



Conflict of Interest

- Describes a *situation*, not a *person*
- Ubiquitous, but not (always) iniquitous
- Can involve individuals
- Can involve organizations



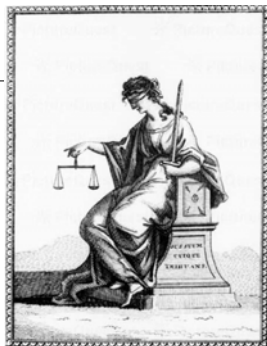
What COIs are *Not*

- Just *any* set of interests in conflict
- Straightforward *bias*
- Conflicts of *commitment*



What is COI?

- A situation that fosters a tendency or temptation to reach a biased judgment, take a biased action, or give biased advice



Why Worry?

- Jesse Gelsinger
 - Adenovirus-mediated gene transfer for OTC
 - Direct infusion in liver
 - First death directly attributable to gene transfer
 - Professional and institutional COIs



Sources of COI

- Genova provided \$2.8M/yr to Institute Director's lab
- Director held substantial equity in Genova
- Institution also held substantial equity



What Went Wrong?

- Gelsinger did not meet inclusion/exclusion criteria at time of trial
- Protocol not strictly followed
- Not all adverse events disclosed



The context of COI

- What is the *relationship*?
- What *judgments, actions or advice* are central to that relationship?
- What *interests* might influence?
- What constitutes "*proper exercise*" of professional discretion?



- "A trustee is held to something stricter than the morals of the market place. Not honesty alone, but the punctilio of an honor the most sensitive, is then the standard of behavior."

– Justice Benjamin Cardozo, 1928



Who Counts?

- Agents
 - Scientists, post-docs, grad students
- Principals
 - Individuals, groups, or institutions to whom the agent has duties
- Society



Relationship: Multiple Principals, One Role

- Lawyers whose firm represents adversaries
- MDs in capitated Managed Care Organizations



Relationship: Multiple Roles, One Principal

- Figure skating judges at Salt Lake City Olympics
- Stock analysts
- MDs recommending enrollment in a clinical trial?



Scientists, Roles and Principals:

- *Patients:* Physician & Investigator
 - “Therapeutic Misconception”
- *Grad Student/Post-Doc:* Supervisor/Mentor & Agent of Corporate Sponsor
- *University:* Employee/Representative & Biotech Entrepreneur
- *Journal Editors:* Peer reviewer & Scientific Rival & Business Competitor



Types of Conflicting Interests

- Relational
 - Nepotism
 - Like/Dislike
 - Sexual
- Reputational
 - E.g., lawyer hedging advocacy for an unpopular client



Types of Conflicting Interests

- Occupational
 - Preserving or enhancing your standing with employer or supervisor



Types of Conflicting Interests

- Financial
 - Why focus on financial?
 - Quantitative
 - Pervasive
 - Mode of action can be subtle
 - Source of public suspicion and mistrust



“Proper Exercise” of Professional Duties

- What should we expect from biomedical scientists?
- What duties do scientists assume to their students, colleagues, institutions, sponsors, society?



Dealing with COIs

- Avoid
 - Firewalls, policies
- Escape
 - Recusal, divestment, resignation
- Disclose
 - Common, but not a panacea
- Manage



Today's "Agents" in Biomedical Research

- Investigators
 - PIs
 - Site-specific leaders
 - Associate investigators
- Other research team members
 - Research nurses
 - Technicians
 - Data gatherers



More "Agents"

- IRBs & their members
- Academic Medical Centers
- Universities
- Community Hospitals
- Physician Practices



More Yet!

- Sponsors
 - Government
 - Private Not-for-profit
 - Pharma
 - Biotech
 - Device manufacturers
- CROs (Contract Research Organizations)
- SMOs (Site Management Organizations)



Business and Science

- By mid to late 1990s
 - >90% of life science firms had UIRRs
 - ~25% of life science research faculty received industry support
 - >50% had consulted
 - ~7% held equity



Business and Universities

1999 survey of US and Canadian universities:

68% held equity in research undertaken by their faculty



The Changing World of Clinical Research

- In 1992 Pharma R&D surpassed NIH R&D
- The gap has grown ever since: Pharma R&D of ~\$20B in 2000; ~10%/yr
- Outsourcing grows 15-20%/yr
- CRO share grows >20%/yr



What SMOs Do

- Market investigative sites to Pharma, Bio, and CROs
- Negotiate contracts
- Get IRB approvals
- Enlist & train investigators
- Recruit & enroll patients
- Standardize site practices



AAMC Task Force on Financial Conflicts of Interest in Clinical Research

Individual COIs (2001)
Institutional COIs (2002)



What is at Stake

- Integrity of Science
- Public Trust
- The Future of Clinical Research