

# **The Perfect Storm: Conflicts of Interest in Research: Ethical, Regulatory, and Practical Considerations**

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## **Overview of today's discussion**

- COI is in the spotlight—expect scrutiny
- A brief history of how we got here: the tragedies, the mixing of marketing and medicine AND
- The result: where there is heat, regulatory action follows—some anticipated actions
- Practical steps to prevent, identify and manage conflicts of interest in research

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## Conflict of Interest—IOM

- A circumstance that creates a risk that professional judgment or actions toward a primary interest will be unduly influenced by a secondary interest
- Primary interests
  - Welfare of patients
  - Integrity of research
  - Quality of medical education
- Secondary interests
  - Financial gain
  - Professional advancement (name and reputation)

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## The Gelsinger Tragedy

- Dr. JW conducted gene therapy experiments at Penn while maintaining a majority interest in Genovo, a biotech company. Penn's Conflict of Interest Standing Committee ("CISC") reviewed the conflict.
- The informed consent did not address the FCOI.
- Jesse Gelsinger died after receiving the experimental gene therapy .
- The bioethical considerations for human subjects research were changed for all investigations.

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### *Taking the Fun Out of Popping Pain Pills*

by Natasha Singer, NY Times, September 20, 2009

- “ ...Drug companies have promoted novel opioids as nonaddictive on other occasions and failed, said... Dr. NK, the chief executive of Analgescic Research, a research and consulting firm in Boston that specializes in the development of pain treatments, who is also a neurologist and adjunct faculty member at Tufts University medical school.”
- “(Dr. K and every other expert quoted here say they have worked as paid consultants for King Pharmaceuticals or conducted research sponsored by the company).”

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### Drugs, devices and doctors: NY Times, Dec. 16, 2005

- “O.K., it's sounding complicated. But the essence is simple: crucial scientific research and crucial medical decisions have to be considered suspect because of financial ties among medical companies, medical researchers and health care providers.” Paul Krugman on COI at Cleveland Clinic

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## 2007 begins Senatorial review of COI: cloudy with a chance of storms

- Senator Grassley focuses on conflicts in academic medicine—waste of public dollars for funding research
- Stanford, Emory, Harvard all have gotten a “Grassley letter”, and have engaged in both the response to the Senator and with the press.
- Ghostwriting, medical journals, IRBs, the NIH—everyone is on the list

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## Threats of undisclosed conflicts of interest

Global concerns:

- Integrity of professional judgment
  - Gelsinger case
  - Harvard students and professorial failure to disclose
- Public confidence
  - Everyone understands the “pizza run”
  - “Look for pens and logo stuff...”

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### *Ghosts in the medical machine*

by Miriam Hill, Philadelphia Inquirer, September 20, 2009

- “When GlaxoSmithKline P.L.C. marketers looked for doctors to promote the antidepressant Paxil, they called the project CASPPER...The name was more than just an offbeat tribute to the friendly cartoon ghost. It was a wink and a nod to "ghostwriting," a questionable practice in which scientists put their names on research written by someone else, usually a writer paid by a drugmaker. “

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### COI in practice

A conflict of interest arises when an individual's private interests (such as outside professional or financial relationships) might interfere with his or her professional obligations to Stanford. Such situations do NOT necessarily imply wrong-doing or inappropriate activities. However, in a research university setting, they can compromise, or be perceived as compromising, important academic values, research integrity, or the university mission.

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## Pay for play in the lab?

- Does a \$2.00 pen sway your judgment?
- How about an all-expense paid trip to Paris?
- How about assistance in preparing a key review of your research topic, right at the time when such a publication would vault you into tenure?
- Payment for service on an advisory board or holding stock in a company?

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## Unconscious bias

- Physicians, like the general public, have an optimistic bias: YOU might be swayed, but not me...
- Gifts and interactions with pharma, reported in numerous publications, show significant differences in prescribing patterns for drugs, favorable comments on company products...

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Existence of Conflict of Interest is not equivalent to lack of integrity or bias. Having a conflict increases the risk that decisions could be influenced by that COI. Thus COI review always must address the reality and the appearance of conflict. Partnership between industry and academia has great contributions to make—but must be managed to support trust in professional judgment.

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## Federal engagement in COI

- Bayh Dole requires translation from bench to bedside
- MedPac addresses COI concerns based on effect on Medicare costs
- FDA has extensive requirements for COI
- NIH considers revisions to PHS COI regulations
- Senator Grassley's "Sunshine Act"
- Six states require disclosure of payments to providers

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## Bayh-Dole Act 1980

- permits recipients of federal funds to obtain the title to the inventions they develop under their federally funded projects, and to transfer the technology to the private sector.
- requires federally funded researchers to obtain a patent for products developed, to seek commercial opportunities, and to report to the National Institutes of Health (NIH) on the use of their discoveries.

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## MedPac Report to Congress: Medicare Payment Policy, 2009

- Concern is for both overt and subtle commercial effect
- At least some interactions associated with rapid prescribing of newer, more expensive drugs and request for addition to hospital formularies
- Influence over medical education may skew information received by students and practitioners

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## MedPac Report to Congress, 2009

### Public Reporting of Physician Financial Relationships

One purpose of establishing a national reporting system [for pharma, device and biological companies] to post payments to providers is “encouraging physicians to reflect on the **propriety** of their relationships with industry...”

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## NIH and Advanced NPR

- Congressional and OIG reviews of NIH COI, both internal and external, have raised concerns
- Current consideration: First comprehensive review of PHS COI since 1995

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## Areas for possible rulemaking

- Expanding Scope of the Regulations and Disclosure of Interests
- Revising Definition of “Significant Financial Interest”
- Adopting New Requirements for Identification and Management of Conflicts by Institutions
- Enhancing Methods for Assuring Institutional Requirements
- Requiring Institutions to Provide Additional Information to PHS
- Amending Regulations to Address Institutional Conflicts of Interest

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## States and the Feds seek disclosure of payments to physicians

- Vermont, Maine, West Virginia, and DC all require disclosure but not in a public data base
- Minnesota and Massachusetts have public data bases but they are not searchable
- Physician Payment Sunshine Act 2009—Grassley-Kohl will require manufacturers and group purchasing organizations to report on payments greater than \$100 to physicians and physician-owned entities

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## Addressing COI

- Remove the conflict
- Disclose the conflict
  - Insufficient to address most COI
  - Human Subjects Research
    - A rebuttable presumption that researchers may not do research when there is a financial COI. Eringhaus and Korn, 2004.
    - Zero tolerance for financial relationships
- Manage the conflict

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## Management of COI

- Monitor research
- Disclosure through informed consent
- Audit informed consents and research process
- Establish Data Safety Monitoring Board
- Education and discussion with students, trainees, junior faculty
- Assure that all contributing authors are named

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## Stanford policies on COI

- Annual Faculty Disclosure
- Stanford Industry Interactions Policy  
<http://med.stanford.edu/coi/siip/>
- Institutional COI (including leadership)  
<http://rph.stanford.edu/4-7.html>
- CME requirements (added to annual disclosure)
- Clinical COI (added to SIIP)
- Overview: <http://med.stanford.edu/coi/>

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## The Storm is Here – What Next?

### COI risks

1. Misunderstanding institutional disclosure requirements—education matters
2. Departmentally- and faculty-funded studies are risky
3. Failure to assess risk adequately--did the institution know what it should have?
4. Failure to document basis for exceptions to rebuttable presumption: reflection of balancing likelihood of influence with seriousness of harm

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## Practical guidelines for COI programs

- Identify all key players and offices.
  - conflicts of interest or commitment reports to the Institution, and the committees that oversee management, mitigation or elimination of these conflicts
  - reports to the NIH and other funders concerning conflicts that relate to externally funded programs
  - for clinical researchers, clinical conflict reports to the hospital and, if the university is separate from the hospital, also to the university
  - disclosures in publications and presentations
  - disclosures in didactic teaching sessions
  - disclosures in informed consent documents
  - disclosures to the Institutional Review Board, IACUC, and Stem Cell Research Oversight Committee

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## Practical guidelines for COI programs

- Establish clear roles and responsibilities.
- Document basis for exceptions to rebuttable presumption: balance of likelihood of influence with seriousness of harm
- Think through the process--practicality and rational analysis matter.
- Address "appearance" concerns realistically
- Communicate, communicate, and communicate.
- Only a well-educated community can follow COI rules.
- Committed leadership is critical

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## After the Perfect Storm: the weather prediction

- Congressional scrutiny, both directly and indirectly by reviews of individual physicians by the Finance Committee will continue—and increase with headlines
- The Sunshine Act, if passed, might be helpful in federalizing a national issue
- Management and mitigation of COI will be more closely reviewed by NIH and other groups
- Clinical COI will increasingly require disclosure and perhaps meaningful disclosure
- Major storm warning: significant harm to patient or research subject...

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