Clinical Research – The Intersection between Commercial Interests and Government Regulation

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Perfect Storm of Pressures on Clinical Research

- Professional Pressures
- Scarce Government Funding
- Commercial Pressures
Agenda

- Recent cases against clinical researchers and institutions
- Strategies to avoid becoming the target of a government investigation
- Intersection between the regulatory framework and the government enforcement agenda
- Ethical considerations
Garden Variety Fraud

- Falsification and fabrication of data in federal grant applications
- Government action under the False Claims Act
- *Qui Tam* actions
United States v. Poehlman: Misrepresentation of Results

- Dr. Poehlman fabricated data in grant applications
- Dr. Poehlman – Principal Investigator
  - Certified that the information contained in the applications was true and correct
Penalties Imposed on Dr. Poehlman

- **Civil Penalties:**
  - $180,000 fine
  - Permanent ban from all federal healthcare programs
  - Retraction of articles

- **Criminal Penalty:**
  - Prison term – one year
Harold F. Farber, M.D.: Misrepresentation Regarding Supervision of Clinical Research

- Dr. Farber was a Principal Investigator on a clinical study of a cream manufactured by 3M Pharmaceuticals
- Substantial portions of the assessments not performed by qualified dermatologist
- Falsely represented to the FDA that he performed all the clinical examinations for the study
Potential Consequences for Dr. Farber

- One year prison sentence
- $100,000 fine
- One year supervised release
University of Pennsylvania and Dr. James M. Wilson

- Jesse Gelsinger case – volunteer gene therapy trial administered by Dr. Wilson at the University of Pennsylvania Institute for Human Gene Therapy (“IHGT”)
- Dr. Wilson and the University had substantial monetary interests in the success of the trial
- Results of the government investigation
  - Improper continuation of the study
  - Misrepresentation of clinical findings
  - Failure to adequately inform participants of the risks associated with the therapy
Financial Conflicts of Interest

- Dr. Wilson was part-owner of Genovo, Inc. which owned the rights to new products developed by Dr. Wilson at IHGT
- In exchange, Genovo, Inc. funded clinical trials at IHGT including the one in which Gelsinger participated
- Biogen, another biotechnology company, paid Genovo, Inc. $37 million for the right to market any liver therapies developed by Genovo, Inc.
- Genovo, Inc. shared a portion of the $37 million with IHGT
Government Action Under the False Claims Act

- False claims and statements in grant applications and other funding documents
- False claims and statements to the FDA
- False claims and statements in connection with informed consent of participants
- False claims and statements to the IRB
Penalties Imposed on Dr. Wilson

- Banned from FDA-regulated clinical trials until 2010
- Training and education requirements for human research participant protections and clinical research
- Restricted clinical activity with a Medical Monitor or Contract Research Organization
- Oversight by a Special Monitor
Penalties Imposed on University of Penn

- Half million dollars in fines
- Increased oversight
- Revised policies and procedures
- Additional training requirements
University of Pennsylvania's Increased Oversight

- The University of Pennsylvania must:
  - Increase the IRB oversight of clinical research
  - Conduct initial monitoring and oversight of clinical research through an independent Contract Research Organization
  - Create an Office of Human Research to review informed consent, adverse events, and compliance with protocols
Corrective Action Taken

- Institute a policy that requires researchers to obtain a certificate that training was completed before an IRB can review a protocol
- Revise and strengthen its standard operating procedures to more clearly delineate roles and responsibilities of sponsors and investigators
University of Pennsylvania Training Requirements

- All investigators and clinical coordinators who participate in clinical research must undergo training on topics including regulatory requirements, conflicts of interest and informed consent.
GlaxoSmithKline ("GSK")

- Intentional suppression of study results showing Paxil might lead to suicidal thoughts in adolescents.
- Failure to disclose negative study results to physicians.
Strategies to avoid becoming the target of a governmental investigation

- Establish a data and safety monitoring plan
- Establish an effective compliance program
- Establish an effective conflict of interest policy
A data and safety monitoring plan should include:

- Mechanism to monitor progress of trials and participant safety
- Procedure for reporting adverse events
- Plan to ensure data accuracy and protocol compliance
- Data and safety monitoring board adds an additional layer of protection
Elements of an effective compliance program must include:

- Written policies and procedures reflecting the institution's commitment to compliance
- Designation of a compliance officer and a compliance committee
- Education and training for all affected employees regarding the institution's compliance program
Compliance Program (cont’d)

- Creation and maintenance of an effective line of communication between the compliance officer and all employees
- An internal monitoring and auditing program to identify problem areas
- Enforcement of standards through disciplinary action
- Policies and procedures to investigate misconduct and take prompt corrective action
- Clearly defined roles and responsibilities and assignment of oversight responsibilities
Draft compliance program released by HHS Office of Inspector General in November 2005

Applied only to Public Health Service grant recipients

HHS withdrew the draft compliance in June 2006

Research Business Models Subcommittee expected to develop guidelines that would apply to all federal agencies

Speculation that new guidelines will be less prescriptive than OIG’s draft compliance program
An effective conflict of interest policy should include:

- Designation of an official to solicit and review financial disclosure statements from each investigator who participates in the research
- A requirement whereby investigators must update financial disclosures during the grant period
- Guidelines to identify conflicting interests
- A plan to manage, reduce, or eliminate conflicting interests
Conflict of Interest Policy (cont’d)

- A policy for maintenance of all financial disclosure records and records of any action taken by the institution in response to any identified conflict of interest
- A policy of making available to the pertinent government agency information regarding all conflicting interests identified by the institution and how those interests have been managed, reduced, or eliminated
- A procedure whereby conditions are imposed on investigators for whom a conflict of interest exists
The Intersection Between the Regulatory Framework and the Government Enforcement Agenda

- False Claims Act
- Qui Tam
- Fraud
1. Are financial relationships bound to influence the way researchers view data?
2. Are there additional concerns aside from the way in which clinical researchers interpret data?
3. Why don’t clinical researchers always disclose conflicts of interest?
4. Can scientists avoid commercial financial ties altogether?
5. What other reforms are likely in the future?