_conflicts of interest in research

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conflicts of interest in research

- what is a conflict of interest?
- why worry about conflicts of interest?
- historical roots of conflicts of interest in research
- what can be done about conflicts of interest?
- columbia policy and process
- changes in 2012

what is a conflict of interest?

a conflict of interest is not a behavior or a bias, but simply a situation in which a primary interest, such as a patient's welfare or the validity of research, could be unduly influenced by a secondary interest, such as financial gain.

1 new england journal of medicine 1993:329 (8).
What are “primary interests” in research?

- The integrity of the research
- The validity of the results
- The safety of research subjects
- The academic mission:
  - To advance knowledge
  - To develop new technologies and treatments
  - But not to increase shareholder values

What are some potential “secondary interests”?

- Career advancement
  - Tenure/Promotion
  - Funding
  - Publications
  - Awards
- Individual financial gain
  - Consulting/speaking fees
  - Stock or equity

Outside Financial Interests

- University faculty are allowed to participate in outside activities that can create financial interests, such as:
  - Consulting
  - Owning equity, including stock options
  - Receiving royalties
  - Serving in a management or fiduciary position (e.g., Board member, executive)
Faculty Handbook regarding Outside Interests:

- “Outside professional activities are an accepted part of academic life. They make faculty better scholars and teachers, and thereby better equip them to serve the University. Nonetheless… [they] create the potential for conflict….” CU Faculty Handbook (2008)

What’s wrong with conflicts of interest?

  Perceptions of conflict of interest disclosures among peer reviewers.
What’s Wrong with Conflict of Interest?

- Metaanalysis of articles concerning industry sponsorship of biomedical research:
  
  “Aggregating the results of these articles showed a statistically significant association between industry sponsorship and pro-industry conclusions.”


Calcium Channel Blockers

- Survey of authors of articles on calcium-channel antagonists to examine their financial interactions with pharmaceutical companies. Results compared with positions authors took about the products.
  - “S[trong] association between authors’ opinions about the safety of calcium-channel antagonists and their financial relationships with pharmaceutical manufacturers.”
  - “Sup[portive] authors were much more likely than critical authors to have financial associations with manufacturers of calcium-channel antagonists.”
  - “C[ritical] authors much less likely to be financially associated with manufacturers.”

  Stelfox HT et al., Conflict of Interest in the Debate over Calcium-Channel Antagonists, NEJM, 1998;338:101-106

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  Stelfox HT et al., NEJM 1998;338:101-106
Author Relationships...

- Metaanalysis of studies of lumbar fusion device with at least one undesirable outcome for 10 or more subjects:
  - “Over half of reports (60%) ... had industry support or evidence of potential conflicts of interest....”
  - “Potential author conflicts of interest ... were associated with significantly more favorable assessment of fusion.”


Why worry?

- Public suspicion or mistrust
- Bias in research
- Recklessness in recruitment or treatment of subjects
- Unfair treatment:
  - of personnel
  - of competitive work
- Can lead to research misconduct

History of Academia/Industry Relationships

- Pre-WWII:
  - Pharmaceutical industry began to develop independent research capability, collaborated with academia.
- Post-WWII:
  - Relationships flagged as government funding increased.
  - But public’s expectation was, taxpayer-funded research should benefit the taxpayer. Therefore need industry collaboration
- 1980s:
  - Government funding slows down; biotech industry develops.
  - Bayh-Dole Act (1980)

Bayh-Dole Act

“It is the policy and objective of the Congress to use the patent system ... to promote collaboration between commercial concerns and nonprofit organizations, including universities....”


1980 - The Bayh-Dole Act

Under the Bayh-Dole Act:
- Universities are permitted to retain intellectual property rights to inventions funded by federal dollars
- Universities are encouraged to commercialize inventions where possible
- Universities can retain royalties earned from those inventions
- The inventor (i.e. researcher) is entitled to a share of royalties

Federal guidelines and professional guidance

Over the past 20-30 years, industry/academic collaborations grew.
In response, federal agencies and professional societies began to define conflict of interest guidelines.
  - NIH Objectivity in Research regulations
  - AAMC/AAU White Papers
What about the research subjects?

- 1999: Jesse Gelsinger, patient in a gene transfer trial to treat a liver disorder, died shortly after receiving study treatment.
- After Gelsinger's death, it was revealed that:
  - Researchers and an office of the university held patents covering several aspects of the study technology.
  - The PI, colleagues, and the university held equity in Genovo, the biotechnology company involved.
  - Relationships not disclosed to Gelsinger in informed consent.
- 2000: Gelsinger's family sued University, Genovo, researchers, and Hospital. Settled out of court.

“Thought Leaders” and “KOLs”

Thought-Leader Management: A Challenge Met

By John Mack

“Pharmaceutical companies are continually working to establish and maintain relationships with thought leaders— influential physicians who play an important role in communicating a new therapy’s benefits to other physicians. Thought Leaders—also known as Key Opinion Leaders, or KOLs—help pharmaceutical companies identify unmet medical needs, shape clinical studies, launch products, and understand critical lifecycle issues. However, across the medical device and pharmaceutical industries, thought leader management programs have not been as effective as internal management would like…. This article reviews Medigent® Thought Leader, a Web-based software suite designed to dramatically improve a pharma company’s communications with Key Opinion Leaders.

Order and pay for this reprint now using your credit card... [Link]
New NIH Regulation

- Broadsens scope of financial interests that investigators need to disclose to the University
- Broadsens scope of University review of disclosed financial interests
- Broadsens requirements for the University to report to NIH
- New requirements for disclosure to the public
Overall CU Policy Approach

- 2009 Policy anticipated some changes in the new regulations.
  - Some technical amendments are needed.
- We will continue to have a single overall Policy governing Columbia research.
- We will continue to have a single set of "Research" questions in our disclosure.
- Some implementation will be specific to NIH-funded research and researchers.

New NIH Regulation: Investigator obligations

- Broader disclosure:
  - All "significant financial interests" (SFI) that relate to investigators' "institutional responsibilities," not to their research.
  - SFI also includes "any reimbursed or sponsored travel".
- Mandatory training every 4 years.

New NIH Regulation: University obligations

- Determinations project-by-project
- Management
- Reporting
- Review/Mitigation
- Public disclosure
New NIH Regulation: University obligations

Project-by-Project Determinations

1. Do the disclosed SFIs “relate” to the research project?
   - Lower threshold for SFI - $10k is now $5k

2. If yes, is there a “financial conflict of interest”?
   - “Stricter standards” provision

New NIH Regulation: University obligations

Management

- Implement a management plan to address FCOI
  - “To ensure, to the extent possible, that the design, conduct, and reporting of research will be free from bias.”
- University must monitor on an ongoing basis

New NIH Regulation: University obligations

Reporting to PHS

- Initial FCOI Report prior to expenditure of funds
- Including: Project #, PI, conflicted investigator, SFI entity, nature and value of SFI (range), relation to research, key elements of management plan
- Annual updates and updates for new issues
New NIH Regulation: University obligations

Review/Mitigation

- **FCOI not identified or managed** in a timely manner (due to failure by an investigator to disclose or the institution to review or manage an FCOI)?
- University has 120 days to conduct a retrospective review of the investigator’s activities and related NIH-funded research
- Was there bias in the design, conduct, or reporting of the research?
- If bias is found, a mitigation report must be submitted to NIH documenting key elements of retrospective review, impact of bias on research, institutional plan to eliminate or mitigate bias

New NIH Regulation: University obligations

Public Disclosure

- Make available to the public – either on a website or promptly in response to requests from the public – information concerning FCOI’s of key personnel identified in connection with PHS research
- FCOI Policy must be publically available

Sunshine Act

- Part of 2010 health care reform law (Patient Protection and Affordable Care Act)
- CMS published proposed regulations in December 2011; public comment period closed on February 17
- Final rule expected in 2012
Sunshine Act

- Group purchasing organizations (GPOs) and manufacturers of covered drugs, devices, biologics and medical supplies must report to CMS:
  - All payments or transfers of value
  - made to physicians and teaching hospitals
  - in excess of $10, with a minimum annual threshold of $100 to each physician and teaching hospital.
- CMS to publish data on website

Sunshine Act

Categories of payment

- Consulting fees
- Compensation for services other than consulting
- Honoraria
- Gift
- Entertainment
- Food
- Travel (including the specified destinations)
- Education
- Research
- Charitable contribution
- Royalty or license
- Current or prospective ownership or investment interest
- Direct compensation for serving as faculty or speaker for medical education program
- Grant
- Other payments as defined by HHS

Is transparency enough?

- “Transparency alone cannot mitigate bias. Because industry relationships can create a ‘pro-industry habit of thought’, having financial ties to industry such as honoraria, consultation, or grant funding is as pernicious a problem as speaker’s bureau participation. Over four decades of research from social psychology clearly demonstrates that gifts—even small ones—create obligations to reciprocate.”
On the other hand…

Can’t we all just get along?

“NCATS aims to re-engineer the translation process by bringing together expertise from the public and private sectors in an atmosphere of collaboration and precompetitive transparency. Through partnerships that capitalize on the respective strengths of each, NCATS works with government, academia, philanthropy, patient advocates, and biotechnology and pharmaceutical companies to overcome translational roadblocks and offer solutions to detect, treat and prevent disease.”
