AGENDA

- Introduction
  - Federal Regulations and Guidance
  - Actions
- Yale Policies
- What Society Thinks about COI
- Yale Procedures
- Questions
Introduction

- Consulting fees or equity interests in a new company have become widely available within the past 20 years to scientists.

- Bayh-Dole Act of 1980 gives grantee and contractor organizations title to inventions resulting from federal research funding.

- Fosters cooperation between the government, academia, the public sector, and provides incentives that encourage the transfer of knowledge and technology that may lead to new product development.
1995 PHS guidance $10,000 identified as significant interest. Recipients of federal awards must disclose their financial interests to the institution.

1998 FDA regulation requiring financial disclosure by clinical investigators. Requires sponsors who are submitting applications to the FDA for review to certify that the investigator has no COI in the product or the sponsor. If they do, then they must disclose the interests.
History and Reaction

- 1999 death of Jesse Gelsinger during a gene therapy clinical trial. Raised questions about the investigator’s interests.

- In 2000, DHHS announced an intent to undertake an extensive public consultation to identify and improve means to manage financial COIS that could threaten subjects or research integrity.

- Call for heightened awareness and surveillance to insure that financial conflicts of interests are not resulting in bias or even the perception of bias.

- Research volunteers deserve the assurance that their protection is top priority.
Challenges for the NIH

- To create the culture of compliance the NIH faced the following challenges:
  - How to distinguish the risks that compromise a scientist’s objectivity?
  - How scientists understand the risks that financial consideration can raise?
  - How to make scientists understand the importance of declaring those risks?

- Disclosure a key understanding.
In 2000-2002: Task forces established and national forums convened.

- AAU, GAO and AAMC
- Recognized direction was needed to address financial COIs.
- Recognized relationships b/w industry and academia are more complex.

Called for every part of the clinical trial process to be “above reproach”.
Transferring university-developed knowledge to the private sector fulfills one of the goals of federally funded research, “by bringing the fruits of research to the benefit of society”. However, it increases the risk of compromising the research in two ways:

- Individual COI in science,
- An Institutional COI.
Conclusion: the problem is rarely a particular conflict itself. Rather what is done with the conflict is the issue. Most cases, problems arise when the conflict is not made apparent, or when it is not assessed or managed.
GAO interviewed 5 institutions, including Yale.

Develop and communicate information on best practices for identifying and managing COI.

Develop guidance or regulation concerning institutional COI.

Extend polices and procedures beyond research that is federally funded.
Association of American Medical Colleges
Definitions of Significant Financial Interest (2001)
AAMC Recommendations

- Review by standing COI committee with individuals who conduct human subjects research and others who are experienced in the oversight of COIs and familiar with applicable laws and regulations.
- A liaison to the IRB
- Consider involving community or patient representatives
Committee Responsibilities

- Review requests by a financially interested individual to rebut the presumption that he or she may not conduct human subjects research.
- Document the committee’s findings.
- Summary report including the nature and the amount of the interest.
- Encourage management or minimize the individual’s direct involvement in the research.
- Communicate with the IRB.
- Disclosure to human subjects, sponsors, editors of any publication and in any substantive public communication of the research results.
AAMC Definition of Significant Financial Interest

- Consulting fees, honoraria, lecturing, travel, service on an advisory board or other purpose expected not to exceed $10,000 annually.
- Equity interests, including stock options of any amount in a non-publicly-traded financially interested company.
- Equity interests in a publicly-traded financially interested company that exceed the defined de minimus amount.
- Royalty income or the right to receive future royalties under a patent license or copyright, where the research is directly related to the licensed technology or work.
- Any non-royalty payments or entitlements in connection with the research.
- Service as an officer, director or in any other fiduciary role for a financially interested company, whether or not remuneration is received for such service.
What non-federally mandated financial interests are included w/in the university’s policy definition of significant interest

- 64% include equity in non-publicly traded companies regardless of % share of equity.
- 64% include non-royalty payments not directly related to reasonable costs of research
Survey Says

- 81% of the respondents permit a researcher with a significant financial interest (SFI) to conduct human subjects research when compelling circumstances are judged to exist.* (only 26% have attempted to define compelling circumstances)

- 83% Processes to reduce the SFI

- 83% Elimination of the SFI

- 86% Disclose the SFI in the consent form

- 26% Involve a patient rep during the consenting and enrollment process

- 54% Use DSMBs
Survey also says.....

- Require clearer guidance on rebuttable presumption.
- Prohibit payments from any source for particular research results.
- Enhance protection (use of) students and trainees.
- Increase institutional education efforts.
- Top 40 recipients of federal funding more strictly aligned with AAMC guidelines.
Yale Policies

I The Institution
II The investigator
III The IRB Member
The Institution

- No Formal Policy. Still in development, but evolving practice;
  - External IRB when research is funded by a sponsor for which Yale has a direct financial interest, e.g., Pfizer-Bioimaging Alliance.
  - Divestiture of financial interest when start up becomes a publicly traded company.
  - Notice to chair that he/she must disclose interest if subordinate conducting research with a company in which the Chair has an interest.
Institutional COI

- Disclosure in protocol when Yale start up company.
- Review by COI C subcommittee when Yale invention being studied in Phase I trial at Yale.
The Investigator or Research Team Member

- A conflict of interest exists when an individual has an external interest that affects or provides an incentive to affect the individual's conduct of his or her University activities. Conflicts of interest can arise naturally from an individual's engagement with the world outside the University, and the mere existence of a conflict of interest does not necessarily imply wrongdoing on anyone's part. When conflicts of interest do arise, however, they must be recognized, disclosed and either eliminated or properly managed.
**Economic interests** include his or her interest in obtaining, maintaining or increasing the value of relationships such as employment, independent contractor or consultant; management positions, board memberships and other fiduciary relationships with for-profit organizations; ownership of stock or other securities and other financial interests such as loans or royalties; and any other activity from which the individual receives or expects to receive remuneration. They also include such interests on the part of the individual's spouse and his or her financially dependent children.
Yale and its researchers have ethical obligations to honor the rights and protect the safety of persons who participate in research. Financial interests held by those conducting the research or the research's sponsor may compromise or appear to compromise the fulfillment of those ethical obligations and the well-being of the research subjects, as well as the integrity of the related research. There is a strong presumption against permitting any person with related significant financial interests to participate in the conduct of such research, particularly if the protocol involves more than minimal risk. Only in rare and compelling circumstances might an exception be made. The HIC has established a policy and procedure for review of COIs related to human subjects research performed at or by Yale researchers. These policies and procedures supplement the Yale University Policy.

Faculty relationships with startup companies - newly-formed, privately-held, for-profit companies based on Yale intellectual property - present conflicts of interest and commitment. Policy guidelines specific to faculty relationships with such ventures appear as an appendix to this general policy statement. These are related to and in part derived from longstanding policies, set forth the Faculty Handbook.
The Investigator

- Protection of students and trainees
- Disclosure on interests annually to the Provost’s Committee on Conflict of Interest and Conflict of Commitment (COIC).
- Disclosure at time of initial submission and renewal to the HIC for each protocol or when relationship changes.
- Earnings limit when working with human subjects ($10,000).
- Provost permission to serve as board member or officer
HIC Policy

- A member of a research team, a member of the HIC Committee or a member of the HIC staff will be considered to have a conflict of interest if the person or the person’s immediate family
  - has a relationship, financial or otherwise, in the protocol’s sponsor or any other organization that could be affected by protocol approval decisions or by the conduct of the research.
  - a financial or a non-financial interest in a competitor of the protocol’s sponsor or in a competing drug or device.
  - a financial interest or non-financial relationship with the manufacturer of any item being evaluated in the protocol
  - a management or fiduciary position with the protocol’s sponsor
  - serves as a consultant or scientific advisor to the protocol’s sponsor or any organization
  - is an inventor of any item investigated in the protocol
  - is personally or professionally affected by a decision to approve or disapprove the protocol for any other reason or believes that he/she has an interest or belief that conflicts with his or her ability to protect participants.
The IRB Member

- Annual disclosure to the IRB
- Forwarded to Provost Committee
- Recuse themselves during discussion and vote when the review of a project presents a conflict of interest.
Society’s Viewpoint – Study I

- 2004: 62% responded that knowing COI information was “extremely” or “very” important.
- 87% felt financial COI should be disclosed as part of the consent process.
- Minority (3-44%) stated that they would be less inclined to participate because of the COI info listed in the scenarios, but only 3 - 17% said they wouldn’t participate.
Study II

- Participants wanted to know about financial interests, whether or not those interests would affect their participation. However, they varied in their desire and ability to understand the nature and implications of financial interests. Whether disclosure was deemed important depended upon the risk of the research.
Study III – Patients in Cancer Research Trials

- 253 patients in cancer-research trials.
- 90% of patients expressed little or no worry about researchers or institutions interests. Most said they would have enrolled even if the drug company paid the researcher for speaking or consulting or if the researcher had received royalty payments or owned stock in the company.
- Most patients believed it was ethical for researchers to receive speaking fees or consulting fees from the company.
- Substantial minority of patients wanted disclosure of the oversight system for researchers and of researchers' financial interests (31%); 17% thought no disclosure to patients was necessary.
- **Conclusions** Most patients in cancer-research trials were not worried about financial ties and would still have enrolled in the trial. A substantial minority wanted to be informed about the oversight system to protect against financial conflicts of interest and about researchers' financial interests
The Process

- File the annual disclosure
- File the HIC form when submitting a new protocol and a Request for Renewal and anytime a member of the research team has a relationship that may impact, or appear to impact, the ability of the study to be conducted without bias.
- Use forms on the website.
- HIC staff review the COI, personally contact the individual and inquire about the activities performed during the last 12 months and the upcoming 12 months and provide a summary of the interest and any study attributes that might help manage the interest present to the HIC Chair for action.
- The Chair may find the study de minimus or take it to Committee for consideration.
- The HIC works closely with the COIC to identify and address all conflicts.
- The COIC checks HIC database for disclosures.
- Individuals not disclosing an interest to the HIC will receive notice.
Questions??

- Is it enough to inform human subjects of the investigators financial or potential financial interests?
- Will disclosing the information to a research volunteer affect their decision to participate?
- Will it make the process any safer for them?
- Can financial conflicts be managed in a way that doesn’t adversely affect patient safety or influence the objectivity of the research conclusions?
References


AAMC (Susan Ehringhause, J.D. and David Korn, M.D.), *U.S. Medical School Policies on Individual Financial Conflicts of Interest, Results of an AAMC Survey*, September 2004


Thank you for your continuing effort to ensure the protection of subjects participating in Yale research!