VOLUME V No. 2
Spring 2002

CONFLICT OF INTEREST

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MICHIGAN STATE UNIVERSITY

Research Integrity

Introduction

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On July 11, 1995 the Department of Health and Human Services published in the Federal Register the final rule for 42 CFR 50 and 45 CFR 94, "Objectivity in Research." In the same issue of the Federal Register the National Science Foundation published a "Notice of technical changes to [its] Investigator Final Disclosure Policy," to conform with the new PHS policy.

The intent of both NSF and PHS policies was to set standards to ensure that the design, conduct, and reporting of research funded by PHS or NSF would not be biased by any conflicting financial interest of those Investigators responsible for the research. The PHS and NSF rules require that faculty Investigators applying to NSF or PHS disclose to the University potential conflict of interests to their universities and that those Universities manage, reduce, or eliminate disclosed financial conflicts of interest.

Sometimes the issuing of federal regulation marks the end of debate, or the substantial diminution of debate over controversial issues. Not so in the debate over the impact on research of financial conflicts of interest. The years since 1995, especially the last three years, have produced a number of reports and position papers by professional groups as well as internal strife in the federal agencies over the future of conflict of interest policy. A number of high-profile cases (or scandals) where financial conflicts of interest allegedly threatened the integrity of research results or the safety and welfare of human subjects of research have occurred. The following (incomplete) chronology illustrates the point.

Chronology of Events and Guidelines Related to Conflicts of Interest

- **September 1999** – Jesse Gelsinger, research subject in gene therapy trial at the University of Pennsylvania, dies. PI (James Wilson), University of Pennsylvania, and Genova (Wilson's biotech firm), revealed to have interlocking financial interests in the research.
- **January 2001** – DHHS publishes *Draft Interim Guidance on Financial Relationships in Clinical Research: Issues for Institutions, Clinical Investigators, and IRBs to Consider When Dealing with Issues of Financial Interests and Human Subject Protection*.
- **September 2001** – The Association for the Accreditation of Human Research Protection Programs, *Interim Accreditation Standards and Procedures*
- **October 2001** – The Association of American Universities' Task Force on Research Accountability, *Report on Individual and Institutional Financial Conflict of Interest*
- **November 2001** – Council on Governmental Relations, *Managing Externally Funded Programs at Colleges and Universities*
- **November 2001** – General Accounting Office Report, *HHS Direction Needed to Address Financial Conflicts of Interests*
- **December 2001** – The Association of American Medical Colleges' Task Force on Financial Conflicts of Interest in Clinical Research, *Protecting Subjects, Preserving Trust, Promoting Progress—Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research*
- **January 2002** – JAMA publishes Morin et al*., Managing Conflicts of Interest in the Conduct of Clinical Trials;* Gelijns and Their, *Medical Innovation and Institutional Interdependence*
- **May 2002** – The Association of American Universities Workshop in Institutional Conflicts of Interest

Research universities are examining their policies on this issue. In his recent article, Peter J. Harrington writes that the "…heightening of pressures favoring university-industry partnerships created by government policy initiatives, increased faculty entrepreneurship, and growing financial constraints on universities" led to resistance to regulate financial conflicts of interest in research. He adds, "That reluctance has given way more recently to a desire to create some more definite ground rules in this area and it now appears that most, if not virtually all, of the leading research universities in the country have adopted some kind of faculty conflict of interest policy. This trend is no doubt due, at least in part, to the great amount of negative publicity in recent years surrounding certain egregious case of conflict of interest and self-dealing by researchers at prestigious universities..."[1]

As to the prospect of more federal regulation, Sara Krauss writes,

"What Now? The AAMC and GAO Reports demonstrate a continued heightened awareness to the issue of financial conflicts of interest in research, and the two reports indicate the existing regulation is insufficient to govern properly this area of significant concern to the public. One would expect HHS to act in the not-too-distant future, promulgating more detailed and expansive regulations governing financial conflicts of interest in connection with research, particularly in areas not addressed at all by current financial conflict regulations, institutionally-held financial interests and a research institution's oversight and management of financial relationships between the institution's affiliated researchers and private sponsors of clinical trials. In light of the media attention to financial conflicts, and recent lawsuits against institutions and researchers that had significant financial incentives to conduct research, institutions are well advised not to wait for HHS action to evaluate their current practices in connection with financial conflicts in research."[2]

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[1] "Harrington, Peter J. "*Faculty Conflicts of Interest in An Age of Academic Entrepreneurialism: An Analysis of the Problem, the Law and Selected University Policies*," Journal of College and University Law: Vol. 27 No.4. P. 776.

[2] Krauss, Sara. "The Latest Developments in Evaluating Conflicts of Interest in Research." Proskauer Rose Health Law Report: Vol. 10,No. 1 Winter 202. P. 4.

This issue of *Research Integrity* contains thoughtful and provocative articles on financial conflicts of interest in research. **Rob Penneck**, Lyman Briggs School & Department of Philosophy, discusses why, ethically it should matter who funds a scientist's research (P.3). **Michael S. Pritchard, PhD,** Willard A. Brown Professor of Philosophy, Director, Center for the Study of Ethics in Society, and Associate Dean, The Graduate College, **Western Michigan University** examines the complexities of COI (P. 6) followed by a summary of the GAO report (P.11) and response by **Jeffrey Brainard** of *The Chronicle of Higher Education* (P.12). **Howard Brody** illustrates some of the potential conflicts associated between pharmaceutical companies' commercial agenda and the values of scientific research (P. 13).

COI effects not only faculty and administration, but graduate students as well. **Antonio A. Nunez,** Associate Dean of The Graduate School writes on the graduate students' or postdocs' perspective pertaining to the consequences of working in a research project supported by corporate resources (P. 14). **William Taylor**, a faculty member of the Conflict Review Committee explains both the purpose of, and his role on, this committee at MSU (P. 17).

Included for review is an article from *Science* entitled, "Clinical Research: Hopkins Reviews Investment In Indian Cancer Drug Trial (P. 18) followed by two responses (P.19 & 21) from **Tom Tomlinson**, Director of the Center for Ethics and Humanities in the Life Sciences, and **Glenn C. Davis,** Dean of the College of Human Medicine.

Loraine J. Hudson gives pertinent advice on conflict of interest and entrepreneurship (P. 22), and excerpts from an interview with **Janie M. Fouke**, Dean of the College of Engineering offers insight into two dimensions of conflict of interest.

Research Funding And The Virtue Of Scientific Objectivity

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Why should it matter ethically who funds a scientist's research? Scientific research is expensive and it won't get done at all unless someone pays for it. Viewed pragmatically, it seems that funding is simply a matter of economics. However, a broader perspective reveals that a variety of ethical issues are indeed relevant, and responsible researchers need to take these seriously. The possibility of conflicts of interest that certain funding arrangements can cause is one important area of concern. This has become increasingly significant as universities, which typically are at the forefront of scientific research, struggle to find new sources of funding to supplement or replace traditional sources.

Attention has recently been focused upon problems that can arise when universities seek funding from industry. If nothing else, funding from industry or other special interest groups can sway what scientific questions get investigated, which can in turn lead to outcomes that are unjust or ethically problematic in some other way. Long-term basic research can get short-changed in the pursuit of applied research that promises a quick return. Public research institutions may begin to neglect research that fulfills their founding mandate of serving the public interest in favor of research that benefits the particular interests of industrial sponsors or their own financial health.

These are all important considerations to keep in mind in sorting

out the ethics of conflict of interest in scientific research, but here I want to focus upon a deeper issue, namely, how financial interests may undermine scientific objectivity. The ethical problem in financial conflicts of interest in research is not at base that of divided institutional loyalties, but rather that such interests can conflict with the scientist's basic responsibility to investigate the world objectively. Of course, financial stakes are not the only source of potential conflict; ideological and other confounding interests can be equally dangerous to objectivity, but in this paper I will keep the focus on what many take to be the bottom line.

By appealing to the central importance of scientific objectivity, I am rejecting a recent view that questions whether science is or even could be objective. An extreme version of this position questions the possibility of objective knowledge under any circumstances. This is not the place to mount a detailed rebuttal of this view, but I must at least briefly explain the way that I think objectivity remains central to science.

The critique of scientific objectivity arose in response to the positivistic claim that science was "value-free". According to this view, saying that science provided objective knowledge meant that it gave us facts that were free of, in the sense of "uncontaminated by", messy values (which were, of course, merely subjective). Critics argued that no knowledge was value-free and concluded that the ideal of an objective science was impossible. I think both of these views misconceptualized scientific objectivity. The concept should not be thought of as meaning value-free. Quite the opposite: Objectivity is itself a value and a value-laden concept, which is linked intimately to other epistemic and ethical norms. For the scientist, I would argue, objectivity may properly be thought of as a special kind of virtue of character, in something like the Aristotelian sense of the term.

One element that is most relevant to the immediate question is, the idea that objectivity involves a certain type of *impartiality*. In particular, objectivity means that the researcher ought to be impartial with regard to which of the several alternative hypotheses that need to be considered is the correct one. It means that the researcher should be committed to determining the answer on the basis of evidence rather than on someone's preference. I would argue that this sense of objectivity carries with it an ethical imperative for the scientific researcher that arises in part from the epistemic values that undergird the evidence-based reasoning that is essential to scientific methods.

With this idea of scientific impartiality in hand, we can return to our original line of inquiry regarding the relationship of objectivity and conflict of interest. Can't scientists be objective in their research, no matter who is providing the funding? It may not be impossible, but it certainly can be difficult. With their future funding always on the line, researchers may feel great or subtle pressure to get results that will keep their sponsors happy. Even if individuals perform their research perfectly objectively, they may find themselves constrained in reporting their full results if external funders have retained some control over what can be published, since it may not be in the interest of the sponsor to reveal every finding.

This is not to say that research sponsors don't care about scientific objectivity. In most cases, objective research is in their own interest as well, and not just because there can be a real economic payoff in the discovery of empirical truths. However, in certain kinds of situations, someone with a financial stake in an outcome might care more about only the appearance of truth. Business advertisers never underestimate the commercial value that scientific

support for the efficacy of their product will bring, or the blow that a negative finding can have. There are already documented cases in which industry funders removed information from university researchers' reports that revealed health dangers in their products. These are clear violations of the sort of impartiality we should expect in scientific research.

There are also more subtle ways that conflict of interest can undermine objectivity. For instance, there is real evidential value to knowing whether the investigator has a financial stake in the conclusion of a study. When we, as third parties, assess reports of the results of scientific studies, we quite properly consider the trustworthiness of the investigator, because we know that researchers are themselves instruments in any study just as spectroscopes and survey forms are. Everything from the quality of the data to the accuracy and fairness of the final report can be affected for better or worse by the objectivity (among other characteristics) of the researcher. Moreover, we understand how a researcher's judgment or actions could be influenced to favor the preferred outcomes of those who hold the purse strings. To cite just one case, it was not unreasonable to doubt studies that supposedly refuted health dangers of cigarettes, once it was learned the research had been funded by the Tobacco Institute.

It should thus be obvious why financial conflict of interest and potential loss of research independence and control ought to be of concern to universities. A major reason why industry and other institutions find it valuable to turn to university researchers is that historically the Academy has placed a premium upon the value of knowledge for its own sake. Because its primary interest (at least in the ideal, if not always in practice) was in the intrinsic value of learning and research, it was trustworthy (again, at least on the whole, if not in every instance) as a source of objective knowledge. The degree to which this basic value of academic research is compromised will in like measure compromise the value of its products.

Another way to look at this is in terms of third-party perceptions. It is probably true that the public tends to overemphasize the degree to which industry funding may be a confounding factor, because most people are never in a position to directly evaluate the quality of the experimental design itself. However, even if the evidence properly supports scientific conclusions, the value will not be appreciated if the public loses trust in the objectivity of scientists and the integrity of the scientific enterprise. The more that university research is perceived as being beholden to special interest funding, the more likely that its reputation for impartiality will degrade over time.

Universities thus have a special stake and role in maintaining and promoting scientific objectivity, but the importance of the virtue extends well beyond the value to the Academy itself. Scientific objectivity is essential to democratic deliberation and governance. As I have argued elsewhere, scientific methods are constructed so as to produce public knowledge, which is what allows it to fill this important social and political role.[3] Even rational negotiation depends in the end upon the possibility of appeal to objectively acquired knowledge. Thus, much is at stake. We would be wise not to dismiss the importance of this and other matters of research ethics.

What is the upshot of such considerations? Do they imply that academic researchers should never accept industry or special interest funding? No, such extreme measures are

[3] Pennock, Robert T. (1999) *Tower of Babel: The Evidence against the New Creationism*. Chapter 8. Cambridge, MA: The MIT Press.

not necessary. However, it does mean that it should be accepted only when adequate protections are in place. Our task during this transitional period, as research universities begin to forge closer ties to industry, will be to conscientiously devise a system of checks and balances that will help safeguard the values of open and impartial research that made industry want to benefit from university research in the first place. I conclude that in the long run it is in the interest of all parties to uphold the integrity of scientific research. If warranted trust in scientific objectivity is undermined, we will lose much of the fundamental value of science. Thus, from an ethical perspective, it is research integrity, not financial gain, that should be the bottom line.

Conflict Of Interest: The Very Idea

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Virtually all codes of ethics in business and the professions contain provisions about conflicts of interest. The details vary, ranging from opposition to even the appearance of a conflict of interest to requiring disclosure of an actual or potential conflict of interest. However, perhaps guided by the assumption that its meaning is clear, 'conflict of interest' is left largely unanalyzed in the codes. In light of the many discussions I have had with colleagues and students, I am convinced that this is a faulty assumption.

For some, it seems that virtually any situation in which two or more interests of any kind are in some sort of tension constitutes a conflict of interest. This broadens the scope of 'conflict of interest' at the expense of depriving it of any analytical power regarding the specific kinds of ethical concerns standard cases of conflicts of interest seem to raise. For others, it seems that only financial or familial interests should count. This takes us into the right arena, but too narrowly. It discourages us from recognizing that virtually identical kinds of ethical concerns can arise in situations involving neither financial nor familial interests. Admittedly, there are many cases that anyone with a minimal grasp of the concept will agree are conflicts of interest. However, I have found generalization from such cases to a satisfactory definition of 'conflict of interest' to be difficult.

In my own attempts to get clearer about what a conflict of interest is,[4] I have turned to Michael Davis's very helpful essays on this topic.[5] In summary, he offers the following account of what he regards to be 'the standard view': I have a conflict of interest if and only if:

- I occupy a certain *role* in which a) I have certain *obligations* that b) require me to exercise good *judgment* in regard to certain matters.
- My being in this role justifies certain others relying on, or placing *trust*, in my

[4] Pritchard, Michael S., "Conflicts of Interest: Conceptual and Normative Issues," *Academic Medicine*, Vol. 71, No. 12, Dec. 1996, 1305-1313; and Borden, Sandra and Pritchard, Michael S., "Conflict of Interest in Journalism," in Michael Davis and Andrew Stark, eds., *Conflicts of Interest in the Professions* (New York: Oxford University Press, 2001), 73-91.

[5] Davis, Michael, *Business & Professional Ethics Journal*, Vol. 1, Summer 1982, 17-28. His most recent discussion is in his "Introduction," *Conflicts of Interest in the Professions*.

exercise of judgment in regard to fulfilling those obligations.

❖ I am actually, or potentially, in a situation in which it would reasonable for others to wonder whether certain *interests* of mine might compromise my ability to exercise the good judgment that can be expected of me.

As a summary, this cannot do justice to Davis's more detailed and nuanced account. However, it can set a rough framework for a discussion in which the concepts of 'interest,' 'role,' 'obligation,' 'judgment,' and 'trust' will be central elements.

Rather than offer a definition, I will discuss some of these central elements, with the aim of helping to explain why, and in what ways, conflicts of interest raise ethical concerns. This approach allows for the possibility, even the likelihood, that there are some conflicts of interest that do not fit comfortably within Davis's standard view. Nevertheless, it is a good place from which to begin. The advantage of having a standard view in mind is that it enables us to focus more clearly on what is ethically at stake.

Davis's 1982 article notes how surprising little analysis of 'conflict of interest' appeared in the literature of that time. He suggests that we look to the legal profession for help. But even there the history of the expression 'conflict of interest' is relatively short, making its entry into court decisions in the 1930's[6], although a notion of 'conflicting interests' was discussed in the American Bar Association's *Canon of Professional Ethics* in the very early 1900's.[7] This does not mean that the ethical issues posed by conflicts of interest were unfamiliar to people prior to the 20th Century. It means only that the first formal attempts to demarcate a special set of concerns in professional practice were made in the early 1900's. So, what are the marks of this special set of concerns that the expression 'conflict of interest' brings to mind?

This choice of words is suggestive, but possibly misleading. Although it appropriately focuses our attention on conflicts, it may suggest to some the much looser notion that anytime one has conflicting interests, one has a conflict of interest. But this would mean that I have a conflict of interest anytime I must choose between two things in which I have an interest, such as going out alone tonight to the basketball game or going to a play's final performance. No doubt this may present me with a difficult choice, but this sort of conflict lacks two elements standardly found in a conflict of interest. First, it is not evident that there is any duty or obligation involved. I could choose a third option, such as taking an evening walk rather than attending either the basketball game or the play, without failing to fulfill a duty, obligation, or responsibility. Second, there is only one party involved, myself. In short, this conflict does not seem to raise any *ethical* issues.

I suggest that the expression 'conflict of interest' is incomplete. It should be taken as shorthand for 'conflict of interest *with*...." A conflict of interest is a conflict of one or more interests with, not another interest, but with an obligation. Of course, I may have an interest in fulfilling my obligation, but it is the obligation rather than the interest that is the primary concern when it is said that I have a conflict of interest. An interest that conflicts with my obligation may itself involve another obligation; but the focus is on the fact that it is an interest.

In the context of a conflict of interest what should count as an interest is

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[6] Luebke, Neil, "Conflict of Interest as a Moral Category," *Business and Professional Ethics Journal*, Vol. 6, Spring 1987, 66-81.

[7] McMunigal, Kevin, "Rethinking Attorney Conflict of Interest Doctrine," *Georgetown Legal Ethics*, Vol. 5, 1992, 844-847.

not entirely clear. According to Davis, the standard view is that an interest includes any influence, loyalty, concern, or emotion that might interfere with fulfilling the relevant obligation.[8] However, without adding important qualifications, this list seems much too broad. For example, if I am very upset because I've just been issued a ticket and fined for going through a red light, this might well temporarily interfere with my ability to grade student papers fairly. Perhaps I should delay grading them for a while--until I'm no longer consumed with anger at the officer for issuing such a heavy fine or making me late for an appointment, or distracted by my concern that my insurance rates may be raised or my driver's license suspended. But, thus described, I do not have a conflict of interest. My suggestion is that we think of an interest as something one might pursue, act in behalf of, or attempt to satisfy or fulfill. My anger at being heavily fined does not qualify as an interest in this sense.

Our emotions and concerns I do reveal interests that we have. If I am angry because I have been heavily fined or concerned because my insurance rates may be raised, this reveals that I have an interest in the state of my finances. However, having an interest that, *as it happens*, may interfere with meeting an obligation is not in itself enough to create a conflict of interest with that obligation. I may have an obligation to meet a student during my office hours on the first sunny, warm day of spring and a strong interest accepting the invitation of my friends to join them on the golf course at that very same time. I am faced with a conflict, one involving my interests and obligations, but this is not standardly viewed as a conflict of interest.

For the conflict to be a conflict of interest, there must be a more special relationship between the interest and the obligation. As a quite contingent matter, it turns out that I cannot fulfil the obligation to meet my student and play golf with my friends. However, there is nothing about the obligation in question or playing golf with my friends that creates the conflict other than the impossibility of being in both places at the same time. So, we might better call this a 'conflict of place and time' than a 'conflict of interest'.

When a conflict of place and time involves a conflict between an obligation and interest alone, the ethical expectation is usually that the interest should give way to the obligation. If the interest is quite significant (e.g., a "once in a lifetime" opportunity), the verdict might go otherwise, depending on what acting on the interest involves, the obligation in question, and the availability of alternative ways of handling the situation. However, there can also be conflicts of time and place that find obligations in tension with one another. One may have taken on too many obligations--several of which are "coming due" at roughly the same time. This is a 'conflict of commitment,' a problem busy professionals commonly face, whether through their own fault or not. Or one may have obligations to be in two places at the same time. This may be the result of poor planning or forgetfulness; but this can also happen through no fault of one's own (e.g., one is scheduled to chair a meeting and one's child has become ill at school just before the meeting is convened). Such conflicts can be quite serious and difficult to resolve in a satisfactory manner. However, unless these commitments stand in some special relationship to each other than simply competing for time and place, we do not yet have a standard conflict of interest.

[8] In Davis and Stark, p. 9. For Davis, the obligation in question is to exercise reliable judgment in behalf of another.

My suggestion is that we reserve 'conflict of interest' for those conflicts between interests and obligations that involve an *inherent* conflict between them. Here is an illustration. Imagine I am serving on an NSF panel reviewing research proposals. As I examine the packet of proposals I am to review, I discover that I am listed in one of them as a paid consultant. My obligation is to exercise independent, impartial judgment in evaluating the proposals. But, seemingly, I have an interest in this particular proposal being funded. Precisely because of this, others may reasonably wonder whether this very special interest could bias my judgment.

It is noteworthy that this instance of a conflict of interest does not preclude my attempting to fulfill my obligation. I may even believe that my interest in a favorable outcome will not bias my judgment of the proposal. In contrast, I know I cannot both go to the game and the play. I know I cannot both keep my appointment with my student and join my friends on the golf course. What can be seductive about conflicts of interest is that I might well believe I can "have my cake and eat it too." This is so for at least two reasons.

First, I may not recognize that I have a conflict of interest. This is because, in general, it is quite acceptable to act in behalf of the interests involved in conflicts of interest. Of course, one might be so determined to obtain a grant or publish one's results that he or she is seriously tempted to fabricate or falsifying data. Giving in to this temptation is not acceptable; it falls under the standard view of 'scientific misconduct'. There is no need to designate this further as a conflict of interest. The concern in the case of a conflict of interest is often not so much that one will engage in behavior that is otherwise objectionable as well; it is that, because of the relationship between certain otherwise perfectly legitimate interests and certain obligations, there is an ethical concern that must be addressed. So, in contrast to cases of deliberate misconduct, finding that I have a conflict of interest may come as a surprise to me--especially if no one is asking me to examine my circumstances to see if I have one.

Second, even if I realize that my circumstance bears all the marks of a conflict of interest, I might believe that my interests pose no serious threat to fulfilling my obligations. Although I am sitting in review of research proposals, I may think that I can fairly evaluate my own proposal along with the rest. Or, if this seems a bit much, I might think that I can fairly evaluate the other proposals provided that I leave the room when mine is being evaluated. However, even this second procedure is very problematic. Once the results are announced and it is learned that I am among the winners, others outside the review process may reasonably wonder whether my judgment was nevertheless affected by my interest in being funded; and the worry might well be shared by other committee members, who were perhaps all too aware of my presence in the review process.

Here, it might be said, we have the *appearance* of a conflict of interest. Once the doubts are raised, how are they answered? Decisions in such cases are not algorithmic. They call for *judgment*, which, as Davis points, out involves discretion, not simply doing sums. How can I convincingly show *others* that my judgment was not biased by having a proposal under consideration? How can I convincingly show *myself* ?

The difficulty, if not impossibility, of satisfactorily answering these questions raises two concerns. Both are related to the *reliability of judgment*. First, there is the question about whether the judgments rendered were, in fact, influenced by my serving on the committee that reviewed my proposal. Conceivably, despite the "coziness" of

the arrangement, good judgment may have been exercised. Second, absent any way of determining that good judgment was exercised, there remains a question of *trust*. If the appearance of a conflict of interest cannot be removed in such cases, we have reason not to place full confidence in judgments rendered, even if, in fact, good judgment was exercised. Given the importance of trust in so many ways, it is important to make serious efforts to minimize risks to that trust. In this case, not allowing one to serve on the committee and submit a proposal at the same time is a positive step. However, depending on other relationships and research interests of committee members, this may not be sufficient.

Bearing all of this in mind, it is important to realize that merely *having* a conflict of interest is not, in general, to have done anything ethically suspect or wrong. This is illustrated in the NSF example above. When I discover that I am listed as a paid consultant on the proposal I am asked to review, I discover that I have a conflict of interest in my role as reviewer. So far, I have done nothing wrong. What I do *next* is crucial. Normally, it would be expected that I recuse myself from reviewing this proposal. Suppose, however, that I am not listed as a paid consultant, but I discover that this proposal is very familiar to me. In fact, I realize, I worked closely with the applicant as he prepared it, and it was clearly understood that I would be working closely with him on the project if it is funded. Lest there be any suspicion of complicity on my part, let us suppose that I was led to believe that the proposal was being prepared for NIH rather than NSF, but that the applicant changed his mind without telling me. I have a conflict of interest that only I know about (assuming the applicant did not know I was serving on the NSF panel). This does not constitute wrongdoing on my part. But, again, what I do next is crucial.

Of course, if I have colluded with the applicant and urged him to send the proposal to NSF because I am on the review panel, I can hardly plead moral innocence. The conflict of interest is of my own, deliberate making. However, there should be no presumption that this is typical of those who have conflicts of interest. This is an ethical point of some practical importance. If I acknowledging that I have a conflict of interest is taken by others, or myself, as some sort of admission of "guilt," it is understandable that one might be reluctant to disclose that I have an actual or possible conflict of interest. For this reason it is important to remove the *accusatory* label from 'conflict of interest' insofar as it is plausible to do so. This can be done while still signaling that there is something ethically significant to which careful attention should be given. Many acceptable, if not required, courses of action may be available at this point, ranging from disclosure to recusal.

Speaking metaphorically, we might think of actual, and even potential, conflicts of interest as yellow traffic lights. Caution must be taken. Depending on the available alternatives, the light may turn red or green--or it may remain yellow for the duration. One significant departure from the traffic signal metaphor is that what happens when the light turns yellow is to a large extent a function of what those addressing the actual or potential conflict of interest *do*. Thus, the conflict of interest signal is quite unlike traffic lights that are preset to turn green, yellow, and red in an invariable, timed sequence independently of driver behavior. Just as professional expertise in general calls for good judgment rather than algorithm determination, so does the ethical handling of actual and potential conflicts of interest.

Biomedical Research: HHS Direction Needed To Address Financial Conflicts Ofinterest Summary

General Accounting Office
(GAO) 02-89
November 26, 2001

Financial relationships between individual investigators or their research institutions and private industry have yielded significant results, including treatments for such diseases as AIDS and strokes. However, some collaborations have raised concerns that the focus on financial reward might compromise the integrity of the research and the safety of human research subjects. GAO reviewed five universities with broad policies and procedures on financial conflicts of interest. All five had difficulty providing basic data on individual investigators' financial conflicts of interest in clinical research involving human subjects. The universities acknowledged a need for better coordination of information on investigators' financial relationships, and several universities were developing ways to do so. Policies and procedures at the five universities addressed financial conflicts of interest affecting institutions, including technology transfer activities and financial relationships with small start-up companies that market products developed by the universities. The Department of Health and Human Services has had limited success in promoting the integrity of biomedical research and protecting human subjects. HHS has taken steps to improve its oversight and monitoring and has drafted guidance on financial conflicts of interest, but this guidance does not provide detailed advice on how to manage institutional conflicts of interest.

Federal Rules On Conflicts Of Interest In Biomedical Research Are Inadequate, Gao Finds

Contributed
By
Jeffrey Brainard

Reprinted from
The Chronicle of Higher Education[9]
Wednesday, December 19, 2001

Federal regulations that give universities much of the responsibility to police financial conflicts of interest involving biomedical researchers have "limitations," the General Accounting Office said in a report released Tuesday. Citing the report, the top Republican on the Senate subcommittee overseeing biomedical research called for hearings and, possibly, additional legislation to improve the protection of volunteers participating in such studies.

The report found that because federal rules now give universities wide discretion to police conflicts themselves, there is variation in how institutions resolve such situations, and university officials in some cases have been confused about the requirements. The GAO, which is the investigative arm of Congress, called on the government to provide more clarification.

The GAO study focused on five universities that are among the top recipients of federal research funds from the National Institutes of Health. The study examined how they had handled situations involving researchers who had a financial interest in treatments that they were testing in experiments using human volunteers.

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The inquiry turned up shortcomings there: The universities had not systematically monitored how investigators complied with conflict-of-interest policies, typically allowing scientists "to self-certify compliance." In addition, the universities' records about financial interests were not well organized, "making it a challenge to ensure that conflicts of interest were appropriately managed and not overlooked."

The five institutions were the University of California at Los Angeles, the University of North Carolina at Chapel Hill, the University of Washington at Seattle, Washington University in St. Louis, and Yale University. GAO officials said that they picked those five universities partly based on the amount of discoveries they had patented. They also interviewed officials at other institutions and higher-education organizations.

The report was prepared at the request of Sen. Bill Frist, a Republican from Tennessee. Dr. Frist, who is a heart-transplant surgeon, began scrutinizing federal rules on biomedical research after the 1999 death of Jesse Gelsinger, a volunteer in a gene-therapy experiment at the University of Pennsylvania. James M. Wilson, the director of the institute that conducted that study, had a financial stake in a company that had financed the institute's work.

In a statement Tuesday, Dr. Frist said that "the report clearly indicates that additional measures are needed." The Senate subcommittee overseeing biomedical research, of which Dr. Frist is the top Republican, had scheduled a hearing on conflict of interest for last October, but it was postponed.

Existing regulations require scientists to disclose significant conflicts of interest to universities, which then must devise ways to ensure that those conflicts are eliminated or do not harm the research. For example, a scientist who owns stock in a company supporting his or her research may have to sell the stock, or submit to reviews by other researchers at the institution.

The GAO cited several limitations in those regulations, however. For example, the NIH and the Food and Drug Administration have established different standards for what constitutes a significant conflict of interest.

In addition, some officials at the five universities were confused about the circumstances under which they were required to report conflicts to the NIH. The NIH requires reporting whenever an institution considers a disclosure from a scientist on an NIH-financed project in which the scientist has a significant conflict of interest. However, the policy requires universities only to tell the NIH whether the conflict was resolved; the university is not required to give the NIH details about the nature of the financial relationships.

In addition, there are no requirements that universities consistently inform institutional review boards about the disclosures by researchers, or how institutions resolved the conflicts of interest. The boards, known as IRB's, are charged under federal regulations with judging the risk posed to volunteers participating in the studies, and board members may need to know about conflicts of interest, the report said. Disclosures of conflicts are typically handled by separate conflict-of-interest committees, or by university administrators.

The report added that the government should spell out how universities should resolve conflicts when the institution itself holds a financial interest in the outcome of research, an area not adequately covered by existing regulations.

The Department of Health and Human Services proposed language providing such guidance last January, but the GAO report said that guidance lacked "detailed advice." In a formal

response included in the GAO report, department officials said they would take up that issue in the final version of the guidance, which is expected to be issued next month.

The department officials added, "It is not surprising that there is much diversity in [institutions'] policies and procedures" on financial conflicts of interest. Ties between universities and corporations vary in size and complexity, they said. "The management of institutional financial conflicts of interest requires tools that reflect this full spectrum of variability, and these tools are best applied at the local level."

The report also noted that department officials have mounted other efforts to provide universities with more help in interpreting government rules. Over the past two years, NIH officials have visited 16 institutions receiving the most NIH grants to remind them about conflict-of-interest regulations, among other topics. (The five universities studied by the GAO were not among them.) The NIH Web site contains information about "best practices" to carry out the rules.

In describing the five universities that GAO officials visited, the report did not specifically identify the practices of any one university. The report also said that the five were not necessarily representative of the hundreds of institutions that receive NIH grants.

The GAO said that the five institutions rarely brought sanctions against scientists who failed to comply with conflict-of-interest rules, and that they relied largely on the scientists to comply voluntarily "because they believed it was important to have faculty support and maintain collegiality with the investigators."

The GAO report, "HHS Direction Needed to Address Financial Conflicts of Interest," is available at the agency's Web site: http://www.gao.gov/

Today's University: Freedom Of Inquiry Or Corporate Cash?

A Response to
E. Press and J. Washburn. "The Kept University."
Atlantic Monthly,
March 2000, 39-54.
www.theatlantic.com/issues/2000/03/press.htm

Contributed by
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Issues surrounding conflict of interest have focused upon concerns with the practices of pharmaceutical companies, and how the commercial agenda and power of such firms sometimes conflicts with values of scientific research. In several of those news items, the university figured as a player, mostly taking the side of the drug company rather than the side of the scientist. This article provides some well-researched background into the current state of the large research university, and argues that we can expect to see more of this behavior in the future unless something changes.

Press and Washburn make the case that with shrinking public funds going to support higher education, large universities are now more dependent upon funding from the corporate world, and previously unrestricted funding has been replaced with strings-attached funding. This has the potential to stifle the free flow of scientific information (due to confidentiality clauses in contracts), tilt the research agenda of the university toward what's profitable and away from what would actually best serve the public interest, and divert funding to lucrative research and away from teaching students and the study of "unprofitable" sectors like the humanities-all the while vastly increasing the opportunities for

individual scientists to become enmeshed in serious conflicts of interest. Moreover, as universities compete for these corporate funds, their own behavior makes them resemble corporations themselves-to the extent that one law review article argues that such universities should, legally, be stripped of their tax-exempt status.

A couple of case examples may illustrate these points. One very close to home is Michigan State University. Press and Washburn note that MSU's patent for the anti-cancer drug, cisplatin, has been one of the most lucrative university patents, netting MSU $160 million in royalties. Recently, with the patent about to expire, and with several companies poised to begin producing cheaper generic versions of cisplatin, MSU applied for and received a slightly revised patent. Repatenting the same product is illegal, but apparently MSU found a loophole that allowed this new patent to appear unrelated to the previous one. Three of the companies planning to make cisplatin are now suing MSU, patients are deprived of a chance for a more affordable drug, and Barnett Rosenberg, the professor (now retired) who discovered cisplatin, has criticized MSU's "selfish, money-hungry" behavior.

Petr Taborsky went from being a graduate student in engineering at the University of South Florida to a member of a chain gang in a maximum-security state prison. His crime: he did research for a private company, then started research on what he (and his dean) said was a new line of investigation for his master's thesis. The new research led to a potentially profitable technique for removing ammonia from wastewater. Both the University and the private company then laid claim to ownership of his process. The university filed criminal charges and (spending 10 times as much for legal counsel than the amount of the original research grant) was able to convince a jury that Taborsky had stolen state property. He began serving his sentence in 1996, and the case became such an embarrassing media spectacle that the governor soon intervened to offer clemency, which Taborsky refused as a matter of principle (thereby suggesting that at least one person in this entire affair had principles).

The authors note the basic conflict between the ethic of science, which depends on sharing and open criticism of data and information, and the ways of the corporation, which treats information as a proprietary product to be kept secret from competitors. They quote Nobel prize scientist Paul Berg on the irony, that the profits now being made in one of the fastest growing sectors of "private science," biotechnology, all depend upon the fact that the basic research tools for replicating and cloning DNA were developed in the university with public funds. Had the present arrangements been in place then, Berg thinks, the restricted flow of information and the need to show an immediate profit would have stifled this technology before it even got off the ground.

The authors conclude with suggestions for reforms that would prevent some of the worst abuses: forbid professors from having direct financial ties to companies sponsoring their research; ban universities from investing in those companies; prohibit confidentiality clauses which delay publication of new findings more than 30-60 days; minimize proprietary restrictions on basic research tools.

Graduate Education And Corporate-Academic Partnerships

Contributed by
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"Secrecy and the pursuit of knowledge for its own sake are uneasy bedfellows"

James B. Conant , President, Harvard University
President's Report Harvard University 1951- 52

Competition, with winners and losers, is as real in academic research as it is in the corporate world. The difference lies in how points are scored. In our universities, the winners are usually those who diligently take their most recent findings to professional meetings for open discussion and dissemination of the data, even before a draft of the resulting paper is rushed to the editor of the most visible outlet that may consider it for publication.

In this environment, investigators proudly display citation records to document the impact that their work is having on the research programs of their peers and competitors, and they eagerly display preliminary findings in grant applications submitted for peer review. This practice, featuring open flow of information, is rarely the best strategy to adopt in the corporate arena. There, it is often necessary to keep preliminary insights and intermediate products unknown to competitors with similar marketing goals. These two cultures clash when university investigators negotiate research relationships with corporate sponsors.

At a minimum, these partnerships entitle the funding company to review research results before they are presented at conferences or submitted for publication, thus restricting the free exchange of information, the signature of academic scholarship. How these issues affect the work and education of graduate students and postdocs is a subject of debate by ethicists, university administrators and practicing scientists (see for example *The Scientist* 15 [22]:34, Nov. 12, 2001).

The Good

From the graduate students' or postdocs' perspective there are attractive consequences of working in a research project supported by corporate resources. For one, contact with corporate partners allows them to assess professional opportunities and career trajectories outside the academic frame. Also, the level of funding by private companies is likely to be higher than what is the norm for university research, but perhaps more important is the unique access to proprietary data bases and other research materials that companies can make available to university investigators as part of the agreement of partnership.

Students and postdocs may also find that their faculty mentors are more accessible to them after their emancipation, by virtue of the private-sector support, from the perpetual grant-writing mode that claims so much of a senior investigator's time. Finally, corporate-sponsored research is often goal oriented with the goals linked to problems present in "the real world". Under such conditions students may find that it is easier to explain and/or justify their work to others outside the discipline (e.g. mom and dad), although they may not be allowed to reveal a lot of information per the constraints of the agreement.

The Challenges

The main challenge for graduate students working in laboratories supported by corporate funds is to be able to accumulate a sufficient number of publications, including the thesis or dissertation, and meeting presentations to

be competitive in the job market, while accommodating the conditions of the partnership that may delay or restrict the dissemination of their findings. Even if the results of the research can be published in a timely fashion, often the particulars of the agreement between the principal investigator and the company limit the students' and postdocs' ability to follow up the results of their projects as independent investigators.

Finally, the extreme specificity of the research goals typical of corporate sponsored projects may curtail the breath of the training that students and postdocs receive in academic laboratories. Lack of breath has been identified as a weakness of many graduate programs (see Nyquist, JD and Woodford BJ, 2000, *Re-envisioning the Ph.D.*). While research is integral to the graduate education process (especially for the doctoral degree), it is not the only activity in which students engage. The graduate student's complete education must be firmly in mind as the major goal of the graduate program.

Conflicts

How much input should students and postdocs have in decisions that affect their intellectual property rights? As considerable research is conducted by teams, how should their rights be balanced with other individuals' rights? What should graduate deans and other administrators do to protect graduate students from possible exploitation by private companies? As these and similar questions are debated in national and local forums, the practice of seeking and accepting corporate support for research is likely to continue to be an attractive alternative to grant writing for support from federal agencies.

No matter what guidelines emerge from the on going discussions, adding private companies as partners in the academic research enterprise will complicate the relationships between students and postdocs and their faculty mentors, thus increasing the opportunities for conflict.

The Conflict Resolution program sponsored by the Graduate School at MSU and developed by J. Beck and K. Klomparens, takes off from the premise that "conflict itself is neither good nor bad – it's how conflict is handled that makes it good or bad". The program's approach emphasizes the importance of clearly identifying the interests of each stakeholder when handling conflicts and when setting expectations between faculty and graduate students.

Effective and honest communication is essential in any effort to identify interests and to use them in evaluating options and making expectations explicit. Students and postdocs need to become aware of the challenges and opportunities that partnerships with private companies present to them. Potential faculty mentors have to be proactive in explaining all aspects of an agreement with a company that in any way could affect the intellectual property rights and the professional development of young scientist being recruited to join a research program. That open and proactive attitude from the principal investigators is a very explicit expectation of The Graduate School.

The MSU Conflict Of Interest Committee

Contributed by
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In July 1995 the Public Health Service (PHS) and the National Science Foundation (NSF) jointly issued rules requiring that all investigators applying for grants from their agencies file a conflict-of-interest certification prior to the award of a grant. NSF will not even process the proposal until the certification has been filed, while PHS will process the proposal, but will not award the grant until they receive the certification. The rules require the investigator to also file a copy of the certification with their university, and require the Universities to develop their own procedure for reviewing any potential conflict of interest issues raised in the certification.

The MSU response to these rules was to create a Conflict Review Committee composed of three faculty members chaired by Dr. David Wright as a non-voting member. The three faculty that serve on this committee are Dr. Charles Given, Dr. Thomas Pinnavaia and me. The membership has not changed since the committee was formed in 1996.

The role of this committee is to manage, reduce or eliminate financial conflicts of interest identified by the applicant for NSF and PHS grants. We do not search for potential conflicts of interest, we respond to such potential conflicts identified by the applicant. The responsibility to identify a potential conflict of interest lies with the faculty member applying for the grant. The two conflicts of interest that must be identified under these rules are both financial. The first is if the immediate family members of the applicant have ownership interests of $10,000 or more in any non-MSU entity related to the commercialization of a product the research is intended to develop or evaluate. The second is if the applicant or the immediate family members receive any form of remuneration equal to or greater than $10,000 for year from such an entity. The entity can be either an enterprise that would gain from a positive evaluation of a product or process, or one that would gain from a negative evaluation of a competitive product or process. The role of the conflict of interest committee is to review proposals to the PHS or NSF and make a determination whether the conflict of interest identified by the applicant exists. If the committee determines that there is a conflict of interest, or even the appearance of a conflict of interest, the committee makes recommendations to the faculty member on how to manage the problem.

A common recommendation is for a full disclosure to the potential sponsor. The sponsoring agency can then weigh the possible conflict in their process of review and award of a contract. On one occasion the committee believed the potential conflict was such that a recommendation was made that the disclosure statement be included in the proposal itself so the proposal reviewers could be aware of the issue, and could consider this in their recommendation.

The committee does not have the authority to require a faculty member to accept our recommendation, nor do we have the authority to prevent a sponsor from awarding a grant if our recommendations are not followed. The committee often meets with the faculty member in an attempt to reach a compromise that is both satisfactory to the applicant, and that the committee believes projects the integrity of the University process. If an agreement could not be reached, we would notify the sponsor of that outcome.

Clinical Research: Hopkins Reviews Investment In Indian Cancer Drug Trial

Contributed by
Pallava Bagla and Eliot Marshall
Reprinted from
Science. Volume 293, Number 5532, Issue of 10 Aug 2001, p. 1024. [10]

Now add financial interest to the mix of combustible elements in the controversy over tests of a new drug for oral cancer in India (Science, 3 August, p. 777). Johns Hopkins University, whose professor helped design a trial at the Regional Cancer Center (RCC) of Trivandrum, India, has also invested in a Minnesota start-up medical company that plans to test the drug at other Asian sites. Hopkins is also trying to explain how it could have sent a check to support the cancer study in India, led by biologist Ru Chih C. Huang of its school of arts and sciences, without first seeking approval from a university ethics panel.

Hopkins's financial involvement in this research will complicate the task of responding to allegations of patient mistreatment, which surfaced last month in Indian and U.S. media. It was another in a string of recent setbacks for Hopkins, which is recovering from the recent death of a research subject at its medical school (Science, 27 July, p. 587). The confusion over who authorized the clinical trial in Trivandrum and who signed the checks feeds into a larger set of concerns about Western companies prospecting for biomedical discoveries in the developing world.

The drug in question is M4N, a methylated extract of the creosote bush. Huang and colleagues discovered a related compound in studies of HIV therapy several years ago at Huang's lab at Hopkins. Because it is insoluble, Huang says, M4N stays put in tissue, where it blocks the cell cycle locally. In 1999 Huang and her Indian clinical co-principal investigator, M. Krishnan Nair, director of the RCC, enrolled 26 patients in a pilot study at the RCC to test whether it could work against solid tumors. In July 2000, Hopkins joined with a Singapore businessman to finance a new company to develop the drug. And in April 2001, Huang and the university obtained a U.S. patent on the anticancer formula now being tested (patent number 6,214,874).

Initial reports of patients responding within days to the injections led Huang to conclude that "this is a wonderful drug, and it's not toxic in humans." But a senior clinician at RCC thought otherwise. V. Narayaman Bhattathiri, a Ph.D. chief of radiology, challenged the trial after seeing some of the patients. "I asked for details of the study, and they were not given to me," he says. "Then I complained to the ethical committee: No action. Two months passed, and then I complained to the Human Rights Commission," a parliamentary body.

Bhattathiri charged that Nair's experiment had begun in 1999 without a proper ethics review or approval of the Drugs Controller General of India. Bhattathiri also alleges that patients were diverted from standard therapy for 3 to 4 days, that they had been led to believe they were getting therapeutic injections (they weren't), and that the experiment might interfere with radiotherapy. He also made a claim--later discredited--that unapproved "toxic" compounds were being used.

Huang told Science that she is baffled by the criticism. She did not apply to Hopkins's Institutional Review Board (IRB) until this year, she says, "because I thought the local IRB in India was sufficient, and none of the Hopkins administrators objected." Last week, Nair released a six-page rebuttal, saying that

the RCC obtained an ethics clearance required by India before beginning the trial and that "discussions were held with the Drugs Controller General. ... All patients received standard treatment," it says, and none developed "any side effects or suffered any harmful effects due to drug injection."

Hopkins spokesperson Dennis O'Shea says that the university first learned of the trial in March 2001--and that it had not gone through Hopkins's IRB. Hopkins put a hold on the research, asking for an IRB review that is still pending. Last month the Indian media reported charges from Bhattathiri that RCC patients were being "used as guinea pigs."

Hopkins never directly funded the trial, O'Shea says. But the RCC clinician in charge, Manoj Pandey, says that the RCC has received two checks signed by Hopkins's treasurer, William E. Snow Jr., for a total of $19,400 and is awaiting a third. In addition, Pandey says that Hopkins has received permission from the U.S. government to import tissue from Indian cancer patients to Baltimore for study.

Huang says that funding for this project comes entirely from private sources, including Hopkins and a new company, Biocure Medical LLC of Edina, Minnesota. In July 2000, according to a press notice on Hopkins's Web site, Huang met with Hopkins vice provost Ted Poehler and Ang Tiong Loi, a Singapore businessman, to form this "groundbreaking new start-up company" for cancer research. Huang says backers have committed about $2.5 million to pilot trials at four sites in Asia, and investments may rise to $50 million.

"I'm not saying we know where these funds came from," says O'Shea. "Just because Johns Hopkins cuts a check doesn't necessarily mean" it approved the project being funded. Making sense of the financial transactions is a task for a new investigative panel, he says, which will report its findings "as expeditiously as possible."

Response

Contributed by
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When it comes to conflicts of interest, it is important to keep two things in mind. First, the appearance can be as important as the reality; and second, institutions are subject to conflicts of interest, not just individuals. These two aspects reveal themselves in the most recent research ethics scandal to hit Johns Hopkins University, involving trials of an experimental cancer drug using patients at a prestigious Indian cancer center.

Conflicts of interest are ethically troubling at the first level insofar as they threaten our capacity to make good judgments (e.g., about the balance of risks and benefits to patients in a clinical trial). They are also troubling at a second level because they undermine the trust that others have in our capacity (or willingness) to act as we should. This is especially worrisome for enterprises, like human research, that rely utterly on the willingness of vulnerable people to put themselves into the hands of others. The appearance of a conflict of interest may undermine their trust as surely as the reality does.

The Indian cancer trials illustrate that the appearance one sees depends on where one is standing. The facts (as reported in various media) seem to be these: A Hopkins faculty member (R.C. Huang), working with Indian collaborators, conducted Phase I trials of a chemical derived from creosote bushes (M4N) in Indian cancer patients. M4N had not undergone adequate animal testing, and the research had not been reviewed, let alone approved, by any Hopkins IRB.

Hopkins, however, held the patent with Huang, had entered into a partnership with a Singapore businessman to commercially develop M4N and related drugs, and had issued checks to the Indian cancer center to pay for the conduct of the trials.

When questioned about the possible connection between the Indian trials and Hopkins' financial stakes in M4N, the university spokesman replied that "The assignment of the patent to the university had nothing to do with the clinical trial in India and it did not in any way alter the researcher's obligation under university rules to submit the proposed trial to an institutional review board."[11] Since the institution didn't even know that the trials were taking place, its financial stake in their outcome couldn't have had anything to do with the design or implementation of the research. Any appearance of a conflict of interest is mere illusion.

The whole affair, however, looks very different from the Indian perspective. The coverage by the Indian media was much more extensive and detailed than anything found in US newspapers; and it was preoccupied with the intricacies of how the trials were financed, and who had economic stakes in their outcome. Once it became known that millions of dollars had been invested in the joint venture, and that there were no trials planned involving US cancer patients, the conclusion drawn in Indian commentary was that poor, semi-literate Indian cancer patients were being used by JHU and its partners in the pursuit of profits. The old adage, "Once burned, twice shy" applies here. Once you've been on the receiving end of mistreatment and exploitation, your index of suspicion will shift dramatically. Hopkins may think there are no grounds for charges of conflict of interest; but for Indians, history gives reason to think otherwise.

Importantly, Indian suspicion did not just focus on Huang or other individuals who stood to gain from the project, but on Hopkins the institution. Hopkins itself was seen as an agent no different than Huang, making decisions under the influence of a set of self-interested motives. It was Hopkins exploiting vulnerable Indian patients, not just Huang.

Hopkins (or rather, someone at Hopkins) may reply that it is not a single agent, but a collection of individuals, each with limited information and discrete responsibilities. Of course, some administrators at Hopkins had to know about Huang's Indian research– but they weren't the administrators responsible for compliance with human subjects research regulations. Sure, someone at Hopkins was cutting checks drawn on Hopkins' accounts– but it wasn't the person responsible for shepherding Hopkins' investment in M4N. If there is any dereliction of responsibility, it occurs only at the level of the individual. This reductive elimination of the very possibility of corporate responsibility may have been at work in the investigation that Hopkins conducted. The report that it issued focused almost entirely on Huang (who is now barred from any further involvement in human research). Hopkins the institution gets only a slap on the wrist for not responding quickly enough once "it" (i.e., the right individuals) found out about the trials.

Just how to characterize corporate responsibility, and its relationship to individual actions, is a complicated question. For now, I'll just point out that however wildly incoherent universities and other organizations may in fact be on the inside, from the outside they look like a single thing. If in conflicts of interest appearance can be as important as reality, Hopkins and other universities need to attend to what they look like.

[11] Krishnakumar, R. "Drug Trials and Ethics." *Frontline* 18 (17), Aug. 18-31, 2001.
(At http://www.flonnet.com/fl1817/18170040.htm, Mar. 20, 2002)

Response

Contributed by
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Patient and subject rights in research studies and scientific standards in biomedical research have changed (improved) radically over recent years. In particular, institutional protection of research subjects has been strengthened due to instances of abuse and through the application of stricter ethical standards. My comments below relate to the piece that appeared in *Science* concerning allegations surrounding a clinical trial of a new anticancer drug. This clinical trial was conducted in India although "backed" by an investigator from Johns Hopkins University (JHU) and the University itself.

The article raises issues that suggest that the University and University faculty members may have violated patients' rights and standards for the conduct of research such as violation of conflict of interest.

When a study is conducted in another country by a North American investigator, is that investigator required to submit the study to an appropriate US institutional review board? Yes, in the case described, the investigator, a member of the John's Hopkins University faculty, should have processed the study through the JHU institutional review board (IRB). Why? North American investigators may not use other countries standards of human protection or human rights. US investigators must abide by US ethical and scientific standards.

When an investigator or institution has a financial interest in a drug (e.g. anticancer agent), that investigator and/or institution has a conflict of interest or appearance of conflict of interest should he/she personally pursue the clinical testing of the efficacy of that drug. Results of a trial (both efficacy and risk) should not be seen through the lens of financial interest. In the case described, it is alleged that both the investigator and John's Hopkins University had a financial interest in the drug. Financial interest is not restricted to ownership in the "new company" but can also involve royalty opportunity through patent and licensing or even consulting compensation.

In defending a conflict of interest allegation, John's Hopkins University stated that it had not funded the clinical trial. It was pointed out that the treasurer of JHU signed checks paying for the study. How can checks be signed by the treasurer and yet the University make the claim it was not funding the study? I presume that the University is claiming that it was holding money from private sources and was merely the "middleman" in dispensing the dollars. If the University "holds and dispenses money" from private sources, is it truthful in stating that it did not fund the project? I do not believe so. The University has, at the very least, an appearance of conflict of interest if only because JHU's name is on the check, a check bearing the imprimatur of that prestigious University, a University with a financial state in the outcome of the study.

It should also be noted that the conflict of interest would have, in all likelihood, been discovered had the investigator submitted the project to the John's Hopkins University IRB. By not submitting the study to the appropriate IRB, the University and investigator did not have appropriate review of scientific standards and of human subject rights and, finally, careful scrutiny of potential conflict of interest. Furthermore, it appears that the right hand of the University was not aware of what the left hand was doing.

Conflict Of Interest And Entrepreneurship

Contributed by
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There are several ways in which potential conflict of interest questions may arise in activities conducted by MSU employees. Conflict of commitment may occur if a faculty member is, for example, running for public office or is otherwise engaged in outside activities which have the potential to conflict with teaching or other essential duties. Some funding agencies, including the National Science Foundation, the National Institutes of Health, and the Michigan Life Sciences Corridor, require that faculty investigators disclose to the University their potential conflicts of interest.

See:
http://www.msu.edu/unit/facrecds/FacHand/guidelinesforconflict.html
for more information.

Finally, state law and university policy require that certain procedures be followed if MSU is to enter into a contractual agreement with an entity owned or partially owned by an MSU employee. This article deals with the third category of conflict.

According to Act 317 of 1968 "Contracts of Public Servants with Public Entities," Sections 15.321-15.323, MSU employees must follow disclosure procedures if they own an interest of more than 1% in a company with which the University is contemplating a contract or license. Board of Trustees policy identifies disclosable *non de minimis* conflicts of interests as situations where the University is negotiating a contract with a company in which a faculty member and his or her immediate family cumulatively own or have options to buy more than 5% of the company's voting stock. Please see http://www.msu.edu/unit/facrecds/FacHand/interimguidelines.html.

Faculty entrepreneurship is an important part of business growth in the community and can result in technology transfer opportunities that are of benefit to both the University and the start-up company. At the same time, many opportunities for conflicts of interest arise from faculty start-ups when the University licenses or contracts with the firms. Thus, it is important for faculty who are financially involved in start-ups to initiate a conflict of interest review as early as possible, so that conflict management procedures may be put in place and appropriate approvals obtained through the MSU Board of Trustees. The process for contract and license approval requires three steps, coordinated through the office of the Associate Vice President for Research and Graduate Studies:

(I) notification to the Board of the University's intent to negotiate with a faculty owned firm;

(2) preparation and submission of a disclosure letter from the faculty member(s) involved in the company outlining their interests and those of their immediate family in the company; and

(3) approval at a subsequent Board meeting of the terms of the proposed contract or license.

Please contact Ms. Lori Hudson, Office of the Associate Vice President for Research and Graduate Studies, 238 Administration Building, 432-4499, ljh@msu.edu, for more information and to discuss entrepreneurship opportunities which may require Board disclosure.

Interview With Dean Fouke

Contributed by
Julie A. Reyes, PhD
Research Ethics Education Coordinator
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In March of this year, I asked **Dr. Janie M. Fouke,** Dean of the College of Engineering for an interview concerning her thoughts on COI. The following article summarizes the main points from this interview.

Dr. Fouke points out, "Institutional COI is a very big problem and is less well discussed in the public domain right now. It is very difficult to figure out how to deal with it. For personal COI, there are any numbers of people who can independently sit down and talk with you about YOUR potential or real personal conflicts. Institutional COI is a completely different issue. The institution may have an enormous investment and stake in the outcome of studies in which MSU is invested. Sometime the investment is a start-up company, with substantial financial stakes and if the study goes well, the University has an opportunity to license the patent and perhaps receive enormous financial gain.

The other two dimensions of COI are "real" and "perceived". It is difficult for some of my colleagues to understand that a perceived conflict of interest is as bad as real conflict of interest. The point is, that someone has cause to question the integrity or independence of the judgment. I have found this to be a harder educational battle than that of the real COI. The top issue concerning COI in the College of Engineering is educating people as to what constitutes a conflict. For instance, we need to help people to understand what the rules are, what do you have to disclose, and to understand what disclosure is trying to achieve.

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