- April 2001 interim rule - final rule 11/04
- ◆ HHS - Advance Notice of Proposed Rulemaking - adults with impaired decision making

ENFORCEMENT IMPLICATIONS OF THE NEW WORLD

- Major efforts at education
- Major efforts at compliance in some institutions and organizations
- Enforcement actions among those who decide not to comply.

IN RE CAREMARK, 698 A. 2d 959 (Del. Ch. 1996)

- “A DIRECTOR’S OBLIGATION INCLUDES A DUTY TO ATTEMPT IN GOOD FAITH TO ASSURE THAT A CORPORATE INFORMATION AND REPORTING SYSTEM, WHICH THE BOARD CONCLUDES IS ADEQUATE, EXISTS. . .” SO THAT THE BOARD CAN REACH INFORMED JUDGMENTS ABOUT COMPLIANCE WITH THE LAW.

In Re Abbott Labs 325 F. 3d 795(7th Cir. 2003)

- “breach of duty to exercise appropriate attention” “unconsidered inaction”
- Press coverage, qui tam suits, government investigations, audit information can be considered in determining whether failure of directors to act “constitutes a lack of good faith”

HOW WILL WE FIND OUT?

- WHISTLEBLOWER PROTECTION
 - ◆ FALSE CLAIMS ACT
 - ◆ CONSCIENTIOUS EMPLOYEE PROTECTION ACT (NJ)
- TORT AND CLASS ACTION CLAIMS
 - ◆ Alan Milstein, sskrplaw.com
 - ◆ Inspection reports, self-reporting

OUR GOALS

- Advancing knowledge
- Protecting human (and other) subjects
- Assuring integrity and accuracy in science
- Assuring fairness in the awarding and use of public funds