





What is Conflict of Interest?

Office of Sponsored Projects Administration



As defined by the University of Kentucky

Who must disclose: *investigators*

- UK AR II-4.0-4: defines “Investigator” as the PI, a Co-principal investigator, and any other person at the university who is responsible for **design, conduct, or reporting** of research
- Usually, who needs to disclose is a subset of the total study personnel
- \$ thresholds on financial disclosure forms are an aggregate for the investigator, their spouse, and/or dependent children

Financial compensation from related business?



Do you or a member of your immediate family receive fees from a business in any way related to your proposed research activities (from consulting, gift fund, salary, dividends, rent, capital gain, real or personal property) that would exceed \$10,000 within a 12 month period?

Equity interest in related business?



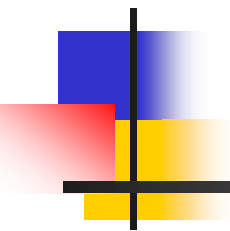
Do you or a member of your immediate family hold financial interests exceeding \$10,000 or 5% ownership in a business enterprise related to your proposed research activities?

Intellectual property and related business?



Are you or a member of your immediate family entitled to receive compensation from a business enterprise due to intellectual property in any way related to your proposed research?

Other relevant financial interests?



Are there other situations not covered in the first 3 questions that might be affected by the research for which funding or IRB approval is sought?



Are Human Subjects Involved?

- Do you or a member of your immediate family hold or expect to hold a board or executive position (regardless of whether the positions are paid or not) with the research sponsor or an entity with financial interest in the results of the research?
- Are you or a member of your immediate family holding equity interest that could be affected by the outcome of the research?
- Are you or a member of your immediate family receiving any type of compensation that could be affected by the outcome of the research?



Why Do We Care About Conflicts of Interest?

- The basis for COI rules is the desire to
 - Promote Scientific Integrity
 - Protect Human Subjects, where applicable
 - Preserve Public Trust
- Conflict is a situation, not a behavior
- UK's mission of research, teaching, and service is enhanced by collaborations with industry, therefore we must manage COI appropriately



Management Strategies: Disclose, Reduce, Eliminate

- Disclosure of financial interest to public, participants, subjects
- Monitoring, verify research by independent reviewers
- Modification of research plan
- Disqualification from participation in some or all research
- Divestiture of part or all of financial interest
- Severance of relationships that create conflict
- Reporting periodically to reviewers
- Public access to data, materials, open publication



How do we typically manage the COI?

- Identify that a conflict exists
- Develop a COI management plan with input and sign-off from the Dean (or AD for Research)
- The role of the central Research COI Committee is changing and will review all COI Management Plans and make recommendations to the VPR
- All research personnel informed in writing of the COI



How do we typically manage the COI? Con't

- Disclose the conflict in publications and presentations
- If human subjects involved, IRB informed, and study volunteers informed in writing of COI
- COI Oversight Committee for the project files a written report, **at least annually**, with OSPA



What Should a COI Management Plan Include?

- Description of the conflict
- Who will independently review the research data, analyses, manuscripts?
- Who will be informed in writing: students and staff working on the project, clinical trial participants, etc?
- Statement of frequency of review and reporting to OSPA by independent reviewers (at least annually)
- Obtain the Office of the Dean's signature approving the Management Plan before submitting to OSPA
- FYI, if the project is funded by the NSF or NIH, OSPA is required to disclose to the federal sponsor



What is the Institutional Motivation for Managing Instead of Prohibiting COI?

- Public benefits of new technology
- Economic Development – new businesses and jobs
- Opportunities for student projects and jobs
- Incentives for faculty to produce results
- Allows the University to compete for/retain talent
- Increased support from industry for research



How COI is Integrated into the IRB Process

- PI submits financial disclosure (FD) forms at time of Initial IRB Application submission to ORI. The check and balance for disclosing COI is: Externally sponsored projects require a FD form to be submitted with the grant/contract application to OSPA. Internally funded projects involving human research require that the PI submit the FD forms with the Initial IRB Application submission to ORI. OSPA & ORI communicate when yes boxes are checked on FD forms.
- If any **yes** boxes are checked on the FD forms, the PI may **concurrently** submit the COI Management Plan signed by the Dean of the College to OSPA
- The central Research COI Committee will review the MGT Plan and make recommendations to the Vice President for Research, who provides final approval



How COI is Integrated into the IRB Process, con't

- OSPA will provide the approved COI Management Plan to ORI to make available to the IRB
- The IRB utilizes the approved COI Management Plan to assess if human subjects will be adequately protected during conduct of the proposed protocol
- The IRB can decide to require additional safeguards to the protocol or Informed Consent in order to adequately protect human subjects during the conduct of the proposed clinical research study



Disclosures to Sponsors e.g. NSF and NIH

The authorized organization official's signature on the face page of application serves as certification of compliance that:

- There is a written, enforced process to identify, manage, reduce, or eliminate conflicting financial interests



Disclosures to NSF

- Institution must have a COI policy as restrictive as NSF's policy (UK's mirrors the NSF and NIH policy)
- Institution must maintain documentation of a system for 1) COI disclosures and 2) annual reviews of the COI management plan
- Institution must inform the NSF if it can not satisfactorily manage a COI



Disclosures to NIH

42 CFR 50.6

- Prior to expenditure of any NIH funds, the organization will inform the Contract or Grant Management Official about the existence of any COI
- The organization will assure that the COI has been addressed, and indicate how
- The organization will continue to make reports
- The organization will make additional information available to NIH, upon request



Disclosures to the FDA

The FDA requires the sponsor of any drug or device marketing application to submit information concerning the compensation to, and financial interests of, any clinical investigator conducting the clinical studies that support the marketing application.



21CFR 54.2

The clinical investigators must report any payments made by the sponsor of a covered study to support their activities that have a monetary value of >\$25,000, exclusive of the costs of conducting the clinical study, (e.g., a grant to fund ongoing research, compensation in the form of equipment or retainers for ongoing consultation or honoraria) during the time the investigator is carrying out the study and for 1 year following the completion of the study.



Recent Reported COI Issues

- Doctors and Drug Companies –Scrutinizing Influential Relationships – NEJM 357:1796-1797 Nov 1, 2007
 - Sen. Grassley & Kohl introduced legislation requiring pharmaceutical & medical device manufacturers to disclose the amount of funds (dinner, consulting fees, reimbursement of costs to attend CME classes, etc.) given to physicians
- Financial Ties are Cited as Issue in Spine Study – NY Times, Jan 30 2008 by Reed Abelson
 - FDA is investigating to determine if the manufacturer of an artificial spinal disc (Prodisc) provided adequate disclosure to the FDA that investigators conducting the CTs required for FDA approval had financial interests in the product. FDA approval was granted in August 2006



Case Study I

Dr. Ramsey is an investigator on a multi-site clinical trial funded by MegaPharma. Dr. Ramsey discloses that he has stock worth about \$12,000 in MegaPharma.



Case Study I Potential Management Strategies

- Include disclosure of the PI's financial interests in the company sponsoring the trial to clinical trial volunteers to ensure informed decision-making by the volunteers prior to enrolling in the trial.
- Other clinicians should consent patients enrolling in the trial.
- Publications and presentations about the trial should acknowledge Dr. Ramsey's financial interest in the company supporting the trial.



Case Study II

Dr. Rafferty is the investigator on a proposed clinical trial, funded by EmergingTech, that will be conducted only at UK. Dr. Rafferty is one of five investors who each own 20% of the company. The company hopes to go public in the next 12-18 months.



Case Study II Potential Management Strategies

- Dr. Rafferty clearly has a financial interest in the outcome of the clinical trial. UK may determine that her equity ownership of the company precludes having the trial performed at UK.
- Conversely, UK might determine, with full disclosure, that the Phase I could proceed at UK. This decision would be strengthened by appointing a data safety monitoring board to be responsible for assuring that the participant recruitment, conduct of the trial, and reporting of the data are independent of Dr. Rafferty.
- If UK permits Dr. Rafferty to act as PI on the trial, all the standard disclosures in written and oral presentations and publications would be necessary.



Breaking News!

- The Association of American Medical Colleges (AAMC) and the Association of American Universities (AAU) Advisory Committee on Financial COI in Human Subjects Research released a report at the end of Feb 2008 titled:
 - Protecting Patients, Preserving Integrity, Advancing Health: Accelerating the Implementation of COI Policies in Human Subjects Research
 - Report is located at: www.aamc.org/jointcoireport



Non-compliance Consequences

- **UNIVERSITY LEVEL**

- UK LOSES CREDIBILITY
- UK LOSES PUBLIC TRUST
- JEOPARDIZES UK'S FEDERAL FUNDING

- **INDIVIDUAL LEVEL**

- REPUTATION LOSS
- PUBLIC DISAFFIRMATION OF THE RESEARCH
- POTENTIAL LOSS OF EMPLOYMENT



What Can You Do to Help Manage COI?

- Ensure that all faculty/staff you come in contact with are aware of the UK COI policy
- Be willing to serve on a COI Management Committee, if asked
- Determine if your research has any COI issues
- If you have a COI, start the process, and follow-up with your COI Management Committee to ensure that annual reports are filed with OSPA

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"Under disclosure rules, I'm required to tell you I own stock in the company whose drug I'm prescribing."



Acknowledgements

1. Code of Federal Regulations
2. National Science Foundation
3. National Institutes of Health
4. University of Michigan
5. Council on Governmental Relations
6. www.CartoonStock.com
7. New England Journal of Medicine
8. New York Times
9. AAMC-AAU Advisory Committee on Financial COI
in Human Subjects Research



Questions?

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