	FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL AND MASSACHUSETTS GENERAL HOSPITAL
	<b>Conflicts of Interest and Rare Diseases</b>  Susan H. Ehringhaus Senior Manager Office for Interactions with Industry
Office for Interactions with Industry	

---

---

---


---

---

---

---

---

	Office for Interactions with Industry
<b>Discosures</b>	
<ul style="list-style-type: none"><li>▪ Spouse: Director of PPD, Inc.; Director of Furiex, Inc.</li><li>▪ Ownership: Equity: PPD; Furiex</li></ul>	
	

---

---

---


---

---

---

---

---

	Office for Interactions with Industry
<b>Nat'l Context for Addressing Financial COIs</b>	
<ul style="list-style-type: none"><li>▪ Since 2005: Federal investigatory and enforcement storm clouds have darkened</li><li>▪ Congressional interest</li><li>▪ 2010: Notice of Proposed Rule Making from NIH</li><li>▪ 2010: Patient Protection and Affordable Care Act</li><li>▪ State transparency initiatives/company websites</li><li>▪ Popular press/scientific press</li><li>▪ <b>LESSON for rare diseases:</b> COIs are not in favor.</li></ul>	
	

---

---

---

---

---

---

---

---

# Conflicts of Interest and Rare Diseases

Susan Ehringhaus, JD


CCRDR September 21, 2010

Office for Interactions with Industry

---

### Current Science: Evidence of Bias in Medicine

- Gifts and favors tend to influence the recipient in favor of the donor (e.g.Dana).
- Prescribing patterns are influenced by the receipt of drug samples (e.g.Steinman).
- People are unlikely to think they're susceptible to being influenced but suspect their colleagues are (e.g.Dana).
- Industry funding of clinical trials is associated with pro-industry results (Wazanza, Jagsi).
- Linkages between undisclosed industry funding and clinical practice guidelines (Cosgrove, Choudhry).
- **LESSON for rare diseases:** Unconscious personal bias is a real risk

 FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL AND MASSACHUSETTS GENERAL HOSPITAL

---

---

---

---

---

---

---


---

Office for Interactions with Industry

---

### What's Different About Rare Diseases & COIs?

- Personal financial interests with industry abound
- For rare diseases, multiple roles = additional conflicts
  - Physician designs the trial
  - Physician enrolls the subjects
  - Trainees involved in the trial
  - Physician is the caregiver
  - Physician is the advisor to the disease foundation
  - Physician's research receives funding from the foundation and the patient's family
  - Industry involvement = Even more vulnerability
- So what are the standards for rare diseases?

 FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL AND MASSACHUSETTS GENERAL HOSPITAL

---

---

---

---

---

---

---


---

Office for Interactions with Industry

---

### Standards for Rare Disease COIs

- IOM Report (2009)
- AAMC standards for financial COIs in research on human subjects (2001, 2002, 2008)
- AAMC standards for financial COIs in clinical care (2010)
- For reconciling multiple roles, standards are derived from fundamental principles of medical professionalism
  - Primacy of the interests of the patient
  - Independence of professional judgment
  - Integrity of medical decision-making

 FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL AND MASSACHUSETTS GENERAL HOSPITAL

---

---

---

---

---

---

---


---

Office for Interactions with Industry

### AAMC Standards: COIs and Research

- Framework for Analysis of COI Cases
  - Risk-benefit analysis
    - Human subjects
    - Possibility/probability of bias
    - Data integrity
    - Benefit to the public, science
    - Alternative approaches
  - If conflicted researcher is allowed to continue, what should be the terms of a management plan?
- **LESSON for rare diseases:** Awareness of conflicting interests leads to evaluation of risks/benefits AND possibility of managing potentially biasing effects.

7



---

---

---

---

---

---

---


---

Office for Interactions with Industry

### How to Manage Research COIs

- Disclosure
  - Informed consent forms
  - Editors of any publications
  - In written and oral presentations
  - To all researchers and trainees on the research project
  - To supervisors, funders, other investigators in multi-site trials
- **LESSON for rare diseases:** Disclosure is a necessary (but rarely sufficient) strategy to address potential bias of the researcher.

8



---

---

---

---

---

---

---


---

Office for Interactions with Industry

### How to Manage Research COIs

- Human subjects
  - Under what circumstances, if any, should a conflicted researcher be allowed to participate in subject recruitment?
  - In subject selection, including prescreening for inclusion/exclusion criteria?
  - In the consent process?
  - In the clinical treatment of subjects?
  - In the clinical evaluation of subjects?
- **LESSON for rare diseases:** Substituting an independent investigator in some roles may mitigate potential bias.

9



---

---

---

---

---

---

---


---

Office for Interactions with Industry

### How to Manage Research COIs

- Research and data integrity
  - Independent, non-conflicted data monitoring?
  - Independent review of study design to address potential bias arising from the conflicts of interest in the roles of the physician/researcher?
  - Prohibition against the conflicted investigator being the principal investigator?
  - Prohibition against involvement in data collection?
  - Prohibition against involvement in data analysis?
  - External, independent analysis of entire project?
- **LESSON for rare diseases:** Independent evaluation of integrity of data and data analysis is not only useful; it can be essential.

10



---

---

---

---

---

---

---


---

Office for Interactions with Industry

### How to Manage Research COIs

- Type of research?
  - Early stage research?
  - High risk research?
  - Development vs. clinical validation
  - Late state research?
- Type of financial interest?
  - Equity stake?
  - Fiduciary position in an interested company ?

11



---

---

---

---

---

---

---


---

Office for Interactions with Industry

### How to Manage **Clinical** COIs

- AMCs should
  - Disclose industry ties of physicians to their communities as one method of managing actual and perceived conflicts in clinical care;
  - Clearly articulate the relationships, the value of the relationships, and the institution's efforts to mitigate bias resulting from them.
  - Use uniform standards and definitions across disclosure sites.
- **LESSON for rare diseases:** General transparency initiatives are essential tools in addressing clinical COIs.

12



---

---

---

---

---

---

---

---

Office for Interactions with Industry

### Managing Clinical COI – Patient Disclosure

- Should individual patients be informed of their physician's COIs?
- Very limited information on effects of disclosure of physician COIs on patients
  - Patients more likely than their physicians to believe that acceptance of company gifts may influence prescribing behavior (Gibbons et al).
  - Patients believed that certain kinds of payment methods to physicians could adversely affect the care they receive, but only half want to know what the financial incentives for physicians are (Kao et al).

PARTNERS  
FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL  
AND MASSACHUSETTS GENERAL HOSPITAL

---

---

---

---

---

---

---

---

Office for Interactions with Industry

### Managing Clinical COI - Patient Disclosure

- Limited information on effects of disclosure of COIs on research subjects
- Interests at stake (Weinfurt et al)
  - Informed decision-making
  - Patients' right to know
  - Maintaining trust
  - Minimizing legal risks
  - Deterrence of troublesome relationships
  - Protecting welfare of research subjects
- Trust is affected by disclosure but direction of effect varies.
- Some subjects don't have the baseline capacity to understand disclosed information and to judge any risks associated with it (Weinfurt et al).

PARTNERS  
FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL  
AND MASSACHUSETTS GENERAL HOSPITAL

---

---

---

---

---

---

---

---

Office for Interactions with Industry

### Managing Clinical COI - Patient Disclosure

- Other studies not involving subjects or patients
  - Experimental studies in psychology suggest unintended consequences from disclosure of COIs, e.g., disclosure resulting in advantage to the discloser rather than to the person to whom the disclosure is made (Cain et al).
- Anecdotal data from AMCs with disclosure websites
  - People don't often access the information.
  - They don't know what to do with this information even if they understand it.

PARTNERS  
FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL  
AND MASSACHUSETTS GENERAL HOSPITAL

---

---

---

---

---

---


---

---

Office for Interactions with Industry

### AAMC Recommendation – Patient Disclosure

- Patients should be informed of the existence of their providers' COIs; additional information should be made readily available to patients.
- The physician should normally be required personally to make the disclosure to the patient and document the disclosure in the medical record.
- Involvement of patient community generally is useful.
- **LESSON for rare diseases:** Specific disclosure to patients is essential.

 PARTNERS  
HEALTHCARE FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL  
AND MASSACHUSETTS GENERAL HOSPITAL

16

---

---

---

---

---

---


---

---

Office for Interactions with Industry

### Managing Clinical COIs – Additional Steps

- Oversight by non-conflicted physician
- Alternative caregivers
- Review of practice patterns
- **LESSON for rare diseases:** Independent review may enhance patient safety and reduce risks from multiple conflicts.

 PARTNERS  
HEALTHCARE FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL  
AND MASSACHUSETTS GENERAL HOSPITAL

17

---

---

---

---

---

---


---

---

Office for Interactions with Industry

### Summary: COIs and Rare Diseases

- **Self Awareness**
- **Transparency**
- **Disclosure**
- **Integrity**
- **Independent Evaluation**
- **Education of the Community**

 PARTNERS  
HEALTHCARE FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL  
AND MASSACHUSETTS GENERAL HOSPITAL

18

---

---

---

---

---

---

---

---