



โครงการฝึกอบรมเชิงปฏิบัติการ “จริยธรรมการวิจัยในคน”
มหาวิทยาลัยเชียงใหม่ ร่วมกับ ชมรมจริยธรรมการวิจัยในคนในประเทศไทย
(FERCIT)

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Conflicts of Interest (COI)



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Outline of Discussion

- Define COI
- Describe specific type and level of COI
- Define and identify issues in COI.
- Understand the specific guidelines on COI.
- How to manage Conflicts of Interest
- Conclusion and Question

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Definition

- “A situation in which a person, such as a public official, an employee, or a professional, has a private or personal interest sufficient to appear to influence the objective exercise of his or her official duties.”

3

Definition

- “A set of conditions in which professional judgement concerning a **primary interest** (such as patients' welfare or the validity of research) tends to be **unduly influenced** by a **secondary interest** (such as financial gain)”.

4

Definition

- Situations in which financial or other personal considerations have the potential to compromise or bias professional judgment and objectivity or reporting research (AAMC, 1990)



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ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in two parts.

1. Identifying information.

2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party. That is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

3. Relevant financial activities outside the submitted work.

This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidemic growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the case of EGFR or lung cancer.

Report all sources of revenue paid for (promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

Use this section to report other relationships or activities that readers could perceive to have enhanced, or that give the appearance of potentially influencing, what you wrote in the submitted work.

Definitions.

Entity: government agency, foundation, commercial sponsor, academic institution, etc.

Grant: A grant from an entity, generally (but not always) paid to your organization.

Personal Fees: Monies paid to you for services rendered, generally honoraria, royalties, or fees for consulting, lectures, speakership, honoraria, expert testimony, employment, or other activities.

Non-Financial Support: Examples include drug/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.

Other: Anything not covered under the previous three boxes.

Pending: The patent has been filed but not issued.

Issued: The patent has been issued by the agency.

Licensed: The patent has been licensed to an entity, whether earning royalties or not.

Royalties: Funds are coming in to you or your institution due to your patent.

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) 2. Surname (Last Name) 3. Date

4. Are you the corresponding author? ☐ Yes ☐ No

5. Manuscript Title

6. Manuscript Identifying Number (if you know it)

Section 2. The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☐ No

Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were present during the 36 months prior to publication.

Are there any relevant conflicts of interest? ☐ Yes ☐ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☐ No

Conflicts of Interest

- ผลประโยชน์ทับซ้อน
- การมีส่วนได้ส่วนเสีย
- ความขัดแย้งกันระหว่างผลประโยชน์ส่วนตนและผลประโยชน์ส่วนรวม



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Types of COI

- Tangible
 - Financial relationship
 - Academic research + commercial interest
 - Financial payment
 - Consulting fee
 - Equity in a company
 - Other monetary reward
 - Gift, trip, etc.



Types of COI

• Intangible

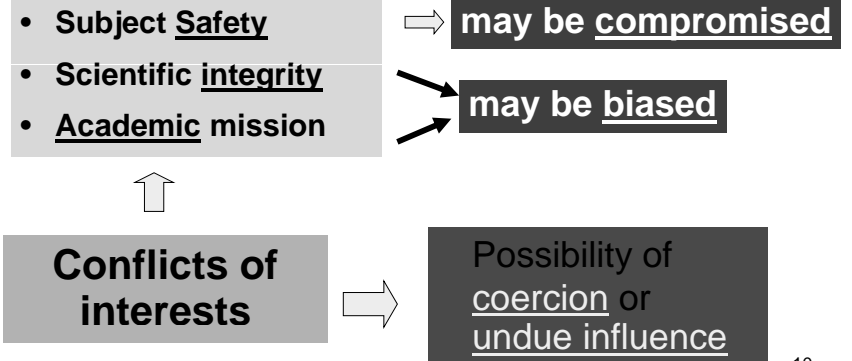
- Academic COI or intellectual bias
- Peer-review process (positive response to a manuscript favoring his/her paper citation; delay publication of competitor)
- Appointment, promotion, grant



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Why should we care about conflicts of interests?

Adverse consequences



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Adverse consequences

• Safety of participants in clinical trial

- Color the consent discussion
- Bias in recruitment or reporting adverse reactions possibly related to the study article, or the analysis and interpretation of data.

• Science enterprise

- Destroy “Trust”



OHRP Draft interim guidance 2001

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Level of conflicts of interest

“A circumstance in which interests, such as career advancement or financial gain, have an influence on the researcher’s judgement of a primary interest, such as patient’s welfare.” (Thompson, 1993)

Conflicts of interest

Individual level

- The investigator
- EC member

Institute level

- University
- Hospital



The investigator level

- Hold significant financial interest in sponsor of research
 - Equity interest, Consulting fee, Honoraria
 - Patent, privilege
 - research-related gift from sponsor
 - stock ownership
- Has monetary reward
 - Finder's fee / per-capita payment
 - Accrual bonus, career promotion



The EC member level

- Member is an investigator on research under review
- Members or staff hold significant financial interest in sponsor of research
- Loyalty to colleagues submitting for review
- Members closely tied to area of research under review

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The EC member level

- Possible impact of decisions on member's own work (e.g., policy changes)
- Personal hidden agendas, deeply held beliefs
- Non-IRB roles of members
 - Contracts and grants office
 - Legal counsel

An institutional conflict of interest

- is when financial interests of the institution or of an institutional official might affect or reasonably appear to **affect institutional processes** including the conduct, review, or oversight of human research

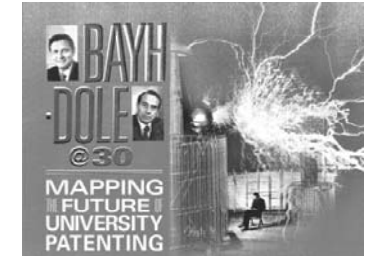
The institution level

- Concern for institution's prestige (Ranking)
 - Institutional equity or ownership
 - Income from indirect cost
 - Research grant competition
- Promoting research vs. protecting subjects
- Underevaluation of EC service/ underbudgeting

http://ccnmtl.columbia.edu/projects/rcr/rcr_conflicts/foundation/index.html

The Bayh-Dole Act (1980)

- Provide recipients of federal funds the opportunity to make income from a patent of products developed
- Remove the ban on campus entrepreneurship
- Consequence
 - Bias on publication practice, drug prescribing pattern, assignment of students to project work



Birch Bayh



Bob Dole

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A Real Case

- Fred Hutchinson Cancer Research Center, Seattle
- T cell-depleted bone marrow transplantation to prevent GVHD
- Since 1981, 20 died.
- 5 series newspaper investigation



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UNINFORMED CONSENT

What patients at 'The Hutch' weren't told about the experiments in which they died

seattletimes.com
The Seattle Times

Uninformed Consent Home

THE BLOOD-CANCER EXPERIMENT

THE WHISTLEBLOWER

THE BREAST-CANCER EXPERIMENT

THE FINANCIER

THE PROSPECTS FOR CHANGE

Continuing Coverage

Q&A on this Series

The Hutch's Response

Supporting Documents

THE BLOOD-CANCER EXPERIMENT

Since 1981



Becky Wright holds her niece after her second bone-marrow transplant in Seattle. She died in 1987.

Patients never knew the full danger of trials they staked their lives on

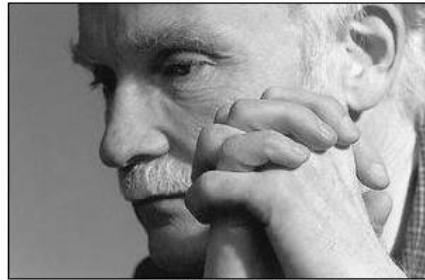
The story of Protocol 126, a blood-cancer experiment at the Fred Hutchinson Cancer Research Center in which at least 20 people died. They were never told that The Hutch and some of its doctors had a financial interest in drugs being tested in the experiment, nor that there were safer, more effective alternative treatments.

- A timeline of events in the Protocol 126 experiment

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THE WHISTLEBLOWER

Since 1991



Harley Soltes / The Seattle Times

"Real people lost their lives, and there was no way to stop it," said Dr. John Pesando, who challenged Protocol 126 both while he worked at Fred Hutchinson Cancer Research Center and afterward.

He saw the tests as a violation of 'trusting, desperate human beings'. For nearly two decades, Dr. John Pesando sounded the alarm over what he saw as a dangerous and unethical human experiment at Seattle's Fred Hutchinson Cancer Research Center. But his complaints were largely ignored — until now.

- A timeline of doctors' complaints and officials' responses

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THE INTERNATIONAL reputation of Seattle's Fred Hutchinson Cancer Research Center was forged with a courageous and sometimes defiant approach to conventional medicine.

It was built by doctors empowered to try new weapons against cancer, even if it meant some patients might die sooner than they would have with conventional treatments.

The center's most respected researcher, Dr. E. Donnall Thomas, won a Nobel Prize for persevering on bone-marrow transplants despite the doubts of peers and the deaths of patients. In his seminal work between 1969 and 1974, he performed bone-marrow transplants on 54 cancer patients. Forty-eight died, but six lived.

In the quarter-century since, "The Hutch" has continued to improve those methods, which have saved thousands of lives around the world.



Dr. John A. Hansen kept about \$10 million stock and broke conflict-of-interest policy



Dr. E. Donnall Thomas took stock worth \$5 million today, if he kept it, which he won't say. Donated the \$350,000 for his Nobel Prize to The Hutch.



Dr. Robert Nowinski started three big biotech. Sold one to Bristol-Myers for \$295 million.



Dr. James Bianco owns \$5.1 million stock after two products flopped then a third took off.

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GENE THERAPY

- Jesse Gelsinger 18 years old in 1999
- suffered from Ornithine transcarbamylase deficiency ("OTC")
- Controlled by medication and low protein diet
- On his 18th birthday, he volunteered in a study on gene therapy at Institute for Human Gene Therapy ("IHGT") U Pennsylvania
- "He wanted to be a hero," his father says. .
- He died 2 days after gene therapy procedures.
- Director of the institute owned stock in Drug company \$13.5 million



Royalty payments to staff researchers cause new NIH troubles

Janice Hopkins Tanne *New York*

Patients who took part in clinical trials at the US National Institutes of Health (NIH) had no idea that scientists at the institute received \$8.9m (£4.8m; €6.8m) in royalty payments and might benefit financially for the use of their discoveries by pharmaceutical companies and device makers, reports from Associated Press allege. This information was not made public until the press agency obtained the information after filing a request under the Freedom of Information Act.

The press agency has reported that 916 present and former

Research Protection, says that patients might have thought differently about the risks of trial treatment if they knew of scientists' financial interests.

The NIH has been criticised before for not disclosing conflicts of interest (*BMJ* 2004;329:10). Five years ago, just before leaving office, Donna Shalala, then secretary of the federal Department of Health and Human Services, issued a requirement that scientists disclose their financial interests. But nothing happened until the Associated Press's investigations.

The NIH has received almost

Patients might have thought differently about the risks of trial treatment if they knew of scientists' financial interest

BMJ VOLUME 330 22 JANUARY 2005

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Guidelines

- **Declaration of Helsinki**

— #13. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

#22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest...

•#27. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication.

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Guidelines

- **CIOMS 2002.**

Investigators must also disclose potential or apparent conflicts of interest on their part to the ethical review committee or to other institutional committees designed to evaluate and manage such conflicts.

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Guidelines

- **ICH GCP 3.2.1**

“Only those IRB/IEC members who are independent of investigator and the sponsor of the trial **should vote/provide opinion** on a trial-related matter”

- **WHO Operational Guidelines 7.1**

“A member should withdraw from the meeting for decision procedure concerning application where there arises a conflict of interest; the conflict of interest should be indicated to the chairperson prior to the review the application and recorded in the minutes”

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Guidelines

The Belmont Principles

- I. RESPECT FOR PERSONS
- II. BENEFICENCE
- III. JUSTICE

- Potential research participants felt they had a “right to know”
- Disclosure promotes trust in the investigator
- **Subject selection should be conducted in a equitable manner and not biased to enhance the investigator's financial interest.**

How to Manage Conflicts of Interest

- **Disclosure** of conflicts of interests
- **Establishing** a conflict of interest committee
- **Divestiture** of significant financial interest by researcher

Elaine L. Brock, Conflict of Interest: An Overview for Administrators, NIH Regional Seminar, Michigan State University, April 12, 2002.

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Managing COI

- **The institution**
 - Established independent COI committee and procedures to deal with individual's / institutional financial interest in research
 - Establish COI Guidance for investigators/sponsors
 - Determining whether particular individuals should report financial interests to the COIC.
- **Establishing policies** regarding the types of financial relationships that may be held by parties involved in the research and circumstances under which those financial relationships and interests may or may not be held.

Federal Register / Vol. 69, No. 92 / Wednesday, May 12, 2004 / Notices

Managing COI

- **EC operation**
 - Reminding members of COI policies at each meeting and documenting any actions taken regarding EC member COI related to particular protocols.
 - Developing educational materials for EC members to ensure their awareness of regulations and institutional policies regarding COI.

Federal Register / Vol. 69, No. 92 / Wednesday, May 12, 2004 / Notices

Managing COI

- **Policy concerning COI**
 - Chair informs policy before meeting begins
 - A member with COI declares and withdraws himself/herself from voting
 - Record in the minute
 - Written SOPs
- Consider if the is significance COI in the protocol and how to manage.

Managing COI

• Investigators

- Including information in the informed consent document, such as the source of funding, etc.
- Having a another individual who does not have a potential or actual conflict of interest involved in the consent process,
- Using independent monitoring of the research.



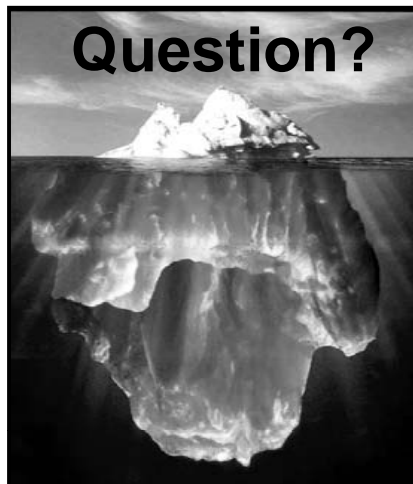
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สรุป

- มีกระบวนการเปิดเผยผลประโยชน์ทับซ้อนที่เกี่ยวข้อง
- จัดทำระเบียบกฎเกณฑ์เพื่อป้องกันและแก้ไขเรื่องผลประโยชน์ทับซ้อน
- นักวิจัยพึงวิเคราะห์ตนเองด้วยใจเป็นกลางและดำเนินการโดยอาศัยหลักแห่งคุณธรรมจริยธรรมและการเปิดเผยอย่างจริงใจ

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**There is more to ethical research
than meets the eye...**



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