

# Addressing Conflict of Interest in Research

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# Overview

- Background and Guidelines
- Concept of Conflict of Interest
- Financial/Economic Conflict of Interest
- Assessing Conflicts of Interest
- Managing Conflicts of Interest
- Case Examples



# Jesse Gelsinger (1999)

- Genetic defect – impaired ammonia metabolism
- Underwent a gene transfer experiment at the University of Pennsylvania's Institute for Gene Therapy
- Injected with the adenovirus carrying the gene
- Died four days after injection
- James M. Wilson, PI & head of Institute had substantial financial stakes in Genovo (Sponsor/founder)



# Jesse Gelsinger (1999)

- Inclusion of Gelsinger as a substitute for another volunteer who dropped out, despite having high ammonia levels that should have led to his exclusion from the trial
- Failure by the university to report that two patients had experienced serious side effects from the gene therapy
- Failure to mention the deaths of monkeys given a similar treatment in the informed consent documentation.



# Jesse Gelsinger (1999)

*After 19-year-old Jesse Gelsinger died in a gene transfer study at the University of Pennsylvania in 1999, conflicts of interest were among the allegations levelled at the research team and the university. The lead investigator and university held equity stakes in a company with a financial interest in the experiment, and the lead investigator and medical school dean held patents on processes used in the trial. Although no causal relationship was established between these financial interests and the irregularities associated with Gelsinger's death, the financial interests raised the suspicion that money clouded judgment.*

<http://www.thehastingscenter.org/Publications/BriefingBook/Detail.aspx?id=2156>



# Guidelines on COI

- *In the protocol (DoH: Art 14)*

*The protocol should include information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest, incentives for subjects and provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.*

# Guidelines on COI

- *In informed consent (DoH: Art 24)*

*In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study.*

# Guidelines on COI

- *In publications (DoH: Art 30)*

Sources of funding, institutional affiliations and **conflicts of interest** should be declared in the publication.

- *Disclosure requirements (National Guidelines)*

Formal disclosure from investigator of information regarding funding, sponsors, institutional affiliations, etc



# Guidelines on COI

- National Guidelines for Clinical Trials
  - Issues to be looked into by ERC: toxicities (Phase I), placebo use (Phases II & III), professional integrity and conflict of interest (Phase IV) (art 3)
  - Clinical trials of medical devices, diagnostic procedures, and preventive measures, including vaccines, raise...potential conflict of interest (art 16)



# Conflict of Interest (COI)

“A conflict of interest is a set of conditions in which professional judgment concerning a primary interest (such as a patient's welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain).”

Thomson D. *Understanding financial conflicts of Interest*. NEJM [serial on the Internet]. 1993 August 19; [cited 2009 June 23]; 329:573-576. Available from <http://content.nejm.org/cgi/content/full/329/8/573>



# COI: Levels of Interest

## Primary Interests

- Determined by the professional duties of the individual (researcher, physician, ethics review committee member, journal editor)
- Primary consideration in any professional decision an individual makes



# COI: Levels of Interest

## Secondary Interests

Interests other than the primary interests, such as:

1. Financial/economic interests
2. Personal fame
3. Ambition
4. Tenure
5. Thirst for knowledge



# COI: Levels of Interest

## Secondary Interest

- Secondary interests are not illegitimate in themselves, and they may even be a necessary and desirable part of a professional practice.
- These interests however must be prevented from dominating or appearing to dominate the relevant primary interests in the making of professional decisions.



# COI: Why regulate?

1. To maintain the integrity of professional judgment – secondary interests are irrelevant to the merits of decisions about primary interest. So, they should be minimized when making professional decisions.
2. To maintain confidence in professional judgment – this is to minimize conditions that would cause reasonable persons to believe that professional judgment has been improperly influenced, whether or not it has.



# Financial/Economic Conflict of Interest

*“Conflict of financial or economic interest occurs whenever financial or economic considerations may have the potential to compromise or have the appearance of compromising an investigator’s professional judgment and independence in the design, conduct, or publication of research.”*

Code of Federal Regulations, Title 42, Volume 1, Parts 1 to 399 (PHS, DHHS)



# Financial/Economic Conflict of Interests: WHO

- Individual (investigator, research assistant, research staff, ethics committee member, journal editor, immediate family member)
- Institution (including sponsor and ethics review committee)





# Financial/Economic Conflict of Interests: INDIVIDUAL

- Equity ownership
- Patent rights, licenses and royalties
- Research funding
- Institutional gifts (endowed chairs, other gifts)
- Gifts to laboratory or research group
- Per capita fee for contracted clinical trial



# Financial/Economic Conflict of Interests: INDIVIDUAL

- Consultant or scientific advisory fees
- Honoraria for speaking at professional meetings
- Informal benefits (e.g.. Entertainment)
- Informal (non-documented) compensation arrangements
- Recruitment incentives



# Financial/Economic Conflict of Interests: INSTITUTIONS

- Equity ownership, including stocks
- Patent rights, licenses and royalties
- Research funding
- Institutional gifts (endowed chairs, other gifts)
- Gifts to laboratory or research group
- Per capita fee for contracted clinical trial
- Consultant or scientific advisory fees
- Informal benefits (e.g. entertainment)

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# COI - Severity

## Severity of conflict depends on

1. The likelihood that professional judgment will be influenced, or appear to be influenced by the secondary interest, and
2. The seriousness of the harm or wrong that is likely to result from such influence or its appearance.



# Assessing COI

1. In assessing the likelihood of conflict, “the greater the value of the secondary interest the more probable its influence”
2. In assessing the seriousness of the conflict, “the greater the scope of consequences, the more serious the conflict”



# Assessing COI

3. In assessing the influence of relationship between parties, “the longer and closer the association, the greater the influence”
4. In assessing accountability and conflict of interest, “the more limited the accountability, the more serious the conflict”



# Managing COI

## 1. Disclosure

Sources of financial /economic support for the research are disclosed to give those who would be affected, or who are otherwise in a good position to assess the risks, information they need to make the decisions

## 2. Mediation

Uses devices such as blind trusts that insulate parties from secondary interests



# Managing COI

## 3. Abstention

Conflicted parties withdraw from cases in which they have substantial secondary interests

## 4. Divestiture

Eliminates secondary interests

## 5. Prohibition

Conflicted parties withdraw





# Case 1. Sexual Satisfaction Study

- Dr. A receives P200,000 a year for speaking at various professional meetings being sponsored by QR pharmaceutical
- He will receive the same amount and a stipend of P25,000 next year in assisting with the preparation of a manuscript for the study sponsored by QR



# Case 1. Sexual Satisfaction Study

- 300 couples from 20 sites will participate in the study with 10 couples enrolled at this site. B, a research nurse who reports to Dr. A will gather the actual measures of these subjects and will also enroll and consent subjects.
- CRC Inc., hired by QR to manage the study and conducted data analysis, offers Dr A and B “recognition of service” award of P5,000 per couple that they are able to enroll within the first 30 days of the trial



# COI

- Dr. A's speaking fees
- Dr. A's and B's "recognition service awards"

# Managing COI

- Paid lectures are not associated with the specific clinical trial
- Being a multi-center study and its other features reduce opportunity for research bias
- Disallow financial enrolment incentives
- PI must disclose financial involvement with company in papers and publications



# Case 2: Yeast Supplement Study

- Drs X and Y conducted a study of yeast supplement that may be helpful in preventing the gastrointestinal discomfort associated with certain types of antibiotics.
- Study is a single-site, double-blind parallel group design in which 20 subjects will be randomly assigned to one of two groups. Subjects will be tracked for 45 days. Reports of GI discomfort and stool samples will be collected at several points by study coordinator A and research assistant B.

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# Case 2: Yeast Supplement Study

- Drs X and Y have been funded regularly by Pharma A over the years. Grants from Pharma A now represent about 75% of the total funding in their lab. Each has also received approximately Php1M in consulting fees each year for the last 5 years.
- Study coordinator A has also received consulting fees of Php100,000 a year from Pharma A for the past several years.



# COI

Lab Funding  
Consulting Fees

## Managing COI

- PI's not to conduct primary analysis
- Remove financially-interested research coordinator
- PI's not do consent or have primary responsibility for reporting adverse events. Person getting consent shall not report to PIs.
- PI's must disclose financial involvement with the company in papers and publications.



# Summary

- Conflicts of interest management is about preventing the secondary interests from dominating the primary interests
- In avoiding or minimizing conflict of interest, self-management is the first step

