Conflict Of Interest In Clinical Research In The U.S.

TOHOKU UNIVERSITY
SENDAI, JAPAN

THEODORE J. ROUMEL PhD MPH

NOVEMBER, 2007
Discussion

- Non Financial Conflicts
- Financial Conflicts
- Institutional Conflicts
- Issues in the U.S.
- Actions To Avoid/Manage
Conflict of Interest—A New Concept?

- Doctor/patient--Trust Relationship
  - Ancient Greece—Hippocratic Oath

- Cultural Differences

- Personal And Institutional Conflicts

- Financial
Definition Of Conflict Of Interest

- Personal And Financial
- Institutional Financial
- Real And The Appearance
Non Financial Conflicts

COI Exists When Two Or More Contradictory Interests Relate To An Activity By An Individual Or An Institution

- Known As Misconduct In Science
- Benefit From Publication And Receipt Of Funding
- Pressure To Publish To Retain Position Or Advance (Tenure)
- Win Recognition---Noble Prize
- Physician vs. Study Director—Patient Or Study Best Interests?
Financial COI

- Equity, Patent Or Other Commercial or Financial Interest By Individual, Family, Others In Research That Could Influence Interaction With Potential Research Participants And Conduct Of Study
Definitions

Conflict Lies In A Situation Not In Any Behavior Or Lack Thereof; Ex. Conflict Between Financial Gain And Completion And Careful Reporting Of A Research Study

COI Are Situations In Which Financial Or Other Personal Considerations May Compromise Or Have The Appearance Of Compromising An Investigator’s Judgment In Conducting Or Reporting Research---AAMC

COI Exists When The Individual Has Interests In The Outcome Of The Research That May Lead To A Personal Advantage And That Might Therefore, In Actuality Or Appearance, Compromise The Integrity Of The Research—NAS
Definitions Cont.

COI Is When Financial Consideration May Compromise Or Have The Appearance Of Compromising An Investigator’s Professional Judgment In:

- Conducting Or Reporting Research
- Affects Collection, Analysis And Interpretation Of Data
- Hiring Of Staff
- Procurement Of Materials
- Sharing Of Results
- Choice Of Protocol
- Involvement Of Human Participants
- Statistical Methods Used
Institutional COI

An Institutional Financial Conflict May Occur When The Institution, Any Of Its Senior Management Or Trustees, A Department, School, Other Sub-unit, An Affiliated Foundation Or Organization:

- Has An External Relationship Or Financial Interest In A Company That Itself Has A Financial Interest In A Faculty Research Project.
- Serve On The Boards Or Have Other Relationships With Organizations That Have Significant Commercial Transactions With The University.

The Existence Or Appearance Of Such Conflicts Can Lead To Actual Bias Or Suspicion About Possible Bias

Failure To Evaluate Or Manage—Issue With Mission, Obligation Or Values Of The University.
Examples Of Conflicts

- Serve As Director, Officer Or Other Decision Maker For Commercial Sponsor Of Human Subjects Research (SHSR) At Your Institution
- Holding Stock Or Stock Options In Commercial SHSR (Unless Held In Blind Trust)
- Receiving Compensation For Service As Consultant Or Advisor To Commercial SHSR
- Receiving Honoraria From Commercial SHSR
- Receipt Of Travel Or Gifts From SHSR
- Receiving Royalties Or Named Inventor On Patents Or Invention Reports For Products Being Evaluated In SHSR
Examples Continued

- Receive Payments Based On Research Outcomes
- Personal Or Outside Relationships With Sponsor Of SHSR
- Have Financial Interest In Companies With Similar Products Know To Investigator To Be Competing With Product Under Study
- Institutional—Taking Company Stock; Alumni; Donors
- Financial Interest Of Others In Outcome
  - SEC—Insider Trading--Even Though Not Make Income
  - ImClone/Martha Stewart Case
Press Reports

- Gene therapy researchers defend trial after death of patient
- Researchers not report adverse events
- Patient was too sick to be in trial
- Key researcher had financial interest in outcome of trial
Press Continued

Late in the afternoon of December 28, 2001, the fax machine whirred at the SoHo offices of ImClone Systems, spooling out a stunning announcement. Citing shoddy data and poor research design, the FDA had spiked the company's application to file for approval for its much-anticipated cancer drug, Erbitux. For the officers and employees of the hot young biotech firm, it was a very bad day -- and the start of two very bad years.

One month later, in January 2002, things got worse. Federal regulators announced that they were launching an investigation into possible insider trading by the company's founder and CEO, Sam Waksal. Within the company, shock was compounded by a sense of betrayal: Waksal had attempted to unload his stock just before the FDA's announcement. When that news surfaced, it undermined investors' belief in Erbitux's efficacy, casting a pall over the entire enterprise.

Waksal given 68 months in prison

Martha Stewart avoided a loss of about $51,000 by selling nearly 4,000 shares of ImClone stock on Dec. 27, 2001, rather than the next trading day, when the stock fell after the FDA rejected the company's application for a key cancer drug. She went to jail for not being truthful to Federal investigators.
Insider Trading

- SEC Investigations

- Buying or Selling a Security While Having Material, Nonpublic Information About the Security, in Breach of a Fiduciary Duty or Other Relationship of Trust and Confidence.

- May Also Include "Tipping" Information, Securities Trading by the Person "Tipped," and Securities Trading by Persons Who Misappropriate Such Information.

- A Felony, Subject to Criminal and Civil Penalties--SEC Can Levy Large Civil Penalties for Violations—Even If You Do Not Benefit.
Why Does It Matter?

- Threaten Central Ethical Core In Scientific Pursuit Of Truth And Undermine The Public Trust In Science
  - Dr. Akihisa Inoue stated goal: it is essential for us to aim at becoming a top-level, world-class research institution
- COI In Clinical Research Settings Can And Have Been Associated With Injury And Death Of Research Participants
Investigators and administrators must consider the perception of investigator or institutional gain may distort the value of the participants role in the trial. Ambiguities or appearance of questionable judgment by individuals or institutions are unlikely to be tolerated by the public when the research places at risk the life or health of a participant. (AAU/AAMC)
Discussion

- It is Not Possible, Nor Necessary to Eliminate All Perceived, Potential or Real COI

- The Concern is How Individuals and Institutions Identify and Respond
History In U.S.

- Long Concern Over Patient Care
- Increased Concern With Full Disclosure To Patients
- Understandable Documents
- Litigation
  - Gelsinger/U Penn And Others
  - Insider Trading
Actions In U.S.


- NIH Conducting Reviews Of Grant Recipients On Selected Basis

- Journals Entered Discussion

- Collaborations Between Academia & Industry to Resolve Concerns

- Goal is to Ensure Clear Understandings
Keys to Managing COI

- Patient Well Being Is Paramount
- Disclose Any Conflict
- Provide Information In Informed Consent Documents
- Oversight Of Conduct Of Research Or Review Of Data Analysis
- Transparency
Clinical Trial View From Industry

- Principle Purpose Of Clinical Trials:
  - To Advance Knowledge Of Researchers And Regulators To Enable New Treatments And Cures To Be Developed

- Conducted In Accordance With Applicable Laws And Regulations, Well Recognized Principles Of Good Clinical Practice (GCP) Wherever In The World Trials Are Conducted

- Must Comply With Standards Published By International Organizations Such As The International Conference On Harmonization (ICH) When Results To Be Used For A Medicine Approved In The US, Europe Or Japan

- Clinical Trial Publications Mimic Academic Concerns
Informed Consent Disclosures

- Benefit And Risk From Research

- Investigator Or Institution Is Receiving Payment For Conduct Of Clinical Trial
Informed Consent Continued

- Payment To Clinical Investigators Should Be Reasonable And Based On Work Performed Not Any Other Considerations—
  - Contract In Place Stating Research Services To Be Provided And Basis For Payment For Those Services;
  - Not Tied To Outcome;
  - Investigators Or Their Immediate Family Should Not Have Direct Ownership Interest In The Specified Pharmaceutical Product Being Studied;
  - Investigators And Institutions Not Be Compensated In Company Stock Or Stock Options For Work Performed On Individual Clinical Trials.
Informed Consent Continued

- Data And Safety Monitoring Board Or Committee (DSMB) And Reports To Regulatory Authorities
  - DSMB—Clinical Investigators In Clinical Trial Of Pharmaceutical Product Should Not Serve On The DSMB Monitoring Team Or Other Trials Of Similar Product
  - Voting Members Of DSMD Should Not Have Any Financial Interests Or Other Conflict That Would Preclude Objective Determinations.
Summary

- COI Exists At Many Levels
- COI Must Be Disclosed
- COI Can Be Managed
Contact Information

Theodore J. Roumel PhD MPH
roumelt@aol.com
202-253-8380

University of Maryland Biotechnology Institute
roumel@umbi.umd.edu
240-314-6509
410-800-4109