

Conflict of Interest: Recognizing, Acknowledging, Managing and Eliminating

Seems simple at first but it's a lot more complicated than you might think...



When you hear “Conflict of Interest” what comes to mind?

- Clinicians receiving money or nice trips from drug companies for endorsing their products?
- A scientist receiving money and discounted stock from a biotech firm to do research on a new product?
- A distinguished scientist receiving a \$25,000N honorarium to give a scientific talk at a meeting sponsored by a drug company?
- A faculty member earning an additional \$50,000N/year in honoraria for seminars, review groups and consulting fees?



When you hear “Conflict of Interest” what comes to mind?

- A person reviewing a grant submitted by:
 - someone s/he knows well professionally
 - someone at their university
 - a former graduate student or postdoc
- A faculty member who last year was away from her lab of 10 people for half of the regular work days?



Ever heard....

- “I’m a good scientist. I would never let anything influence how I interpret or present my data! Only big name people getting big bucks from industry have to worry about Conflict Of Interest.”
- “I know the boss likes to travel to give talks, review grants, meet people, but I have been waiting for a month for him to read the first draft of my paper!”



Goals for this session...

- Clear understanding of research community-wide policies and expectations regarding financial conflict of interest
- Broader view and understanding of common non-financial conflicts of interest
- Understand the broader implications of 'conflicting interests' and 'competing interests'
- Heighten awareness of unconscious COI and how it can affect judgment without you knowing it



Goals continued...

- Recognition that the risk of real and perceived COI is ever-present, learning how to:
 - Identify
 - Acknowledge - Disclose
 - Minimize
 - Manage
 - Eliminate if possible but it's not always possible
- Prepare you for how COI is often not black and white, and people often disagree, but highest ethics are essential to you and science



Conflicts of Interests (COI)

- A set of conditions in which professional judgment concerning a primary interest tends to be unduly influenced by a secondary interest
- A *clinical* role conflict between professional duties to a patient and obligations (express or implied, real or perceived) to the interests of a third party
- A relationships with industry that may unduly influence or supersede the primary interest of a researcher/clinician



Elements of COI

- Conflict of values
- Conflict of commitments
- Dual loyalty
- Potential for scientific misconduct



Examples of COI

- Gifts and incentives from drug companies to physicians
- Industry-sponsored research
- Research on patients
- Consulting fees or compensation for personal services to a company
- Attending professional meetings and lectures
- Examining own trainees and students
- Reviewing grants application or publications for close peers



Why Regulate COI?

- To maintain the integrity of professional judgment
- To maintain confidence in professional judgment
- To enhance and maintain scientific objectivity
- To eliminate/minimize potentials for scientific misconduct



Consider the following...

- You are in your third year as a new Assistant Professor
 - You just got your first R01- a 3 year grant
 - Bench Malaria research, potential to translate to treatment
 - Everyone in your group excited with positive career impacts
- Break up into groups of 4. Each take one of the roles below. Assume the perspective of the person and identify as many, and the most important, INTERESTS YOU HAVE and how this may influence how you approach the upcoming research
 - The young PI
 - A third year PhD postdoc hoping to become a PI herself
 - A second year graduate student in your lab
 - A clinical fellow just starting 1 year of research time
- 5 minutes - think about your interests and write them down
- 5 minutes - share your list and discuss them with others
- 5 minutes - identify interests that are compatible and those that conflict



What key interests did you identify for...

- The PI
- The PhD postdoc
- The graduate student
- The clinical fellow



Did you consider...

- For the PI, the research may have commercial value so he may want to keep the results very quiet until he knows enough to apply for a patent.
- For the postdoc, she will be trying to get a job in the next 2 years and she desperately needs publications.
- The postdoc also needs to begin establishing independence but the lab needs to focus on this high profile work that will stay at the university
- How will the interests of the postdoc and the Fellow differ?



Would you consider it a COI if...

- The PI prohibited everyone in the lab from talking about the research to anyone outside the group...
 - For the first year?
 - For the first two years?
 - For the first two years even though the chances of it commercializing became slim?
- The postdoc ignored the PI and gave a seminar on the work in a job interview.
- The PI would not let the grad student stop working on a piece of the work with high potential but which had gone nowhere in 18 months.



Do you see any COI here?

- As the PI, you start having real concerns the work is not going to pan out. You go to your Chair and the Dean and express the intent to pull back from the work and shift your attention to other safer studies. Due to the potential for commercial value, they advise you to keep going, even offering to provide funding for a year or two if your grant is not renewed.



Brief History

- US
- Mid 1990s, US Public Health Service (NIH) and National Science Foundation implemented regulations addressing individual conflicts of interest
- Goal of regulations: “promot[ing] objectivity in research by establishing standards to ensure there is no reasonable expectation that the design, conduct, or reporting of research funded under [PHS or NSF] grants or cooperative agreements will be biased by any conflicting financial interest of an Investigator”



What is the NIH policy on Financial COI?

- Late 2007, updated to make more specific and establish minimum standards
 - Institution must have policy on Financial COI that is enforced
 - Before submission must receive written statement from PI if any Significant Financial Interest of \$10,000 or more that could benefit from the proposed research
 - Also includes spouse and children
 - Before funds spent, must report if any financial COI of Investigator exists – does not require the details in report
 - Must certify that appropriate measures are being taken to “...identify and manage, reduce or eliminate conflicting interests...”
 - Applies to students and postdocs too!



What is “Significant Financial Interest”

- Defined by the regulation as anything of monetary value, **including** but not limited to:
 - salary or other payments for services (e.g., consulting fees or honoraria);
 - equity interests that exceed 5% of ownership (e.g., stocks, stock options or other ownership interests);
 - intellectual property rights (e.g., patents, copyrights and royalties from such rights).



What “Significant Financial Interest” is not...

- It does **not** include:
 - salary, royalties, or other remuneration from the Institution;
 - income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities;
 - income from service on advisory committees or review panels for public or nonprofit entities;



Problems/Limitations of COI Regs

- No requirement to reveal the amount of financial interest
- “Honor System” – no requirements for checking accuracy and honesty
- Similar honor system reporting financial interests by reviewers of grants and papers
- Industry has not been required to reveal who they pay how much for what services
 - Under threat of legislation they are beginning to!
- Assumption often is industry is only interested in financial gain and will hide or distort truth



Ghost Writing and Refocoxib (Vioxx)

- Vioxx is a Non-steroidal anti-inflammatory drug that was a blockbuster for Merck - used by millions
- Several years ago evidence began mounting some patients with CVD had increased risk of death using Vioxx
- Led to decision to pull it from the market
- Lawsuits based on evidence Merck knew of risk but suppressed or down-played
- Court cases led to millions of company documents being made public



Ghost Writing and Refocoxib (Vioxx)

- Authors started looking for patterns in emails and letters – led to JAMA article on ‘ghost writing’ of original research papers and review articles
- Written by Merck employees or for-profit publishing companies - little or no initial input from faculty authors
- Once articles largely written, went ‘shopping’ for academics who would agree to be authors
 - Unspecified level of involvement with revision
 - Many received payment - \$750-\$2,500
 - High fraction never disclosed their level of involvement with the work or that they received payment from Merck
- Not just occasional incident - high frequency pattern



Questions to consider...

- What conflicts of interest do you see?
- Why does it matter who writes an article if the ultimate authors agree with what it says?
- Would it make a difference if the article presented a truly accurate account of the topic rather than a view slanted to maximize benefit and minimize apparent risks of taking Vioxx?
- Discuss these questions with 3-4 others around you for 10 minutes and then we will reconvene in local groups to discuss your discussions
- NU and many other institutions/organizations have totally banned ghost writing



Recent 'Scandals'

- Dr. Charles Nemeroff removed as chair of Psychiatry at Emory University for not reporting income from Glaxo
 - He said he did not think the policy applied as they were "CME-Like" talks he gave
 - Last year named Chair of Psychiatry at U of Miami
- U of Wisconsin Chair of Orthopedics reported to have received \$19.4 million from Medtronic 2003-2007
 - U of WI policy does not require reporting how much
 - Big issue of did it influence his clinical US practice and promoting of devices/materials with Food and Drug Administration (FDA) concerns
 - He said he has been telling patients about his relationship with Medtronic for years



More Scandals

- NIH intramural researchers and administrators had consulting arrangements with pharmaceutical and biotechnology companies
- Fall-out:
 - Bad press
 - Congressional hearings
 - Loss of public trust
 - Did NIH have sufficient oversight of its own researchers?
- NIH adopted stricter conflict of interest rules for intramural investigators – I was there at the time...big reaction by NIH PIs



COI Policy Changes Emerging...

Institutions receiving US Public Health Service (includes NIH) funding should:

- Comply with 1995 regulations;
- Revise policies;
- Establish procedures for compliance;
- Train Investigators; and
- Continue to report FCOIs to NIH.

Institutions that implement the regulation prior to August 24, 2012 signify their compliance by making the institutional FCOI policy publicly accessible.



Is COI a bigger issue in biomedicine than other fields?

- Yes and no...
- Politics...can you think of any local or national examples?
- Business...
- Stock market...insider trading
- Pretty much anywhere profit to be made and there are winners and losers
- Core element is honesty and ethical behavior



Public trust, vulnerability and a self-policing system

- All put a special demand on biomedical field
- Physicians in high regard, huge trust placed in them, expected to put needs of patient first – patients vulnerable
- Public in no position to make informed decision among treatments and drugs – vulnerable again
- Research also enjoys public trust – huge sums of money invested for good of all
- Trust among scientists that what is reported is accurate and unbiased – otherwise science can be led into huge black holes/wasted resources



Public trust, vulnerability and a self-policing system

- Both medicine and research are largely self-policing, ESPECIALLY research
 - sheltered from strict laws and rules
 - makes it especially prone to public outcry with lapses
- The whole requirement by NIH for formal training in RCR caused by high profile ethical lapses in research clinical studies
- It all really comes back to conflict of interest, or more accurately conflicting interests..



Professional gain vs. financial gain...

- Most COI discussions center on money as a reward
- What about other kinds of rewards might cloud judgment and lead to COI?
 - Publications
 - Grants
 - Promotion
 - Invitations to give talks
- Do you think the desire for these rewards is greater or less than direct financial gain for most scientists?
- How many of you have ever witnessed a situation where data was 'massaged' just a bit to make it more convincing so a paper is more likely to be accepted? Where are the conflicting interests?



Peer Review and Conflict of Interest

- From the perspective of Peer Review:
 - Who is the best person to review a publication or grant application?
 - Who is the person most likely to have a competing interest in the research done or proposed?
 - What does a person submitting a paper or a grant expect of a peer reviewer?
 - What is the central assumption of Peer Review?

OBJECTIVITY!!!

...



Institutional COI

- Can a university be guilty of a COI?
- Definitely and seems to be a growing problem – with more to be gained from for-profit relationship more risk of COI
- Stagnant NIH budget also contributing
- Institution might look the other way when investigator behavior presents a COI
- More pressure on PIs to bring in money so more risk
- Universities spinning off for-profit ventures so now THEY become the responsible party



How much risk is there?

- Just how easily do you think you can insulate your judgment from being influenced by your conflicting interests for:
 - completing your postdoc
 - getting publications
 - supporting your family if you have one
 - making it to the next professional step in a very competitive world
 - being honest and objective so that science is best served



It can be harder than you think...

- Best strategy is to consciously begin to:
 - Think about it
 - Identify potential conflicting interests
 - Acknowledge/disclose them
 - Minimize
 - Manage
 - Eliminate
 - The “grandmother” and Daily Newspaper rules!
 - Think about and plan how you guide others



What do you do if you become aware of something you think is a conflict of interest?

- It really depends on who it involves, your relationship with them and how certain you are
 - Your mentor/advisor
 - Another PI
 - A peer in your research group
 - A peer not in your research group
- Are you not sure of what is going on or not sure if it is ok to do?
- If you are not sure if it is ok, discuss in general terms with your mentor/advisor
 - “I am trying to get a better idea...What if...”
- You can also discuss with peers but some caution
- If it concerns your PI, look to someone in leadership you can talk with confidentially



What is ahead for you?

- Constantly recognize and balance competing interests
 - Recruiting enough clinical research subjects vs. protecting their safety and informed decisions
 - Getting your paper published vs. not including an author who really did not contribute
 - Talking about your newest finding at your poster vs. competing with others to be first to publish
 - Going along with a senior researcher who is cutting corners vs. standing up for what you know is right
 - Including an undergraduate who worked for a summer but didn't accomplish much as an author vs. keeping a high expectation for what authorship means



It really does matter

- Constantly recognize and balance competing interests
- “Everyone else does it” is a very slippery slope
 - Would you be ok with others doing the same?
- Conflicting interests really can lead you to unconscious bias
 - Professional gains more frequent and perhaps more powerful than financial gains
 - Definitely longer lasting
- Perception is just as important as reality
- Repairing a tarnished reputation is really tough



Remedies for COI

- Prevention
- Individual discretion
- Delegation of key research activities
- Development of protocols and guidelines
- Professional regulation
- Governments regulation



Prescriptions for COI

- Disclosure
- Mediation
- Abstention
- Prohibition

(discuss the pros and cons of each)



University Policies and Procedures

- Ethics Policy, University of Ibadan 2010, 2013



Questions & Discussion

