Scientific Integrity and Academic Fraud

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Presentation Outline

• Provide historical background to research and its regulation
• Discuss the concept of shared values in research
• Highlight investigator and institutional responsibilities in maintaining scientific integrity
• Discuss academic fraud and highlight implications on medicine and academic discipline
Conflict Declaration

No conflicts to declare related to this presentation
Goals of Research

• To advance knowledge through critical inquiry and scientific experimentation

• Assumptions
  – Research rigor expects honesty and self-regulation
  – Research activities by nature monitors itself
  – No specific rules are needed
The Historical Facts

- Ronald Ross, Nobel prize winner for discovery of malaria disease mechanism
  - Exposed his Indian servant to malaria material
- Giovanni Battista Grassi (1854-25)
  - Infected a chronic hospital patient with malaria
- Sir Patrick Manson (1844-22), father of tropical medicine, filariasis and mosquitoes
  - Exposed son and lab assistant to malaria
  - Son was medical student, developed malaria, was treated with quinine, had relapse (vivax)
Historical Facts

- Armauer Hansen and leprosy
  - Head physician of leprosy hospital in Bergen, Norway
  - Injected leprous material from one patient into another patient to prove infectious nature of leprosy
  - Without her consent
  - Justified action by arguing that she would not consent to procedure because she would not understand the significance of the research and the fact that Hansen was capable of dealing with any adverse reactions that could occur as a result of the injection
## Protection of Human Subjects

### Timelines

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>~400 BCE</td>
<td>Hippocratic Oath</td>
</tr>
<tr>
<td>1938</td>
<td>Food &amp; Drug Act</td>
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<tr>
<td>1947</td>
<td>Nuremberg Code “Nazi Trials”</td>
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<td>1962</td>
<td>Kefauver – Harris Amendments</td>
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<td>1964</td>
<td>Helsinki Declaration signed by US</td>
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<tr>
<td>1966</td>
<td>FDA Regulations: 21 CFR</td>
</tr>
<tr>
<td>1969</td>
<td>Informed consent requirements defined</td>
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<tr>
<td>1979</td>
<td>Belmont Report</td>
</tr>
<tr>
<td>1983</td>
<td>45 CFR 46 Subpart D</td>
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<tr>
<td>1991</td>
<td>10 CFR 745 Common Federal Policy for Protection Of Human Subjects</td>
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### Additional Events

- 1949 International Code of Medical Ethics of the World Medical Assembly
- 1979 Belmont Report
- Respect
- Beneficence
- Justice

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**BELMONT REPORT**

- Respect
- Beneficence
- Justice

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**ICH**

- Good Clinical Practice
International Regulatory Authorities

- International Conference on Harmonization (ICH)
- Council for International Organizations of Medical Sciences (CIOMS)
- World Health Organization (WHO)
- World Medical Association (WMA)
- Food & Drug Administration (FDA)
Scientific Integrity Synonyms

• Honesty
• Truth
• Truthfulness
• Honor
• Veracity
• Reliability
• Uprightness
Road to Responsible Conduct of Research

Driving vs. Research rules
Shared Values in Research

• **Honesty**
  – Convey information truthfully and honor commitment

• **Accuracy**
  – Report findings precisely and avoid errors

• **Efficiency**
  – Wise use of resources and avoid waste

• **Objectivity**
  – Allow facts to speak for themselves and avoid bias
Scientific Integrity in Research

Essentials

• Trust and accountability
• Objectivity of researchers
  – Essential for advancement in science
  – Basis for Public trust
• Integrity and purity of data
Scientific Misconduct

-Misbehavior that risks corrupting the scientific record or compromising the integrity of scientific practices.

-Such behavior is unethical and unacceptable in proposing, conducting, or reporting research, or in reviewing the proposals or research reports of others.

US Commission on Research Integrity 1996
Research Misconduct

"Behaviour by a researcher, intentional or not, that falls short of good ethical and scientific standards."

British consensus panel (1999)
Common Motivation for Scientific Misconduct

Academic Pressure
• Maintaining successful academic career
  – Grant renewals
  – Publish or perish
  – Career advancement
  – Satisfaction of accomplishment
  – Reputation

Financial pressure
• Supplemental income
• Advisory Board membership
• Stock ownership
Types of Misconduct in Science

• Fabrication, falsification, plagiarism or other practices that deviate from acceptable standard by the scientific community for proposing, conducting or reporting research.

• DOES not include honest errors or honest differences in interpretation or judgment of data.
Taxonomy of Research Misconduct

- Fabrication: invention of data or cases
- Falsification: wilful distortion of data
- Plagiarism: copying of ideas, data or words without attribution
- Failing to get consent from an ethics committee for research
- Ghost authorship
- Gift authorship

Richard Smith (Editor, BMJ www.bmj.com/talks)
Scientific Misconduct

25-30 cases from Public Health service and NSF
1 case per 10,000 researchers
Scientific Misconduct

Eric Poehlman, University of Vermont

Researcher admits fraud in grant data
Ex-Vermont scientist won nearly $3m from US
By Carey Goldberg and Scott Allen, Globe Staff | March 18, 2005

Eric T. Poehlman won acclaim at the Université de Montréal and other schools for his work on obesity and metabolism. (Univ. De Montreal)

The Boston Globe

AAAS Forum on Science and Technology
Scientific Misconduct

Researcher Faces Prison for Fraud in NIH Grant Applications and Papers

In the most extensive scientific misconduct case the National Institutes of Health (NIH) has seen in decades, a researcher formerly at the University of Vermont College of Medicine in Burlington has admitted in court documents to falsifying data in 15 federal grant applications and numerous published articles. Eric Poehlman, an expert on menopause, aging, and metabolism, faces up to 5 years in jail and a $250,000 fine and has been barred for life from receiving any U.S. research funding.

Scientists say the falsified data—including work in for total cholesterol, insulin, resting metabolic rate, and glucose—were falsified or fabricated, said a statement Poehlman signed last week. In an effort to portray worsening health in the subjects, DeNino tells Science, “Dr. Poehlman would just switch the data points.”

After DeNino filed a formal complaint, a university investigative panel looked into Poehlman’s research and uncovered falsified data in three papers. These included a much-cited 1995 Annals of Internal Medicine study that suggested hormone replacement therapy could prevent declines in energy expenditure and increases in body fat during menopause. In that paper Poehlman presented metabolic data on 35 women taken 6 years apart. Most of the women did not exist, according to the statement Poehlman signed. (In 2003 the paper was retracted.) Poehlman left Vermont in 2001, before the investigation ended, for the University of Montreal. He left there in January and now lives in Montreal.

AAAS Forum on Science and Technology
Created 35 imaginary women and data over 6yrs
Scientific Misconduct

Jon Sudbø, Norwegian Radium Hospital, Oslo

Research scam makes waves

A Norwegian doctor’s fabrication of cancer research is making waves far beyond Norway’s borders. The fraudulent research may have led to faulty treatment of cancer patients, international investigations have been launched into how the fraud could have occurred, and top Norwegian officials all the way up to the ministerial level are desperately trying to control the damage.

The editor of the respected magazine, The Lancet, in which the fabricated article was published, calls the fraud “the worst the research world has seen.”

Richard Horton told Oslo newspaper Aftenposten that he also can’t understand how the Oslo doctor’s 13 co-authors and colleagues on the fraudulent cancer research project could have been duped as well.

Horton claims at least six of the doctor’s co-authors corresponded with The Lancet, and were highly involved with the substance of the article.

AAAS Forum on Science and Technology
13 co-authors involved
Korean stem-cell case, Woo-suk Hwang

Who Is Telling the Truth?
Hwang Defends Stem Cell Work; Coauthor Repeats Fabrication Claim

By Kim Tae-gyu
Staff Reporter

Korea’s cloning scientist Hwang Woo-suk contended his team did create several tailor-made stem cells and will prove the authenticity of the medical potential-laden cells in about 10 days.

During a press conference Friday at Seoul National University (SNU), Hwang apologized for disputes over the stem cell research and said he had requested the withdrawal of the stem cell paper in question featured by U.S. journal Science in May.

However, the 52-year-old geneticist rebuffed the claim of his close aide Roh Sung-II, head of Mizmedi Women’s Hospital, who argued on Thursday that Hwang admitted the stem cells were fake.
Implications of Scientific Misconduct

• Injury to patients
  – Change of practice standards
  – Death

• Emotional torture from dashed hopes

• Delay in progression of scientific knowledge

• Waste of resources
  – Replication of bogus studies
  – Grant awards from corrupt data
Principles of Maintaining Scientific Integrity in Research

• **Expectations**
  - Understanding guidelines for ethical conduct of clinical research (ICH-GCP)
  - Commitment of scientists to intellectual honesty
  - Appropriate mentor trainee relationships
  - Careful data acquisition, management and ownership
  - Collaborative science
  - Declaration and management of conflict of interest
  - Peer review process in grant reviews and publications
  - Awareness of investigator and author responsibilities
What Does an Institution or Country Need to Respond to Research Misconduct?

- Protection for whistleblowers
- A body to investigate allegations
- A fair system for reaching judgements
- An established code of good practice
- Systems for teaching good practice
What Does an Institution or Country Need to Respond to Research Misconduct?

• A recognition of the problem by the medical community and its leaders
• An independent body to lead with investigations, prevention, teaching and research
• Clear definition and agreement on what fraud is
Misconduct Inquiry

- Information gathering
- Initial fact finding

**Goal**

To determine if an allegation or apparent instance of misconduct warrants an investigation.

**Does not determine**

Conclusively if wrongdoing has occurred

Guilt

Innocence
Misconduct Investigation

• A formal examination and evaluation of all relevant facts to determine if misconduct has occurred.

• If confirmed, the investigation will determine its seriousness and identify responsible parties.
Sanctions for Scientific Misconduct

• Dependent on severity of misconduct
• Federally or Privately funded research
  – Debarment from eligibility from research funding
  – Disqualification by FDA from use of investigational drugs
  – Disqualification from serving on Advisory or Peer review committees
  – Termination of employment
The Role of the IRB

- Following review of a specific protocol, they should determine that
  - Risks to subjects are minimized
  - Risks to subjects are reasonable in relation to anticipated benefits
  - Selection of subjects is equitable
The Role of the IRB

- Informed consent will be sought from each prospective subject and appropriately documented
- When appropriate, determine that research plan makes adequate provision for monitoring data collected, safety of and privacy of subjects and confidentiality of data
The Role of the Institution Federal Wide Assurance in Research

“Institutional pledge that all research activities involving human subjects are guided by the ethical principles as set forth in the Belmont report, regardless of funding. This includes human subject research conducted by faculty, adjunct faculty, staff, students on the University premises”
US Commission on Research Integrity (1996)

• Research misconduct is significant misbehavior
• Improperly appropriates the intellectual property or contributions of others
• Intentionally impedes the progress of research
Summary

• “Integrity embodies a commitment to intellectual honesty in proposing, performing, reporting and reviewing research, and fairness in interactions with colleagues”

• “Investigators must continue to show individual accountability in decisions to enter relationships, complying with institutional, government, journal policies, and proactively addressing conflict of interest challenges”

IOM and National Research Council 2002
Suspected Misconduct Case

• Case essentials
  – Dr. Okonta is at the top of his career
  – His laboratory publishes a lot and he is always included as an author on publications
  – Drs. Okonta and George are friends, worked together for 5yrs and have published together
  – Dr. Adeola, a post Doctorate of Dr. Okonta suspects scientific fraud by Dr. George on a recent publication
  – Dr. Okonta does not know Dr. Adeola very well
Suspected Misconduct Case

• How should Dr. Okonta respond to the complaint?
  – Very seriously
  – Conflict of interest exists for him as co-author
  – Refer case to the Institutional office of Scientific Integrity for inquiry and investigation
Suspected Misconduct Case

- How should Dr. Okonta deal with Drs Adeola and George, data called into question, institution where they work and Journal where possibly fraudulent data was published?
Suspected Misconduct case

• Dealing with Dr. Adeola
  – As the head of the laboratory, it is reasonable for Dr. George to discuss Dr. Adeola’s suspicions about the research data.
  – Understand he is also involved in the suspected misconduct and may be conflicted
  – Refer the case to the Institutional office for research
  – Ensure that her privacy, rights and confidentiality during the inquiry and investigation are maintained
Suspected Misconduct case

• Dealing with Dr. George
  – Inform him of complaint by Dr. Adeola
  – Advise Dr. George to avoid direct discussion of case with Dr. Adeola
  – Inform Dr. George of case referral to the Institutional office for Conflict of Interest and Scientific integrity
  – Instruct Dr. George to cooperate with the inquiry
  – Request protection of data in question for the investigators
Suspected Misconduct case

• Data called into Question
  – Expect a detailed review of the Laboratory data involve
Suspected Misconduct case

• Dealing with the Institution where all 3 work
  – Refer case to the relevant institutional office

• Dealing with Journal where data published
  – Defer specific notification until the investigation is completed
  – Once completed and if data found fraudulent, inform Journal about need for retraction of the publication
Suspected Misconduct case

• Assume Dr. Okonta is unresponsive to Dr. Adeola’s complaints.

• How might Dr. Adeola follow-up on her concerns?
  – Refer case to the Institutional office for research
Suspected Misconduct case

• Assume that Dr. Okonta proceeds by asking Dr. George obliquely about the assay used for the project, mentioning that Dr. Adeola seems to have some problems with it.

• In spite of Dr. Okonta’s subtlety, Dr. George suspects that his inexperienced postdoc has planted some serious suspicions in Dr. Okonta’s mind.

• Since Dr George is confident of the accuracy of his work, how should he respond to Dr. Okonta?
  – Pledge to make the laboratory data available and fully cooperate with the initial inquiry and subsequent investigation.
Suspected Misconduct case

• Should Dr. George approach Dr. Adeola and if so, what should he say to her?

  – Best to let the review and inquiry process proceed without “tampering with the witness”
Anything that can be misunderstood has been misunderstood.
How Common is Research Misconduct?

• Redundant publication occurs in about 20% of publications

• About 20% of authors on publications have done little or nothing to justify authorship

• Most authors of studies in medical journals have conflicts of interest, yet they are declared in less than 5% of cases
Conflict of Interest

Conflict of interest is the most debated issue regarding relationship between academic scientists, physicians and the pharmaceutical industry.
“Edict of Palermo”

By early 13th century, Holy Roman Emperor Frederick II of Hohenstaufen enforced legislation which no longer allowed physicians to sell medicines and separated the professions of physicians and pharmacists.
Conflict of Interest

Arises when an activity is in divergence between personal or institutional benefit when compared to the responsibilities to patients and to society

This can be in the context of research, medical education, guideline development, purchasing, leadership and investments
When does a Conflict of Interest Exist?

Occurs in a situation in which professional judgment regarding a primary interest, such as research, education or patient care, may be unduly influenced by a secondary interest, such as financial gain, family interest or personal prestige.

Lemmens. CMAJ 1998:159960-65 and Singer
Conflict of Interest in Research

• Dr. K’s long awaited grant was not funded
• Approached by CRO to be PI in a clinical trial comparing a new drug to an established one
• Benefits of acceptance of offer
  – Enable payment of reliable technician of 5 years
  – Compensation of $5K per enrolled subject
  – Sponsor OK with PI keeping extra $2K beyond all study related costs
• In return, PI is expected to sign to waive rights to publish or disclose study findings
Conflict of Interest in Research

• Dr. N is a famous University Professor and cardiologist and Cardiology program director
• She is invited to attend a 2-hour CME program in Hawaii. No presentation is expected
• All expenses for her travel and 10 days stay in Hawaii will be covered
• Her expert opinion is expected in a 1-hour post-conference retreat dinner in New York
• She will receive $5,000 for her efforts
Conflict of Interest in Research

What is wrong with these scenarios?
Apparent Conflict of Interest

- When participation in an official or personal capacity on any matter (primary interest) has a direct and predictable effect on a secondary or personal interest
Apparent Conflict of Interest

- A member or researcher serving as a reviewer may have an apparent conflict of interest in an application or proposal if the application or proposal is submitted by
  - Person with whom a business relationship exists
  - Person from researcher’s family
  - Organization for whom the researcher’s family serves as an officer, trustee, consultant or seeking employment
Appearance of Conflict of Interest

• Arises where a researcher or committee member is involved in a particular matter involving specific outside parties and the circumstances are such that a reasonable person with knowledge of the relevant facts would question the member’s impartiality
Appearance of Conflict of Interest

• Specific outside parties (examples)
  – A member of household or a close relative
  – Person with whom the member has or seeks a business, contractual, or other financial relationship.
  – Any organization for whom the member’s spouse, parent or dependent child is serving or seeking to serve as an officer, director, trustee, consultant or employee
Conflict of Interest in Research

• Very common and unavoidable
• Having a conflict of interest is not unethical
• Failure to recognize or declare a conflict of interest is unethical
• Consequences of unmanaged conflicts
  – Compromise of patients’ trust in physician
  – Undermines public trust in the profession
  – Damages scientific integrity
Common Causes of Conflict of Interest in Research

Lack of Institutional COI policy
- Poorly developed IRB/Ethics Board
- Poor understanding of ethical standards in conducting research

Pressure of Academia
- Maintaining research enterprise
  - Difficult grant environment
  - Need for soft research money
Financial Conflict of Interest

- Most common source of conflict of interest
- Includes any monetary interest of the researcher, the spouse or minor children
- May also include but are not limited to royalty or licensing agreements with or stock ownership in such organizations as drug companies, non-Federal research institutions etc
How Common is Conflict of Interest?

- 75 articles
- 89 authors
- 69 (80%) responded
- 45 (63%) had financial conflicts of interest
- Only 2 of 75 articles disclosed the conflicts of interest

## Relationship Between Financial Interest and Safety Recommendations on Calcium Channel Blockers

<table>
<thead>
<tr>
<th>Variable</th>
<th>Supportive</th>
<th>Neutral</th>
<th>Critical</th>
<th>P Value</th>
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<tr>
<td># Articles</td>
<td>30</td>
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<td>23</td>
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<tr>
<td># Author Survey Response</td>
<td>24</td>
<td>15</td>
<td>30</td>
<td></td>
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<tr>
<td>Authors with Financial ties</td>
<td>24 (100%)</td>
<td>10 (67%)</td>
<td>13 (43%)</td>
<td>&lt;0.001</td>
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<tr>
<td>Honorarium from Manufacturer</td>
<td>75%</td>
<td>40%</td>
<td>17%</td>
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<tr>
<td>Research Funding support</td>
<td>87%</td>
<td>40%</td>
<td>20%</td>
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<tr>
<td>Consulting for Calcium channel manufacturer</td>
<td>25%</td>
<td>33%</td>
<td>17%</td>
<td>0.45</td>
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</table>

*Stelfox et al: NEJM 1998; 338: 101-105*
Industry Support and Professional Opinions

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Supportive Authors (N = 24)</th>
<th>Neutral Authors (N = 15)</th>
<th>Critical Authors (N = 30)</th>
<th>Chi-Square for Linear Trend</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer of calcium-channel antagonist</td>
<td>23 (96)</td>
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<td>Manufacturer of competing product</td>
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<td>8 (53)</td>
<td>11 (37)</td>
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<tr>
<td>Any manufacturer</td>
<td>24 (100)</td>
<td>10 (67)</td>
<td>13 (43)</td>
<td>22.68</td>
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</table>

## Industry Support and Professional Opinions

<table>
<thead>
<tr>
<th>Interaction and Manufacturer</th>
<th>Supportive Authors (N = 24)</th>
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<th>Chi-Square for Linear Trend</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of authors</td>
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<tr>
<td>Support to attend symposium</td>
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### Author Position on Rosiglitazone Safety and Financial Interest

<table>
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<tr>
<th>Manufacturer Relationship</th>
<th>Favorable N=31</th>
<th>Neutral N=84</th>
<th>Unfavorable N=65</th>
<th>Rate Ratio (95% CI)</th>
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<td>52 (62)</td>
<td>47 (72)</td>
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Wang et al: BMJ 2010: 340;c1344
## Author Position on Rosiglitazone Safety and Financial Interest

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<tr>
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<td>3 (12)</td>
<td>70 (60)</td>
<td>28 (74)</td>
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</table>

Wang et al: BMJ 2010: 340;c1344
Pfizer Admits it Paid out $35m to Doctors

• Pfizer admitted it had paid $35m over a six month period to 4,500 doctors who worked with the company on the development and marketing of new drugs and helped “educate” other doctors on their use.

• Disclosure made as part of a government settlement after it pleaded guilty to illegally promoting more than a dozen of its own drugs.

• Pfizer paid a record $2.3bn fine in connection to the deal.
Conflict of Interest Studies

• Lexchin (2003), *BMJ*

Meta-analysis of 30 COI studies

Positive correlation (4.05 OR) between industry sponsorship and positive outcomes
Conflict of Interest Studies

- **Bekelman (2003), JAMA**
  
  Meta-analysis of 37 COI studies (1,000s of trials)

  Positive correlation (3.60 OR) between industry sponsorship and positive outcomes
Conflict of Interest Studies

• Friedman (2004)
  398 publications, NEJM and JAMA

Positive correlation (2.35-2.64 OR) between industry sponsorship and positive outcomes
Are All University-Pharmaceutical Partnerships Bad?

### Table 1 Selected partnerships between universities and big pharma

<table>
<thead>
<tr>
<th>Company</th>
<th>Date</th>
<th>Partner</th>
<th>Deal</th>
</tr>
</thead>
<tbody>
<tr>
<td>AstraZeneca</td>
<td>October 2008</td>
<td>Columbia University Medical Center</td>
<td>Study of neurogenesis with respect to depression and anxiety</td>
</tr>
<tr>
<td></td>
<td>June 2008</td>
<td>Columbia University Medical Center</td>
<td>Study of metabolic diseases, obesity and type 2 diabetes</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>June 2008</td>
<td>Immune Disease Institute</td>
<td>$25 million over five years for joint research projects on immunoinflammation</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>November 2008</td>
<td>University of California, San Diego</td>
<td>Research, education and training collaborations with a focus on new clinical applications</td>
</tr>
<tr>
<td>Merck</td>
<td>September 2007</td>
<td>Harvard University</td>
<td>Funding for six labs in oncology and central nervous systems disorders</td>
</tr>
<tr>
<td></td>
<td>April 2008</td>
<td>Harvard University</td>
<td>Funding for two labs working on osteoporosis</td>
</tr>
<tr>
<td>Pfizer</td>
<td>January 2008</td>
<td>Washington University, St. Louis</td>
<td>$25 million over five years for joint research projects on immunoinflammation</td>
</tr>
<tr>
<td></td>
<td>June 2008</td>
<td>QB3 Institute</td>
<td>$9.5 million for projects that will speed translation of discoveries to drugs</td>
</tr>
</tbody>
</table>
Can University-Industry Relationships be Managed?

- Developing clear policies, efficient processes and support mechanisms to guide Investigator relationships with industry
- Maintaining access to all phases of data analysis and interpretation is essential
- Avoid agreements that prevents or delays publication of research results > 60 days
- Peer review and monitoring of industry relationships to protect primary interests
Conflict of Interest can Always be Managed

• Advise researcher on remedial actions
• Disqualification from matters specifically involving or affecting those interests
• Limitation of duties, voluntary resignation, or transfer to another committee
• Divestiture of a conflicting interest
• Establishment of a qualified blind or diversified trust
• Resignation from a position with business or other entity
• Authorize or deny participation of faculty in any research project
Avoiding COI Institutional Obligations

- Create standing Institutional COI committee
- Maintain a written and enforced COI policy
- Ensuring faculty awareness of policy
- Yearly ethics training for ALL researchers
- Provide adequate guidelines for enforcement mechanisms and sanctions
Managing Conflicts of Interest
International Implication

- **Federal wide Assurance**
  - Represents the University’s pledge that all research activities involving human subjects are guided by the ethical principles as set forth in the Belmont report regardless of funding source.
  - This includes human subject research conducted by faculty, adjunct faculty, staff and students.
Role of the IRB in Managing Conflicts of Interest

• No regulatory requirement for IRB to consider investigator financial conflict of interest

• Up to 30% of IRB’s routinely consider and deal with Investigator and IRB member conflicts of interest
Role of the IRB in Managing Conflicts of Interest

• Ensure that **ALL** IRB members make COI declaration at election and update information annually or more frequently as needed

• **ALL** researchers should be made to declare financial and potential relationships that may pose a conflict during a research study as part of the IRB review process
Guiding Principles to Investigators in Reducing Conflict of Interest

• Commitment to conduct scientific research with **highest professional standards**
• Understanding that primary responsibility as full-time faculty is to one’s academic institution
• Outside activities should **complement** and not compromise institutional responsibilities
• Consulting and advisory board relationships should be carried out in a transparent and accountable manner and disclosed as they are initiated.
• When a consulting relationship exists with an investment firm related to one’s area of expertise, all parties shall be aware of the specific circumstances involved.
Is Dr. Johnson’s participation appropriate?

- **Pros**
  - Suitable academic environment
  - Relevant expertise
  - Important clinical trial with potential for significant impact
  - Lead investigator role
  - Financial relief for self and department
  - Important academic accomplishment
Is Dr. Johnson’s participation appropriate?

• Cons
  – Significant investment in 3 Biotech firms
  – Drug available to her patients only through study participation
  – Need for augmenting division income
  – Ability to maintain objectivity as lead investigator
  – Involvement of a placebo controlled arm in light of her familiarity with the preliminary data and potential for compromised judgment
Does Dr. Johnson have a conflict of interest? What’s the nature?

- Definitely
- Nature of Conflict
  - Mostly Financial with the financial gains and potential for fame likely to impair or influence her judgment
  - Possibly ethical conflict in having a control group
- How can the conflict be mitigated?
  - Specify extent of stock involvement in Bio-tech firms
  - Place equity holdings in a blind trust
  - Divest her stock holdings
  - Have someone else serve as lead investigator
  - Create as advisory committee to monitor the study results
Conflict of Interest case 1

• Would the conflict be different if she had not owned stock but instead had been offered stock as a form of compensation?
  – YES
  – The payment in stock makes the financial incentive for participation even greater especially if the study outcome is good as anticipated.
  – Potential for fame and gain puts more pressure on researcher’s objectivity, judgment and data integrity
Conflict of Interest Case 1

• Can Dr. Johnson honestly assign patients randomly to treatment or placebo?
  – Probably, but the appearance of conflict may undermine her credibility as lead investigator

• What if she believes the drug is deleterious because it has adverse effects on the kidney late in the treatment?
  – As long as her belief is unproven, the planned prospective, randomized and placebo-controlled studies should answer the questions
What should be the role of the University?

- Make Dr. Johnson declare her conflicting equity ownership in Biotech sector
- Suggest an alternative lead investigator
- Remove Dr. Johnson from decision making position during the clinical trial
- Create an Advisory committee to provide oversight
Conflict of interest Case 1

• Dr. Johnson is able to tell who is on the study drug based on the presence of a facial flush. Might that further influence her ability to remain objective?
  – Definitely

• What considerations apply in answering that question?
  – Knowing that study subjects are flushed in a way unblinds the investigator to the study drugs
Approach to Conflict of Interest Management

• Awareness
• Disclosure
  – Asking the question “would I feel comfortable if patients or other people find out about my interest in this matter?”
• Review and authorization
• Prohibition