Assuring Integrity while Facilitating Innovation in Medical Research

IMPACT OF CONFLICT OF INTEREST POLICIES ON INNOVATION

June 5, 2013
IOM Proposed Questions

• What is the industry perspective on the impact of COI policies on medical innovation? Has the relationship between industry and academia changed because of COI policies?

• Have institutions and investigators been impacted by COI policies? Has there been an impact on publicly funded research (e.g. CTSA’s)?

• What are the drivers of success to spark development and commercialization of needed medical products? Have COI policies been a help or a hindrance to success?
Background and Study Objectives

Background

- The desire to preserve public’s trust in the credibility and transparency of biomedical research has prompted many public and private institutions to adopt more restricted conflict of interest (COI) regulations.
- There is significant concern that tightening of COI policies across and within many institutions (e.g. academia, government, industry) could be impeding access to and sharing of crucial scientific and clinical research knowledge.

Study Objectives

- Map the different stakeholders impacted by COI policy restrictions
- Collect expert views on what constitutes a COI
- Understand how tightened regulations on COI have impacted stakeholder’s work, with a particular focus on the ability to get access to and/or share scientific knowledge.
Project primarily focused on evaluating the impact of COI on three main aspects of Research & Development

**Examples**
- All receiving PHS funding must disclose financial relationships
- Research collaborations between researchers, industry, and government (NIH) governed by policies
- Trial PIs required to disclose relationships
- FDA committees for drug evaluations must disclose financial relationships
- Companies required to report all gifts to physicians, including samples

**Those Impacted**
- Academic and Research Institutions
- Government: NIH Research
- Industry: Basic Research/Drug Discovery
- Industry: Drug Development
- Physicians/Trial PIs
- FDA
- Physicians/Experts on FDA Panels
- Industry: Drug Approval
- Advocacy Groups: Pushing for unbiased but quick evaluations
- Industry: Drug Success
- Physicians/Medical Centers Prescribing Therapies
- Physicians writing Treatment Guidelines
While the term COI means the presence of improperly influenced judgment, more frequently it refers to a perceived COI due to a financial relationship with industry.

- In order to avoid a true COI, stakeholders require disclosure of relationships that could influence judgment or the integrity of research.
- Since financial relationships are the most straightforward to quantify and track, the most focus is on financial relationships.
- As a result, in many cases a definite assumed conflict is attached to research or collaborations with pharma, payers, or others that result in financial gain.
Conflict of Interest: Spectrum

Full disclosure of financial relationships is important to avoid future conflicts. The difficulty lies in then determining when a true conflict is present vs. a perceived conflict.

Unbiased:
- Research is not influenced by any other interests

True Conflict:
- Example: An expert that stands to gain financially from a product being approved should be recused from the approval process
- Collaborators or evaluators have a similar vested interest, working towards a common goal

Source: Health Advances interviews and analysis.
# Types of Conflict

Policies are largely focused on financial relationships due to the ease of tracking them and because they are thought to be the most likely relationship to result in a true COI.

<table>
<thead>
<tr>
<th>Type of Potential Conflict</th>
<th>Likelihood of Resulting in True Conflict</th>
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<tbody>
<tr>
<td><strong>Tangible financial</strong> conflicts of interest could occur if a person has a direct financial tie to the success of a product or research</td>
<td><a href="#">Bar Graph</a></td>
</tr>
<tr>
<td><strong>Intangible financial</strong> conflict of interest could occur if a person has received payment for a service tied to the success of a product or research</td>
<td><a href="#">Bar Graph</a></td>
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<tr>
<td><strong>Personal</strong> conflict of interest could occur if someone’s personal beliefs or goals are tied to the research</td>
<td><a href="#">Bar Graph</a></td>
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<tr>
<td><strong>Professional</strong> conflict of interest could occur if a person could gain professionally from the results of a study</td>
<td><a href="#">Bar Graph</a></td>
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<tr>
<td><strong>Institutional</strong> conflicts of interest could occur if the interests of an institution or an institution official could affect institutional processes for the design, conduct, reporting, review, or oversight of research</td>
<td><a href="#">Bar Graph</a></td>
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</tbody>
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Weighted Score (n=27) 7
Relationships of Key Stakeholders

Influencers impact the COI policies of the stakeholders responsible for maintaining research and treatment integrity. The impact of these policies on patients remains a key question.

Policy Makers
- Government (Congress, HHS)

Influencers
- Media
- Professional Medical Associations (Institution Specific)
- Advocacy Groups

Key Stakeholders Responsible for Enacting COI Policies
- Academic/Research/Medical Centers
- Physicians and Researchers
- Industry
- Government (FDA, NIH)
- Professional Medical Associations (Physician or Disease Specific)

Source: Health Advances interviews and analysis.
# Effects of COI Policies/Perceptions

<table>
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<tr>
<th>Key Effects of COI Policies/Perceptions</th>
<th>Description</th>
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<tr>
<td>Impaired Collaboration</td>
<td>- Decreased ability for experts to collaborate on research through studies, consulting, etc., particularly with industry</td>
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<tr>
<td>Increased Resource Burden</td>
<td>- More resources/time required to be compliant with COI policies and monitor COI disclosures</td>
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<tr>
<td>Limited FDA Access to Best Experts</td>
<td>- Inability of FDA to fill advisory committees with best expertise</td>
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<tr>
<td>Decreased Physician Education</td>
<td>- Less funding, fewer events and less expertise for CME and physician education</td>
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<tr>
<td>Decreased Communication</td>
<td>- Company-sponsored talks, physician talks on behalf of companies</td>
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Impact of COI on Academic Research Activities

Impact of COI Policies

$n = 16-19^*$ academic researchers

Paid company speeches
Resources invested to monitor policies
Time personally spent complying with policies
Paid consulting for industry
Ability to fill FDA advisory committees
Time to initiate collaboration
Paid educational speeches
CME/Fellowship Programs
Collaboration with industry
Collaboration with government
Collaboration with academia

* Respondents were able to select “Don’t know” for each factor, so ns vary from 16-19 for each bar.

Question: Q18 In your opinion, in the past 1-3 years, have conflict of interest policies and rules had an impact on any of the following?

Source: Health Advances survey and analysis.
Impact of COI Policies

Impact of COI Policies

\[ n = 8 \text{* industry researchers, } n = 18-19 \text{* academic researchers} \]

Feedback

- "The number of potential collaborations with industry are reduced. My research productivity is therefore reduced." – Academic Researcher

- "[Policies] have made it very difficult for companies to work with academic investigators who are prescribers, even if the work is entirely nonclinical.” – Industry Researcher

- "The perception of conflict of interest makes working and collaborating with industry incredibly difficult.” – Government Researcher

* Respondents were able to select “Don’t know” for each factor, so N’s vary for each bar.

Question: Q18 In your opinion, in the past 1-3 years, have conflict of interest policies and rules had an impact on any of the following? Q22 In your opinion, in the past 1-3 years, has fear of being perceived as having a potential conflict of interest had an impact on any of the following?

Source: Health Advances survey and analysis.
Impact: Resource Burden by Stakeholder

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**Impact of COI Policies**

* $n = 7-8^* \text{ industry researchers, } n = 17-19^* \text{ academic researchers}*

Industry

- “The increase in resources and money required to enact these policies is probably more than before because of greater technology required and more complex policies – for instance it used to take about 3 months for a company to set up a policy or compliance program, now it can take up to a year.” — Legal Expert

Academia

- “We recognize that there are burdens on investigators, some of which are measurable, some of which are not quantifiable but are certainly well known to the institution.” – AAMC
- “Conflict of interest policies do dramatically increase the additional regulatory burden for institutions and individuals and add to costs because more administrators are needed and more time is lost complying with the policies.” – Academic Researcher

Government

- “It’s created a new industry of full time COI ethics people, a specialty that costs an enormous amount of money and slows everything down, and then there are also the people who are on the committees that review everything and that takes their time away from their primary duties.” – Government Researcher

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* Respondents were able to select “Don’t know” for each factor, so N’s vary from 7-17 for each bar.

Question: Q18 In your opinion, in the past 1-3 years, have conflict of interest policies and rules had an impact on any of the following? Q22 In your opinion, in the past 1-3 years, has fear of having a potential conflict of interest had an impact on any of the following?

Source: Health Advances survey and analysis.
Experts

IBD
- Gastro: >13K
- IBD (1.4M patients)
  - >80 published, more seeing many adult patients

Epilepsy
- Neurologists: >13K
- Epilepsy and seizures (3M patients)
  - >100 published, more seeing many patients
- Infantile spasms (6-9K patients)

Diabetes
- Endocrinologists: 5-6K
- Type 1 Diabetes (1.16M patients)
  - >100 published, more seeing many patients
- Specific MOAs
  - Handful of KOLs are specialized in insulin studies

Pediatric IBD (150K patients)
- Pediatric Gastroenterologists: <40 KOLs
- Pediatric IBD: <10 KOLs

Infantile Spasms (6-9K patients)
- Infantile spasms: <10 KOLs

Example in FDA
- 2011 - Waiver granted for evaluation of Remicade in Ped. UC after FDA reached out to 31 experts who were recused due to COI or scheduling
- 2008 - Meeting on vigabatrin for infantile spasms delayed due to advisory committee vacancies
- 2012 – Evaluation of insulin-degludec: More than half of invited experts were in conflict
  - 13 invited, 6 unable because of conflicts, 1 waiver granted

Note: IBD = inflammatory bowel disease, UC = ulcerative colitis.
Source: Health Advances interviews and analysis, BiomedExperts, FDA, Dendrite, NORD, Epilepsy Foundation, eMedicine.
Reasons for Advisory Committee Declines

Outcome of Invitations to Serve on FDA Advisory Committees Where Waivers Were Granted
2009-2012

- Unable to Participate
- Participated with Waiver
- Participated
- Incomplete Paperwork
- Scheduling
- Combination
- Recused due to COI

All Invitations (n = 217)
Unable to Participate (n = 75)

Note: The combination outcomes are an unspecified combination of COI, scheduling, and/or paperwork.
Source: Health Advances interviews and analysis, FDA website.
FDA Committee: Factors Impacting Recruitment

The low recruitment of FDA panels is due to a variety of factors

Potential Reasons for Low Recruitment on FDA Panels

Policy
- Current guidelines are too strict on what constitutes a COI
- Experts are either not allowed to participate or not even invited

Perception
- After all the negative publicity, people are afraid of being perceived as having a COI and electing not to serve

Not COI
- Vacancies are unrelated to COI policy, and instead related to resources or expert availability

Source: Health Advances analysis.
Executive Summary

• While the actual term “conflict of interest” means the presence of improperly influenced judgment, more frequently it refers to a *perceived* COI due to a financial relationship with the industry.

• Extreme instances of true COI have sparked attention and led to negative perceptions of industry relations and stricter policies which have increased fear of perceived COI and burden of compliance. Specifically, our research found that COI policy restriction has led to:

  • Impaired Collaboration
  • Increased Resource Burden
  • Limited FDA Access to Best Experts
  • Decreased Physician Education
  • Decreased Promotional Relationships
Currently, COI is largely handled through avoidance. There is an opportunity to manage COI and promote shared access to scientific knowledge without concerns of conflict.

**Today**

Avoidance of Beneficial Relationships

- Negative perception of ties to industry leads to fear of perceived conflict of interest
- Inefficient policies lead to increased resources

**Future Goal**

Manage Relationships Efficiently and Effectively

- Standardize policies; narrow definition of true COI to remove perception that all relationships are automatically a COI
- Research best practices for monitoring and create standards to use resources efficiently and increase confidence COI is being managed appropriately
- Promote beneficial relationships

Source: Health Advances analysis.
Q&A