

Chapter 4: CONFLICTS OF INTEREST (COI)

A. Definitions

Interest

An interest may be defined as a commitment, goal, or value held by an individual or an institution.

Examples include a research project to be completed, gaining status through promotion or recognition, and protecting the environment. Interests are pursued in the setting of social interactions.

Conflict of Interest (COI)

A conflict of interest exists when two or more contradictory interests relate to an activity by an individual or an institution. The conflict lies in the situation, not in any behavior or lack of behavior of the individual. That means that a conflict of interest is not intrinsically a bad thing.

Examples include a conflict between financial gain and meticulous completion and reporting of a research study or between responsibilities as an investigator and as a treating physician for the same trial participant.

Institutional examples include the unbalancing of the institutional mission by acceding to the space requests of a large donor for an idiosyncratic program.

Other definitions include:

Conflicts of interest are “situations in which financial or other personal considerations may compromise, or have the appearance of compromising, an investigator’s judgement in conducting or reporting research.” AAMC, 1990

“A conflict of interest in research exists when the individual has interests in the outcome of the research that may lead to a personal advantage and that might therefore, in actuality or appearance compromise the integrity of the research.” NAS, Integrity in Scientific Research

B. Consequences of a COI

When an individual COI exists, then independent of the behavior of the investigator, those knowledgeable about the study must take the COI into account when judging the validity of the study.

Beyond that, in clinical research, the well being of the subjects may also be compromised by a COI and this has become an overarching factor in the

regulation of financial COIs in clinical research. As noted above, the well being of the participants is paramount and trumps the completion of the research.

C. Government intervention

The Bayh-Dole act of 1980 made it possible for institutions and individuals to recover substantial financial rewards for their intellectual property as royalties and as equity. Furthermore, the reliance of research sponsors on the expertise of faculty to support a trial agent encouraged substantial payments to accrue to faculty as consultants, often on a continuing basis. Optimizing these financial interests produces a COI situation in relation both to the conduct of the research and to the welfare of trial subjects. Responding to these realities, the NIH, FDA and individual institutions developed rules for investigators to limit the impact of investigator COIs under Federal rules. A reminder follows

<http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-05-013.html>

The actual rules can be found at this URL

<http://grants.nih.gov/grants/guide/notice-files/not95-179.html>

The key provisions are, redacted:

“Investigators are required to disclose to an official(s) designated by the institution a listing of Significant Financial Interests (and those of his/her spouse and dependent children) that would reasonably appear to be affected by the research proposed for funding by the PHS. The institutional official(s) will review those disclosures and determine whether any of the reported financial interests could directly and significantly affect the design, conduct, or reporting of the research and, if so, the institution must, prior to any expenditure of awarded funds, report the existence of such conflicting interests to the PHS Awarding Component and act to protect PHS-funded research from bias due to the conflict of interest.

The definition of "Significant Financial Interest" in 50.603 has been changed in several respects. The exception for financial interests in business enterprises includes salary, royalties or other payments not reasonably expected to exceed \$10,000 per annum. Alternative measures of \$10,000 in value include stock or no more than five percent ownership interest.”

In my view, \$10,000 or an ownership position even if it has no cash value constitutes a significant COI and should be at least disclosed. Disclosure requirements are very poor in that the statute limits them to the institutional administrators and the COI committee. They should be required to disclose every time they present or publish research.

D. Industry Sponsorship

Studies of industry sponsorship reveal profound influence over study design, analysis and interpretation of data (bias). They also engage in suppression of results (negative, AEs). They promulgate secrecy among researchers by negotiating confidentiality clauses in contracts.

Sometimes results are made public while bypassing the peer review system.

“Drug company money and investigator COIs have so corrupted clinical trials research that drug companies control what clinicians and patients know and don’t know about the \$200,000,000 worth of drugs and devices they are consuming.”

“This is all about bypassing science. Medicine is becoming a sort of Cloud Cuckoo Land, where doctors don’t know what papers they can trust in the journals.” Drummond Rennie of JAMA

E. Professional Societies

Professional societies take huge amounts of pharmaceutical money to support their annual meetings and other activities. The funding may unbalance the science presented at the meeting. They permit highly biased Continuing Medical Education segments.

Professional societies do not carefully control the listing of COIs in the scientific presentations. They foster over-the-top media presentations of advances. They permit biased articles and supplements in their journals.

F. Clinical Practice Guidelines

The practice of “evidence based medicine” has led to the development of guideline for the treatment for many medical conditions, based on meetings of “experts,” often from professional societies. Treatment guidelines generally support the use of more procedures and medications. It was recently shown that

33% of guideline authors have financial interests in the drug

50% guidelines had no COI documentation

34% of guidelines stated no COIs

50% had at least one author receiving research support

43% had at least one author who had been a paid speaker for the company

Derived from National Guideline Database

Nature, Oct 20,2005

G. Other initiatives

The people who need to know about the COI are those who learn about the results of a study and have to interpret it.

The decision about disclosure of a COI should never be left to the possessors of the COI because they are susceptible to self-deception or worse about the influence of the COI on their research behavior.

Thus, NIH and other funding agencies, Professional Societies sponsoring research meetings, and the leading journals now require disclosure of COIs as a precondition for reviewing, editing, presenting and publishing research and research proposals but there is no means of enforcing the requirement. Voluntary revelation of a COI precludes the reviewing, of a grant or paper. A COI must be disclosed in presenting science.

The Appearance of a COI must be avoided or disclosed. Consider the NY Times test. “Would you want the relationship published in the NY Times?” The presence of Conflicts of Interest tends to diminish the credibility of a study.

The most common conflicts of interest in research are between financial or career rewards and the integrity of a research study, report, presentation, or review.

**It's necessary to manage outside income,
for consultations
for lectures,
for courses,
for research
when conducting a clinical trial.**

Full disclosure of conflicts of interest should be required in consent forms, papers, lectures and presentations. COIs may result in:

- 1. Loss of objectivity**
- 2. Reordering of priorities towards applied research**
- 3. Degradation of the *nature of science* as an open and collegial enterprise**
- 4. Exploitation of trainees**
- 5. Transfer of time and interest to Commercial ventures**

H. COIs in Financial Consulting

A new kind of COI has just come to light as the practice has become much more widespread through investigative reporting of the Seattle Times. Many investigators are recruited to consult for financial entities including venture capital firms, hedge funds and investment houses to inform them of the latest developments in their field. The pay is good and the investigators feel quite

flattered. Sometimes, the investigators have provided privileged information about an ongoing clinical trial about which both they and their institutions signed confidentiality statements. In all instances, the goal of the consulting groups is to learn information of investment value before the competition. After the initial concern, apparently this area of concern has lost immediacy.

Cases: Chapter 4

Case: Remembra

Dr. Zhivago, in NIH supported research, made remarkable progress in memory studies by identifying a new receptor “C” responsible for instilling and preserving memories. In mice and rats substantial improvements in memory were produced in a short time as demonstrated by performance studies. Activating C in monkeys permitted substantial acceleration in achieving cognitive skills and great enhancement in cognitive capability. Zhivago approached her institution’s Office of Technology to arrange for patent and licensing.

The University had just established a research incubator to carry its inventions to a more advanced stage so that it would be able to retain a greater portion of the financial benefits to come from the products of discovery.

The Office of Technology suggested that Zhivago establish a company with the university to exploit her discovery and develop small molecule receptor agonists for use in treating certain forms of mental retardation as well as Alzheimer’s and other disorders. Neither Zhivago, nor the university officials were unaware of the fact that once approved, the agonists would most likely be taken by normal persons to augment their intellectual capabilities.

Zhivago was told that the university would advance up to 1 million dollars of its endowment on this company and that as funding requirements grew, depending on the situation, either more new funds would be allocated or venture capitalists would be invited to invest.

Zhivago, figuring that if she reduced her clinical burden and got out of teaching, which were easily arranged, she could spare 30% of time for this project and suggested to her senior technician Anna Karenina that she take a job at the new company, LEARN, with a significant salary increase, and manage the practical details of creating C-receptor agonists under Zhivago’s direction. When the time came, Zhivago would test her drug first in mentally retarded children, her specialty.

Dr. Zhivago delayed publication of her discovery for four months in order to accomplish the patent and license work.

Upon learning of the discovery, a couple of very large drug companies with an interest in mental health volunteered financial support for priority in the bidding for the new agent when it was developed.

The entire university leadership was highly attuned to this activity as the result of their big stake in the outcome.

Zhivago found that it was very difficult to recruit someone as effective as Anna to run her lab where she was expected to continue to perform at a high intellectual level.

Zhivago found that she needed a lot of assistance with designing, synthesizing and testing CR agonists. Pharmacologists from the university were asked to help and they asked for equity in return. The Pharmacologists were knowledgeable but unwilling to commit enough time to oversee the effort.

Three and one half million dollars and two years later, a potent CR agonist was available for testing. It was called Remembra.

The IRB, with an inquiry from the university President urging expediency, approved the Phase I and II trials. In a total of 25 subjects the pharmacokinetics and acute toxicity studies were completed satisfactorily.

As Dr. Zhivago gears up for the clinical test of Remembra, she learns that her NIH renewal was not going to make the grade because of poor recent productivity. She thinks, "If this works, I won't need to keep applying for grants."

While the IRB was initially reluctant to approve Dr. Zhivago's role in both managing and carrying out the Phase III placebo controlled double blinded trial, with a little institutional encouragement the protocol was approved and Zhivago began testing Remembra on mentally retarded adolescents who required special schooling. Even though the study was double-blinded, the progress on Remembra was so dramatic that everyone thought they knew who was taking the real drug. Treated students were able to learn and retain much more rapidly than ever before.

Enthusiasm at the school got out and reached university administration, which revealed in the possibility that one of their investments might pay off.

About 3 months into the six-month trial it was noted that some of the participants began to have episodes of sweating and confusion that came and went. The teachers and investigators reported these events and when the Data and Safety monitoring Board was informed, one of the investigators suggested measuring the blood sugar during episodes and sure enough, the symptoms were found to be due to hypoglycemia (very low blood sugar).

Since there were no severe episodes and the episodes were treatable with orange juice, the DSMB suggested providing frequent meals and teaching the families and teachers of the students how to treat hypoglycemia. The IRB required an amendment to both the protocol and the consent form recognizing the adverse event.

By the fifth month the adolescents were gaining a lot of weight and on one occasion a participant went into hypoglycemic coma and had to be treated in the E.R.

The DSMB decided to stop the trial for safety reasons even though the participants on Remembra were learning at an impressive rate and the teachers wanted it continued. The DSMB heard an appeal from the university president for the sake of the mentally retarded to continue the study but they did not budge.

One of the teachers told the story of Remembra to the N.Y. Times, which published a long article on the story. Shortly thereafter Dr. Zhivago received a call from a major drug company about the possibility of developing Remembra as a treatment for diabetes.

1. What conflicts of interest exist in this scenario?
2. Remembra has potential. How can the ethical issues surrounding its testing be resolved?
3. How does the idea of improving on human intelligence strike you ethically?
4. If you were the CEO of LEARN what actions would you take now?

Case: Conflict of Interest Committee

You are a member of your institution's conflict of interest committee charged with the responsibility of determining the significance of Eric Jensen's conflicts of interest (COI) and to manage it. You are the primary reviewer for Jensen's proposal. He has invented an electrical device that markedly accelerates the fracture-healing rate. This was brought to the intellectual property office where a patent was requested. Jensen also formed a company to exploit the patent with the University. They induced a large medical apparatus company to manufacture and market the device. The university and Jensen's company would receive equity and royalties.

Jensen receives a prototype of the commercial version of the device and decides to conduct a clinical trial on healing rates comparing the device with conventional treatment. He will carry out a blinded study using the device appropriately or in an inactive mode.

1. Please comment on the proposed arrangement as primary reviewer for the COI committee.
2. What are the limits on a faculty member's interest in his/her company's ownership and function?
3. What does "conflict of commitment mean in this setting?"

Case: Expert consultant

Going through your E-mails you find the following:

Hansen and Question, a commercial analysis company, is conducting in depth 30 minute interviews with thought leaders in your field about dilational cardiomyopathy for which a new molecular mechanism was just uncovered.

The E-mail indicates that they have been commissioned by a pharmaceutical company to get a further understanding of approaches to the management of this condition. They are willing to pay you \$500 for a 30 minute, one on one interview. The E-mail indicates that all your opinions will be reported anonymously in the final report.

As an expert on cardiomyopathy with definite views, you feel that might have a lot to offer the company; after all, you are the PI on a sophisticated study of cardiomyopathy at this very moment.

- 1) **Should you respond to the E-mail?**
- 2) **What questions should you ask if you chose to respond?**
- 3) **Are there any constraints in relation to giving your opinion?**
- 4) **What is the university's involvement in this kind of activity and what should it be?**

Chapter 4 Bibliography

Cohen, J. J. (2001). "Trust Us to Make a Difference: Ensuring Public Confidence in the Integrity of Clinical Research." *Acad Med* 76(2): 209-214.

Investigators' and institutions' financial conflicts of interest in clinical research raise serious questions about the objectivity of such research, the safety of human subjects, and the threat to public trust in the integrity of clinical research. Yet the author makes clear that a conflict of interest is a state of affairs, not a behavior, and therefore not automatically a manifestation of improper actions. But it is clear that both non-financial conflicts of interest and financial ones are double-edged: they can motivate individuals to do their best work but also can compromise judgment and undermine objectivity. The author offers eight suggestions for what academic medicine's leaders might do in this regard (comply with existing full-disclosure requirements; establish principles governing institutional conflicts of interest; etc.). He closes by reiterating that the pursuit of clinical research depends entirely on the ability and willingness of the research community to merit public trust.

(2003). "Protecting Subjects, Preserving Trust, Promoting Progress I: Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research." *Acad Med* 78(2): 225-236.

(From the Executive Summary) In December 2001, the AAMC Task Force on Financial Conflicts of Interest in Clinical Research released this report, the first of two (both published in this issue of *Academic Medicine*). This report focuses on gaps in existing federal financial disclosure regulations of individual conflicts of interests, finding that additional scrutiny is recommended in two areas: human subjects research and privately sponsored research. The task force suggests that when potential conflicts exist, a conflicts of interest committee should apply a rebuttable presumption against engaging in human subjects research. The task force recommends that the circumstances giving rise to the presumption against the proposed activity be balanced against compelling circumstances in favor of the conduct of the research. The AAMC task force delineates core principles to guide institutional policy development. First, an institution should regard all significant financial interests in human subjects research as requiring close scrutiny. Second, in the event of compelling circumstances, an individual holding a significant financial interest may be permitted to conduct the research. Whether circumstances are deemed compelling will depend in each case upon the nature of the science, the nature of the interest, how closely the interest is related to the research, and the degree to which the interest may be affected by the research. Four other core principles for development of institutional policies are identified in the report, pertaining to reporting, monitoring, management of conflicts, and accountability.

(2003). "Protecting Subjects, Preserving Trust, Promoting Progress II: Principles and Recommendations for Oversight of an Institution's Financial Interests in Human Subjects Research." *Acad Med* 78(2): 237-245.

(From the Executive Summary) The AAMC Task Force on Financial Conflicts of Interest in Clinical Research issued this report, the second of two, in October 2002. (The first report is also published in this issue of *Academic Medicine*.) This report offers a unique perspective on the new phenomenon of "institutional" conflicts of interest. The task force acknowledges the diverse obligations of academic institutions that conduct research and also invest in--and accept the philanthropy of--commercial research sponsors. The task force emphasizes the importance of disclosing institutional financial interests as an integral part of the research process, critical to allaying public concerns, and to strengthening the trust relationship between research subjects, the public and the scientific community. The task force found that the safety and welfare of research subjects and the objectivity of the research could be--or could appear to be--compromised whenever an institution holds a significant financial interest that may be affected by the outcome of the research. Thus, the task force recommends separating the functional and administrative responsibilities related to human subjects research from those related to investment managing and

technology licensing, and encourages the establishment of institutional conflicts-of-interest committees. As in the first report, the task force recommends that institutions should develop policies establishing a rebuttable presumption against the conduct of research at or under the auspices of an institution where potential conflicts in human subjects research are identified. This presumption against engaging in the research is to be balanced against compelling circumstances in favor of the conduct of the proposed research activity.

Kelch, R. (2002). "Maintaining the public trust in clinical research." *N Engl J Med* 346(4): 285-7.

This is a laudatory commentary on the AAMCs report on individual conflicts of interest.

(2003). *Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection*. Federal Register. 68: 15456-15460.

The Office of Public Health and Science (OPHS), Department of Health and Human Services (HHS) announces a final guidance document for Institutional Review Boards (IRBs), investigators, research institutions, and other interested parties, entitled *Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection*. This guidance document raises points to consider in determining whether specific financial interests in research could affect the rights and welfare of human subjects, and if so, what actions could be considered to protect those subjects. This guidance applies to human subjects research conducted or supported by HHS or regulated by the Food and Drug Administration.

Angell, M. (2000). "Is Academic Medicine for Sale?" *N Engl J Med* 342(20): 1516-1518.

This position paper uses evidence mostly from publications to argue that conflicts of interest are so pervasive so as to compromise the integrity of much medical publication.

Bekelman, J. E., Y. Li, et al. (2003). "Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review." *JAMA* 289(4): 454-465.

This was a meta-analysis of the quantitative analytic literature on conflicts of interest in biomedical research from 1980 to 2002 using a variety of search techniques for materials. In 34 studies meeting all their criteria they show that about 1/4 of the investigators had industry affiliations and 2/3 of academic institutions hold equity in start-ups that sponsor research. They claimed a relationship between industry sponsorship and positive conclusions. Industry sponsorship was also associated with restrictions on publication and data sharing. They concluded that conflicts of interest can have a powerful effect on biomedical research reports.

Bentley, J. P. and P. G. Thacker (2004). "The influence of risk and monetary payment on the research participation decision making process." *J Med Ethics* 30(3): 293-298.

This study used pharmacy students' reactions to scenarios varied by risk and payment to determine the extent to which they affected decisions to participate in a clinical trial. They found that money did help enlist subjects but they were not blinded to the risks.

Blumenthal, D. (2003). "Academic-Industrial Relationships in the Life Sciences." *N Engl J Med* 349(25): 2452-2459.

The author describes the evolving set of relationships between academic institutions and industry as it pertains to biological developments. He points out the rapid progress of biotechnology and the significant support of research by industry. He also points out the influences on scientific integrity and diminished quality of treatment of research subjects. A very important paper.

Blumenthal, D. (2004). "Doctors and Drug Companies." *N Engl J Med* 351(18): 1885-1890.

The author describes the evolving nature of the relationships between doctors and drug companies over the 20th century and the influences that the companies have come to exert over medical practice and research. He also discusses efforts to manage these relationships. Conflicts of interest pervade. This is a very powerful statement and uncomfortable reading for physicians.

Blumenthal, D., N. Causino, et al. (1996). "Relationships between Academic Institutions and Industry in the Life Sciences -- An Industry Survey." *N Engl J Med* 334(6): 368-374.

Despite growing acceptance of relationships between academia and industry in the life sciences, systematic, up-to-date information about their extent and the consequences for the parties involved remains scarce. They surveyed a representative sample of life-science companies in the United States to determine their relationships with academic institutions by telephone from senior executives of 210 life-science companies (69%). Ninety percent of the companies had relationships with an academic institution in 1994. Fifty-nine percent supported research, providing approximately 11.7 percent of their research-and-development funding. Over 60 percent of those companies had received patents, products, and sales as a result. The companies also reported that they often had agreements to keep the results of research secret beyond the time needed to file a patent. These relationships need greater scrutiny.

Bodenheimer, T. (2000). "Uneasy Alliance -- Clinical Investigators and the Pharmaceutical Industry." *N Engl J Med* 342(20): 1539-1544.

The author details the uncomfortable relationship between clinical investigators who carry out research on new drugs and industry that has a powerful vested interest in the success of their products. Conflicts of interest are widespread with adverse consequences for the science.

Boyd, E. A. and L. A. Bero (2000). "Assessing Faculty Financial Relationships With Industry: A Case Study." *JAMA* 284(17): 2209-2214.

The authors reviewed disclosure forms at UCSF to determine more about clinical and basic science faculty relationships with industry. By 1999, almost 7.6% of faculty investigators reported personal financial ties with sponsors of their research, including paid speaking engagements 34%. 33% had consulting agreements, and 32% involved the investigator holding a position on a scientific advisory board or board of directors. 14% involved equity ownership, and 12% involved multiple relationships. The advisory panel recommended managing perceived conflicts of interest in 26% of the cases. They considered this to be a growing problem that required management.

Boyd, E. A., M. K. Cho, et al. (2003). "Financial Conflict-of-Interest Policies in Clinical Research: Issues for Clinical Investigators." *Acad Med* 78(8): 769-774.

They questioned faculty at UCSF and Stanford who conducted clinical research about their knowledge of and attitudes towards conflict of interest policies. The campus COI policies were a mystery to more than half of those interviewed. Many investigators felt that, rather than the university, monitoring COIs was the job of professional societies, (who have no clout) the public (that understands nothing about this) and, individual investigators (who routinely engage in self-deception) should monitor conflicts of interest. Administrators and policymakers have to find a way to convince investigators, both clinical and nonclinical, of the serious problems of bias and co-optation associated with financial relationships with industry.

Brainard, J. (2001). *Federal Rules on Conflicts of Interest in Biomedical Research Are Inadequate*, GAO Finds. The Chronicle of Higher Education. Washington.

The GAO pointed out what everyone knew and was glad of, namely that COI regulations were weak and unenforceable.

Bramstedt, K. (2003). "Research subject advocates: to whom are they loyal?" *Clin Invest Med* 26(2): 64-9.

The author deals with the issue of conflicts of interest in the activities of Research Subject Advocates. This is based largely on who is paying them. Of course, the main issue is what are they paying them for. GCRC RSAs, for example are paid to support the subjects and they should normally operate in that manner. She deals with the Abiomed artificial heart case in which the subject advocate was sued as wrongly representing the institution. How hard is it for subjects to get the kind of support they need in difficult studies with considerable risk?

Brownlee, S. (2004). *Doctors Without Borders: Why you can't trust medical journals anymore*. Washington Monthly.

This reporter discusses the Nemaroff case in which a physician wrote a review article for *Nature Neuroscience* in which he failed to reveal his many and profitable conflicts of interest in recommending

drug treatments for psychiatric illness. She goes on to discuss in vivid terms the insidious downside of these conflicts and the great efforts made by industry to involve prominent physicians in supporting their drugs.

Calfee, J. E. (2001). "Pharmaceutical Price Controls and Patient Welfare." *Ann Intern Med* 134(11): 1060-1064.

He argues forcefully against price controls for drugs as inhibiting innovation and eliminating the risk capital necessary to bring new ideas to market by killing incentive.

Campbell, E. G., J. S. Weissman, et al. (2001). "Market Competition and Patient-oriented Research: The Results of a National Survey of Medical School Faculty." *Acad Med* 76(11): 1119-1126.

They tried to determine the impact of carrying out clinical care in a competitive environment on research productivity by surveying research faculty (2336 responses). They found that both basic and clinical research productivity was adversely affected by the need to do more clinical care in the most competitive markets. Good study demonstrating the impact of changing priorities for survival.

Cech, T. and J. Leonard (2001). "Science and business. Conflicts of interest--moving beyond disclosure." *Science* 291(5506): 989.

As director of the Howard Hughes Institute the author makes his point about conflicts of interest in research and indicates a strong position in avoiding them.

Cho, M., R. Shohara, et al. (2000). "Policies on faculty conflicts of interest at US universities." *JAMA* 284(17): 2203-8.

This excellent study has become somewhat dated because of the impacts of studies and changing policies secondary to various forces acting on universities. It reviewed COI policies of 89/100 polled Institutions. They found that there was great variability in types of relationships that were controlled, the financial limits, and the disclosures required. They recommended much more specific and consistent rules throughout the country.

Coyle, S. L. (2002). "Physician-Industry Relations. Part 1: Individual Physicians." *Ann Intern Med* 136(5): 396-402.

This is part 1 of a 2-part paper on ethics in physician-industry relationships. Part 1 offers advice to individual physicians; gives recommendations to medical education providers and medical professional societies. While physicians and commerce share an interest in advancing medical knowledge they diverge in that the former is a fiduciary for the patient and the latter has responsibility primarily toward its investors. This can lead to conflicts of interest, biased reporting and issues with appropriate experimental design. While physicians and trainees think they are impervious to Drug Company blandishments, the companies know better. So physicians have to decide for themselves what gifts raise no problems and which do. A general guideline is inexpensive and no strings attached. But, in our society, the very act of accepting a gift creates an obligation. Other financial ties between physicians and industry include honorariums for speaking or writing and payment for doing clinical research. These also can influence a physician's beliefs and practices. The paper goes into considerable detail.

Coyle, S. L. (2002). "Physician-Industry Relations. Part 2: Organizational Issues." *Ann Intern Med* 136(5): 403-406.

This is part 2 of a 2-part paper on ethics and physician-industry relationships. Part 1 offers advice to individual physicians; part 2 considers medical education providers and medical professional societies. While industry develops advances in medicine it also plays a key role in disseminating up-to-date medical information. The problem is bias and providers of the education must protect against that bias by presenting objective and balanced information. To do that, they must be careful of conditions under which money is collected to carry out their programs. They should insist on control of the content and conditions of the learning process Disclosure of industry sponsorship to students, faculty, and continuing medical education trainees is mandatory. This also applies to medical societies.

Dana, J and G. Lowenstein (2003). "A social science perspective on gifts to physicians from industry." *JAMA* 290(2): 252-5.

The article uses behavioral science to examine the nature of conflicts of interest. It examines the “self-service bias” in our perceptions of fairness, indicating an individual’s notion of fairness is inherently biased toward his/her own self-interest. This makes the article very good in uniting cross-arguments into one inherent principle: human nature.

DeAngelis, C., P. Fontanarosa, et al. (2001). "Reporting financial conflicts of interest and relationships between investigators and research sponsors." *JAMA* 286(1): 89-91.

JAMA was one of the first journals to insist on disclosure of COIs in all papers, editorials, etc coming out of their shop.

Drazen, J. M. and G. D. Curfman (2002). "Financial Associations of Authors." *N Engl J Med* 346(24): 1901-1902.

Having come upon scathing criticism for publishing review articles written by persons with substantial conflicts of interest without identifying those interests, the authors (editors of *NEJM*) reiterate past policies and frame a new policy. They ended up, eventually, requiring disclosure of all conflicts of interest, but not in this article.

Drazen, J. M. and G. Koski (2000). "To Protect Those Who Serve." *N Engl J Med* 343(22): 1643-1645.

Patients submitting themselves to a clinical trial are inherently vulnerable; they understand the risk associated with their reward. When these clinical trials are industry-sponsored and may contain ambiguous COIs, they are in direct conflict with the patients’ interests and therefore violate the physician-patient bond. This article calls for physicians to consider this when enrolling patients in clinical trials.

Duyk, G. (2003). "Attrition and Translation." *Science* 302(5645): 603-605.

The recently published NIH Roadmap proposes that public-sector science should place increased emphasis on the development of new therapeutics and diagnostics based on the fruits of fundamental research. Such "translational research" activities, traditionally the province of the private sector, have long been compromised by high rates of attrition (failure during the course of preclinical or clinical development of therapeutics). Attrition has led to growing financial costs, as well as opportunity costs. The new focus offers a way to reverse these trends, especially if the scientific community can improve on its ability to reconcile molecular genetic research with integrative organ- and organism-based research.

Eichenwald, K. and G. Kolata (1999). When physicians double as entrepreneurs. Hidden interests: a special report. *NY Times* (Print). New York City: A1, C16-17. November 30, 1999.

A very important report worth noting and reading. It chronicles not only COI’s in medicine, but also the culture around them, questioning whether physician-inventors can ethically promote their products. Although there is much to be gained from new technology and increased competition, much is lost when physicians ignore patient interests and focus on profits.

<http://query.nytimes.com/gst/fullpage.html?sec=health&res=9D07E6D6103FF933A05752C1A96F958260>

Elliott, C. (2001). "Pharma Buys a Conscience. Bioethicists increasingly find their work underwritten by pharmaceutical companies. Who passes on the ethics of ethicists?" *The American Prospect* 12(17): 16-20.

Do as I say, not as I do. Does that apply to bioethicists? Unfortunately developing a center on bioethics requires lots of money and the usual deep pockets, drug and other companies seem to be the most willing sources of funding. This article bears some of the funding sources of prominent bioethics programs and questions bioethicists’ behavior in the face of drug company dependence. He also indicates support of IRB members, of the FDA and of bioethics consultants tends to build favorable reviews.

Field, K. (2004). Medical School Reaches Agreement with Cancer Survivors in Suit over Canceled Study. *The Chronicle of Higher Education*.

If a study promises a therapeutic regimen and the company decides that the agent is not worth pursuing from the preliminary data, it can cancel the study. The participants argued that they were promised a full course of treatment by the university and sued.

Friedberg, M., B. Saffran, et al. (1999). "Evaluation of Conflict of Interest in Economic Analyses of New Drugs Used in Oncology." *JAMA* 282(15): 1453-1457.

Recent studies have found that when investigators have financial relationships with pharmaceutical or product manufacturers, they are less likely to criticize the safety or efficacy of these agents. In this study of a number of oncology drugs of different kinds, when comparing company vs non-profit supported studies, it was found that overstatement of positive results were less of a problem than a reduced likelihood of reporting unfavorable qualitative conclusions.

Friedman, P. J. (2002). "The Impact of Conflict of Interest on Trust in Science." *Sci Eng Ethics* 8(3): 413-420.

This paper is a deep analysis of the corrosive effects of conflicts of interest on trust in science, with the public and even among investigators. This lack of trust can have an adverse effect on the scientific record as well. Disclosure, our major method of dealing with COIs is really inadequate even if it were well- and completely carried out. We need new rules and new approaches and the author discusses some possibilities. He points out that managing COIs is not institutions of learning's best suite and that institutions can get into COI problems themselves.

Gelijns, A. C. and S. O. Thier (2002). "Medical Innovation and Institutional Interdependence: Rethinking University-Industry Connections." *JAMA* 287(1): 72-77.

The authors attempt to present a balanced account of the great benefits associated with Industry-Academic collaborations in research and development and the negative impacts of the relationships. This paper reviews institutional patterns of innovations and suggests organizational and public policy implications. This is important reading because many of the papers in this area deal with the negative aspects of university-industry relations and do not deal with the importance of these collaborations for advances.

Hahn, R. (2002). "Conflicts of Interest and the False Comfort of "Full Disclosure"." *Professional Ethics Report* 15(4).

The concept that revealing conflicts of interest in all presentations and publications eliminates their insidious effects on research. Not true, this article claims. The problem is that other mechanisms of control severely limit the incomes of successful scientists.

Hall, S. S. (2001). *Claritin and Schering-Plough: A Prescription for Profit*. The New York Times. New York. March 11, 2001.

This article purports to show that Schering used inadequate science to demonstrate that a mediocre antihistamine was less soporific than the older variety and therefore supplanted the older versions at great cost to society. Ironically, branded clariton sells well as an over-the-counter antihistamine even though it is expensive.

Hart, D. (2002). "The "Corporatization" of Science." *Science* 295: 439.

This letter reviews the history of the support of basic research after WWII and reviews the changes in the scientific community that supported Bayh-Dole and indicated the importance of continuing attention to the new relationships developing as a result.

Horton, R. (2004). "The Dawn of McScience." *The New York Review*.

This review of Seldon Krimsky's book *Science in the Private Interest: Has the Lure of Profits Corrupted Biomedical Research?* The reviewer indicates that Krimsky produced a polemic indicating that declaring conflicts of interest will not solve the problems but that the separation of science from industry never truly existed and that, to some extent, the moral requirement to tell the truth in science was always blemished when it related to practical products. The Nancy Oliveri case, as well as the purchase of investigators and physicians by gift giving of pharmaceutical houses, are thoroughly discussed. I think that we are moving in the direction of balance by now, but my naivete may be showing.

Johns, M. M. E., M. Barnes, et al. (2003). "Restoring Balance to Industry-Academia Relationships in an Era of Institutional Financial Conflicts of Interest: Promoting Research While Maintaining Trust." *JAMA* 289(6): 741-746.

This paper deals with University-Industry relationships from the point of view of the research managers and other leaders at academic institutions. The authors discuss divestiture, firewalls and other methods to ensure that industrial affiliations do not corrupt the activities of the university and adversely affect the public trust.

Johnston, J. (2004). "Outing the Conflicted: Et Tu, NIH?" *Science* 303(5664): 1610b-.

This report outlines the findings on NIH senior investigator and administrator conflicts of interest and their potentially serious consequences.

Kaiser, J. (2004). "BIOMEDICAL RESEARCH: Feeling the Heat, NIH Tightens Conflict-of-Interest Rules." *Science* 305(5680): 25-26.

This news article describes the first responses of NIH administration to revelations about intramural conflicts of interest.

Kaiser, J. (2004). "NATIONAL INSTITUTES OF HEALTH: Paid Consulting: Good for the Staff, Not for the Chiefs." *Science* 304(5673): 936a-937.

A news report on the extent of NIH staff involvement in conflicts of interest.

Kaiser, J. (2005). "CONFLICT OF INTEREST: NIH Chief Clamps Down on Consulting and Stock Ownership." *Science* 307(5711): 824-825.

A news report on the NIH ruling on conflicts of interest among its employees.

Kassirer, J. P. and M. Angell (1993). "Financial Conflicts of Interest in Biomedical Research." *N Engl J Med* 329(8): 570-571.

An early voice indicating the growing involvement of with industry and the conflicts of interest and of commitment they engender. Worthwhile reading.

Kassirer, J. P. and M. Angell (1997). "The High Price of Product Endorsement." *N Engl J Med* 337(10): 700-.

Product endorsement by a professional or scientific organization raises serious ethical problems. The endorsement is worth a lot to the product's company and it is willing to pay well for it. The question is whether the organization has done the comparative testing to determine whether this is a superior product worth endorsing. Organizations take risks to their credibility and financial risks when they endorse a product.

Kjaergard, L. L. and B. Als-Nielsen (2002). "Association between competing interests and authors' conclusions: epidemiological study of randomized clinical trials published in the *BMJ*." *BMJ* 325(7358): 249-.

To assess the association between competing interests and authors' conclusions in randomized clinical trials the authors conducted an epidemiological study of randomized clinical trials published in the *BMJ* from January 1997 to June 2001. Financial competing interests were defined as funding by for profit organizations and other competing interests as personal, academic, or political. They reviewed 159 trials from 12 medical specialties. Authors' conclusions were significantly more positive towards the experimental intervention in trials funded by for profit organizations alone compared with trials without competing interests, trials funded by both for profit and non-profit organizations, and trials with other competing interests. The authors' conclusions were that randomized clinical trials significantly favored

experimental interventions if financial competing interests were declared. Other competing interests were not significantly associated with authors' conclusions.

Krimsky, S. and L. Rothenberg (1998). "Financial interest and its disclosure in scientific publications." *JAMA* 280(3): 225-6.

Journal policies and requirements of funding agencies on financial disclosure of authors and grant applicants have divided editors and scientists who disagree on whether such policies can improve the integrity of science or manage conflicts of interest. Those opposed to such disclosure policies argue that financial interest is one of many interests held by scientists, is the least scientifically dangerous, and should not be singled out. Those who favor open reporting of financial interests argue that full disclosure removes the suspicion that something of relevance to objectivity is being hidden and allows readers to form their own opinions on whether a conflict of interest exists and what relevance that has to the study. The authors believe that the scientific community and the public will be best served by open publication of financial disclosures for readers and reviewers to evaluate.

Lawler, A. (2003). "UNIVERSITY-INDUSTRY COLLABORATION: Last of the Big-Time Spenders?" *Science* 299(5605): 330-333.

This review of the fate of large corporate gifts for research to universities suggests that the universities continued to do their thing but that the yield of marketable products to the companies was small. He concludes that on balance the agreements were win-win.

Levinsky, N. G. (2002). "Nonfinancial Conflicts of Interest in Research." *N Engl J Med* 347(10): 759-761.

The author considers his longstanding interest in his career and how that might have affected his objectivity in research. A worthwhile read.

Lo, B., L. Wolf, et al. (2000). "Conflict-of-interest policies for investigators in clinical trials." *N Engl J Med* 343(22): 1616-20.

There is substantial concern that financial conflicts of interest on the part of investigators conducting clinical trials may compromise the well being of research subjects. They analyzed policies governing conflicts of interest at the 10 medical schools in the United States that receive the largest amount of research funding from the National Institutes of Health. All 10 universities required that faculty members disclose financial interests to university officials. They conclude that policies governing conflicts of interest at leading medical schools in the United States vary widely. We suggest that university-based investigators and research staff be prohibited from holding stock, stock options, or decision-making positions in a company that may reasonably appear to be affected by the results of their clinical research. Of the 10 medical schools we studied, only 1 had a policy that was close to this standard.

Martin, J. B. and D. L. Kasper (2000). "In Whose Best Interest? Breaching the Academic-Industrial Wall." *N Engl J Med* 343(22): 1646-1649.

McCarthy, M. (2000). "Conflict of interest taints vaccine approval process, charges US report." *The Lancet* 356(9232): 838.

McCrary, S., C. Anderson, et al. (2000). "A national survey of policies on disclosure of conflicts of interest in biomedical research." *N Engl J Med* 343(22): 1621-6.

Conflicts of interest pose a threat to the integrity of scientific research. The current regulations of the U.S. Public Health Service and the National Science Foundation require that medical schools and other research institutions report the existence of conflicts of interest to the funding agency but allow the institutions to manage conflicts internally. They surveyed all medical schools (127) and other research institutions (170) that received more than \$5 million in total grants annually from the National Institutes of Health or the National Science Foundation; 48 journals in basic science and clinical medicine; and 17

federal agencies in order to analyze their policies on conflicts of interest. There was a very high response rate.. Fifteen of the 250 institutions (6 percent)--5 medical schools and 10 other research institutions--reported that they had no policy on conflicts of interest. Among the institutions that had policies, there was marked variation in the definition and management of conflicts. They concluded that there is substantial variation among policies on conflicts of interest at medical schools and other research institutions. This variation, combined with the fact that many scientific journals and funding agencies do not require disclosure of conflicts of interest, suggests that the current standards may not be adequate to maintain a high level of scientific integrity.

Moses, H., III, E. Braunwald, et al. (2002). "Collaborating with Industry -- Choices for the Academic Medical Center." *N Engl J Med* 347(17): 1371-1375.

This is a core paper that defines the issues in the various relationships between industry and academic medical centers. They take a drastic step in outlawing (at Harvard) most conflicts of interest with industry.

U. S. G AO (2003). *University Research: Most Federal Agencies Need to Better Protect against Financial Conflicts of Interest*. G. A. Office.

This extensive study of Federal agencies and universities indicated that at the time of the report protection against conflicts of interest was inadequate. Among Federal agencies only the NIH and NSF had policies requiring review and reporting of conflicts of interest related to research support.

Orlowski, J. and L. Wateska (1992). "The effects of pharmaceutical firm enticements on physician prescribing patterns. There's no such thing as a free lunch." *Chest* 102(1): 270-3.

They examined the impact on physician prescribing patterns of pharmaceutical firms offering all-expenses-paid trips to popular sunbelt vacation sites to attend symposia sponsored by a pharmaceutical company. Drug usage patterns were tracked for 22 months preceding each symposium and for 17 months after each symposium. Ten physicians invited to each symposium were interviewed about the likelihood that such an enticement would affect their prescribing patterns. A significant increase in the prescribing pattern of both drugs occurred following the symposia. These changed prescribing patterns were also significantly different from the national usage patterns of the two drugs by hospitals with more than 500 beds and major medical centers over the same period of time. These alterations in prescribing patterns occurred even though the majority of physicians who attended the symposia believed that such enticements would not alter their prescribing patterns.

Patricia, B., D. Jocelyn, et al. (2002). "MEDICINE: Clinical Trials and Industry." *Science* 297(5590): 2211-.

Royal Australasian College of Physicians (2000). *Ethical Guidelines in the Relationship Between Physicians and the Pharmaceutical Industry*.

The Australians were able to agree on a set of ethical guidelines related to physicians and the pharmaceutical industry. They were opposed to most forms of gifts and proposed a skeptical position. It was not clear the extent to which these guidelines penetrated the profession..

Psaty, B. M., C. D. Furberg, et al. (2004). "Potential for Conflict of Interest in the Evaluation of Suspected Adverse Drug Reactions: Use of Cerivastatin and Risk of Rhabdomyolysis." *JAMA* 292(21): 2622-2631.

In recent years, US patients have increasingly been the first to receive new medications, some of which are subsequently discovered to have suspected adverse drug reactions (SADRs). As a result, the challenge of early detection has largely shifted to the US postmarketing systems. They sought to review the association between the use of cerivastatin sodium and the risk of rhabdomyolysis in an effort to illustrate the operation and limitations of the current US postmarketing safety-surveillance system. In the published literature, cerivastatin was associated with much larger risks of rhabdomyolysis than other statins. Analyses suggested that compared with atorvastatin calcium, cerivastatin monotherapy substantially increased the risk of rhabdomyolysis. To our knowledge, these findings were not disseminated or published. The company continued to conduct safety studies, some of them inadequately designed to assess the risk of rhabdomyolysis, until cerivastatin was removed from the market in August 2001. They concluded that

despite limitations of the available data, the asymmetry between the information available to the company and the information available to patients and physicians seems striking. A subjective element is present in the effort to infer whether or not the occurrence of untoward outcomes in users of a particular drug was actually the consequence of the use of that drug, and, under the current system, a pharmaceutical company's appraisal of SADR's may be influenced by economic considerations. Such an appraisal would best be made by an independent group. They claim US Congress should mandate and provide adequate support for independent reviews and analysis of postmarketing data.

Psaty, B. M. and D. Rennie (2003). "Stopping Medical Research to Save Money: A Broken Pact With Researchers and Patients." *JAMA* 289(16): 2128-2131.

This report documents a case in which a drug company decided that its cancer drug was no longer worth developing and stopped a trial even though they had promised a longer trial in writing. Both the company and the institution were sued.

Ramsay, S. (2001). "Online database reveals researchers' industry ties." *The Lancet* 357(9269): 1977.

This neat idea reveals the great extent to which those conducting clinical research have industry income associated with that activity. The list proceeds apace.

Roberts, T. G., Jr. and B. A. Chabner (2004). "Beyond Fast Track for Drug Approvals." *N Engl J Med* 351(5): 501-505.

Clinical Trials. Deals with fast track mechanism and the importance of selecting probable responses to each new drug. Proposes "selective approval mechanism."

Scherer, F. M. (2004). "The Pharmaceutical Industry -- Prices and Progress." *N Engl J Med* 351(9): 927-932.

This report examines the cost and pricing structures of pharmaceutical companies and tries to deal constructively with the demands for lower prices while at the same time supporting costly research. It is a very worthwhile read.

Schulman, K. A., D. M. Seils, et al. (2002). "A National Survey of Provisions in Clinical-Trial Agreements between Medical Schools and Industry Sponsors." *N Engl J Med* 347(17): 1335-1341.

Concerned about threats to the integrity of clinical trials in a research environment increasingly controlled by private interests, the International Committee of Medical Journal Editors (ICMJE) has issued revised guidelines for investigators' participation in the study design, access to data, and control over publication. It is unclear whether research conducted at academic institutions adheres to these new standards. From November 2001 through January 2002, they interviewed officials at U.S. medical schools about provisions in their institutions' agreements with industry sponsors of multicenter clinical trials. The results demonstrated limited adherence to the standards embodied in the new ICMJE guidelines. Scores for coordinating-center agreements were somewhat higher for most survey items. They suggest that a reevaluation of the process of contracting for clinical research is urgently needed.

Univ. of California_Senate. (2004). Report of the University Committee on Research Policy: Problematic Restrictive Clauses in Contracts, Grants and Gifts for Research, University Committee on Research Policy.

Steinbrook, R. (2004). "Conflicts of Interest at the NIH -- Resolving the Problem." *N Engl J Med* 351(10): 955-957.

This intermediate report discusses the various ideas that were considered at the NIH in an attempt to silence criticism while maintaining leeway for extra income for investigators.

The, Editor. (2004). "Publishing Commentary by Authors with Potential Conflicts of Interest: When, Why, and How." *Ann Intern Med* 141(1): 73-74.

This describes their policies at the time.

Weiss, R. (2004). NIH Bans Collaboration With Outside Companies. *Washington Post*. September 24, 2004.

This was the first response to the revelations of the extent of conflicts of interest at the NIH.

Williams, S. (2002). "Handle With Care: Avoiding Financial Conflict of Interest in Clinical Research." *Academic Physician and Scientist* January/February: 1, 10-12.

This paper begins by discussing the plight of the Fred Hutchinson Cancer Research Center when sued by research subjects' families. The issue of the Center or its physicians deriving financial benefit from the research put the organization in a weak position. This has led to the two AAMC reports on individual and institutional conflicts of interest that are referred to elsewhere in this bibliography.

Willman, D. (2001). Risk Was Known as FDA OKed Fatal Drug. *Los Angeles Times*. Los Angeles, CA. March 11, 2001.

The article chronicles Warner-Lambert's push and subsequent approval of the kidney drug Rezulin. Although liver damage was apparent in the clinical trial, Warner-Lambert's "partnership" with the FDA allowed for swift authorization. This should be a warning to all regulatory bodies about attaching themselves too closely to studies.

Willman, D. (2003). Stealth Merger: Drug Companies and Government Medical Research. *Los Angeles Times*. Los Angeles: A1, A32. December 7, 2003.

Some of the National Institutes of Health's top scientists are also collecting paychecks and stock options from biomedical firms. Increasingly, such deals are kept secret.

Willman, D. (2004). The National Institutes of Health: Public Servant or Private Marketer? *Los Angeles Times*. Los Angeles, CA: A29. December 22, 2004.

Another in a series of Willman's articles that deals with conflicts of interest. This one points out key scientists in the NIH with blatant COIs and the effect this has on research.

Willman, D. (2005). NIH to Ban Deals With Drug Firms. *Los Angeles Times*. LA, CA: A1, A17. February 1, 2005.

After initially breaking the COIs at the NIH, Willman announced the ban placed on industry-physician consulting relationships as well as other financial interests. These two Willman pieces on the NIH were monumentally influential in bringing to light gross inconsistencies in policy and their negative effects on the public.

Ziegler, M., P. Lew, et al. (1995). "The accuracy of drug information from pharmaceutical sales representatives." *JAMA* 273(16): 1296-8.

To provide quantitative data about the accuracy of the information about drugs presented to physicians by pharmaceutical sales representatives the authors investigated one hundred six statements about drugs made during 13 presentations by pharmaceutical representatives. Statements were rated inaccurate if they contradicted the 1993 Physicians' Desk Reference or material quoted or handed out by the sales representative. They found that twelve (11%) of 106 statements about drugs were inaccurate. All 12 inaccurate statements were favorable toward the promoted drug, whereas 39 (49%) of 79 accurate statements were favorable. None of 15 statements about competitors' drugs were favorable, but all were accurate, significantly differing from statements about promoted drugs. In a survey of 27 physicians who attended these presentations, seven recalled a false statement made by a pharmaceutical representative, and 10 said information from the representatives influenced the way they prescribed drugs. They claim that eleven percent of the statements made by pharmaceutical representatives about drugs contradicted information readily available to them. Physicians generally failed to recognize the inaccurate statements.

Brennan, T. A., D. J. Rothman, et al. (2006). "Health Industry Practices That Create the physician's roles Conflicts of Interest: A Policy Proposal for Academic Medical Centers." *JAMA* 295(4): 429-433.

Conflicts of interest between physicians' commitment to patient care and the blandishments that pharmaceutical companies and their representatives lavish on them impair professionalism in medicine. Although the involved groups, including the Federal government have instituted self-regulation of marketing, research into gift receipt and giving indicates that current controls will not satisfactorily protect the interests of patients. More stringent regulation is necessary, including the elimination or modification of

common practices. They propose a policy for academic medical centers to take the lead in eliminating these conflicts of interest that impair patient care.

Stossel, T. (2005). Mere Magazines. *The Wall Street Journal*. Washington, DC: A16. December 30, 2005.

In this brief article Dr. Stossel raises important questions about the arrogance of major medical journals and their persistent negative attitude towards the companies that are responsible for all the advances in medicine that we have seen over the past half-century. Whether or not you end up agreeing with the arguments, this is a refreshing contrast with the uniformity of the beating big Pharma has been taking in the medical literature and the media.

(2004). Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection. DHHS. Services, Federal Register. 69 (92): 26393-7.

This federal guideline asks IRBs and institutions to consider a variety of means to eliminate, document, disclose, and manage conflicts of interest. It is not overly prescriptive but it expects institutions to actively and effectively deal with conflicts of interest both of individual investigators and of IRB members. Conflict of interest committees distinct from IRBs are expected to be developed. Required reading for research administrators.

Brody, B., C. Anderson, et al. (2003). "Expanding Disclosure of Conflicts of Interest: Views of Stakeholders." *IRB Ethics and Human Research* **25**(1): 1-8.

Kim, S. Y. H., R. W. Millard, et al. (2004). "Potential research participants' views regarding researcher and institutional financial conflicts of interest." *J Med Ethics* **30**(1): 73-79.

This empirical study of the attitudes of potential research subjects towards the revelation of financial conflicts of interest and their existence gave strong evidence that subjects wanted to know. Some would be less inclined to participate in the proposed study knowing of the conflicts of interest. A very nice study.

<http://jme.bmjournals.com/cgi/content/full/30/1/73>

Taylor, R. and J. Giles (2005). "Cash interests taint drug advice." *Nature* **437**(7062): 1070.

This paper and the accompanying editorial deal with groups empanelled by professional societies primarily to write "evidence based" clinical practice guidelines. A study by Materal found that substantial number of the panel members receive income or own stock in companies whose products are under consideration. The influence of these companies may be indirect in promoting drug use in the filed or to encourage use of a specific product. Better methods of developing guidelines are suggested.

<http://www.nature.com/nature/journal/v437/n7062/full/4371070a.html>

Brody, H. and F. G. Miller (2003). "The clinician-investigator: unavoidable but manageable tension." *Kennedy Institute of Ethics J* **13**(4): 329-46.

This paper addresses the two roles of the Clinician-Investigator as scientist and caregiver. The authors indicate that research is very different from care and thus there is ethical tension in doing both (the difference position). Those that argue that the physician's role is similar in both circumstances (similarity position) are claimed to be in error because the position denies the ethical tension. A very worthwhile read.

Mello, M. M., B. R. Clarridge, et al. (2005). "Academic Medical Centers' Standards for Clinical-Trial Agreements with Industry." *N Engl J Med* **352**(21): 2202-2210.

This critical paper delineates the weaknesses of academic institutions in writing contracts that protect data and investigators from bias. This is very important reading.

<http://content.nejm.org/cgi/content/abstract/352/21/2202>

(2003). "American Society of Clinical Oncology: Background for Update of Conflict of Interest Policy." *J Clin Oncol* **21**(12): 2387-2393.

The new version of their conflict of interest policy that is based on complete disclosure and a number of prohibitions. A good set of rules that others could emulate.
<http://www.jco.org/cgi/content/full/21/12/2387>

Bentley, J. P. and P. G. Thacker (2004). "The influence of risk and monetary payment on the research participation decision making process." *J Med Ethics* **30**(3): 293-298.

This questionnaire study attempted to determine the impact of various levels of payment on willingness to participate in a trial. Knowledge of the characteristics of a trial and whether it would lead to behavior damaging the quality of the study. Money was an incentive. The other effects did not seem to be present.
<http://jme.bmjournals.com/cgi/content/full/30/3/293>

Miller, F. G. and A. F. Shorr (2002). "Ethical Assessment of Industry-Sponsored Clinical Trials*: A Case Analysis." *Chest* **121**(4): 1337-1342.

These authors review a single randomized control trial of asthma therapy in children for its ethical characteristics and find it faulty. This is worthwhile reading.
<http://www.chestjournal.org/cgi/content/abstract/121/4/1337>

Schroter, S., J. Morris, et al. (2004). "Does the type of competing interest statement affect readers' perceptions of the credibility of research? Randomised trial." *BMJ* **328**(7442): 742-743.

<http://bmj.bmjournals.com/cgi/content/full/328/7442/742>
An empirical study noting a competing financial interest on receiving research support on various aspects of a study. Believability and relevance were both significantly reduced in the presence of a financial conflict. All in all, a weak paper, but provocative.

Resnik, D. (2004). "Disclosing conflicts of interest to research subjects: an ethical and legal analysis." *Accountability in Research* **11**(2): 141-59.

The author makes the case that investigators have an ethical and now a legal obligation to disclose their conflicts of interest in a manner such that the study participants will have enough information to sign an informed consent. He argues that disclosure of conflicts of interest should be required in informed consent documents.

Campbell, E., B. Moy, et al. (2004). "Institutional academic industry relationships: results of interviews with university leaders." *Accountability in Research* **11**(2): 103-18.

The investigators conducted interviews of university leaders to get their viewpoints on academic-industry relationships. Generally, there were many such relationships and these were generally thought to be constructive. There was understanding that conflicts of interest were pervasive and sometimes risky.

Holmes, D. R., B. G. Firth, et al. (2004). "Conflict of interest." *American Heart Journal* **147**(2): 228.

This report of an expert meeting reviews conflict of interest issues from the level of the investigator on to the FDA. It has become somewhat dated because of the recent NIH revelations and rule development and progress in registering clinical trials.

Bernstein, M. (2003). "Conflict of interest: It is ethical for an investigator to also be the primary care-giver in a clinical trial." *Journal of Neuro-Oncology* **63**(2): 107.

The author addresses one of the issues of the day. He comes down in opposition to the AAME report on individual conflicts of interest in clinical research, as supporting such research in many instances.

<http://www.springerlink.com/openurl.asp?genre=article&id=doi:10.1023/A:1023959021758>

Komesaroff, P. (2005). "Ethical issues in the relationships with industry: an ongoing challenge. New Guidelines open for public comment." *J Paediatr Child Health* **41**(11): 558-60.

In this paper the author explains the extent to which medical decision-making in Australia is influenced by industry. He provides guidelines to Australian physicians as to their behaviors, including the rejection of gifts, subsidized attendance at meeting, and samples. They should not endorse specific products. Clinicians should also avoid recruiting their patients into studies in which they are investigators, as well as only doing studies in which there is a commitment to make the results public. This should be followed by an empirical study on compliance.

<http://www.blackwell-synergy.com/doi/abs/10.1111/j.1440-1754.2005.00719.x>

Topol, E. J. and D. Blumenthal (2005). "Physicians and the Investment Industry." *JAMA* **293**(21): 2654-2657.

<http://jama.ama-assn.org/cgi/content/full/293/21/2654>

In this excellent paper the authors identify and discuss the new practice of clinical researchers providing information to investment groups as consultants. In a number of instances it appears that confidential information was leaked that gave investors significant advantages. The questions as to the ethical standing of this activity versus the right of professors to communicate about what they know was introduced. How can we be sure that the information is in the public domain before discussing it?

Weiss, R. (2004). NIH to Set Stiff Restrictions on Outside Consulting. *Washington Post*. Washington, D.C.: A01. August 4, 2004.

After a scandal revealed by the LA Times in which many NIH personnel including investigators and those with responsibilities for dispensing grants and contracts received substantial sums from drug and biotech companies the NIH took. Head of investigations by congress, internal reviews, and the report of an independent expert committee developed rules for NIH personnel. Familiar rules once being adopted by most major research institutions.