

Chapter 11

Reforming Research Ethics in an Age of Multivested Science

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UNIVERSITIES AND THEIR faculty have embraced a new role for science that combines its classical mission (“knowledge is virtue”) with postindustrial goals rooted in the Baconian tradition (“knowledge is productivity”). The new symbiosis between academia and commerce, amply nurtured by public policies, is forcing a critical reexamination of research ethics on issues such as sharing of information, commodification of knowledge, conflicts of interest held by scientists and their institutions, and the mingling of medicine and business in clinical trials. Government agencies, universities, journal editors, and professional societies are beginning to reexamine the norms under which academic science has functioned for more than one hundred years. At stake is public trust in the autonomy of university research and the extent to which, in the words of Columbia University historian Richard Hofstadter, [the pursuit of knowledge] “is esteemed not as a necessary instrument of external ends, but as an end in itself” (Press and Washburn 2000, 54). This chapter explores the indicators of changing patterns of research support at universities; the connection between these patterns and the current trends in university entrepreneurship; and the new ethical norms under consideration by professional groups, research institutions, journal editors, and government agencies in response to the growth in conflicts of interest in academic science and medicine.

The changing patterns of funding for university research indicate the growth of university entrepreneurship. Research universities and their faculty have become more dependent on and accepting of private funding and, along with such funding, a business model of research. The rapid development of

university entrepreneurship in the past twenty years—what Sheila Slaughter and Larry Leslie (1997) term *academic capitalism*—has effected changes in the traditional norms of science. New guidelines in research ethics, mostly focused on transparency of interests and disclosure, are a response to the conflicts of interest and the growth of public mistrust of science arising from the mixture of pure and profit-oriented research that has become endemic within major academic institutions.

Indicators of Change

To understand the emergence of the new entrepreneurial university, we can examine five factors that characterize the changes taking place in academic institutions:

- Private funding of research
- Faculty consulting and service on company advisory boards
- Faculty equity and personal involvement in companies
- University-industry partnership
- Intellectual property held by faculty and universities

For several of the indicators the trends have been quantified. Other trends, such as increases in faculty consulting and personal involvement in new companies, are revealed through indirect measures as well as national and site-specific surveys.

The incentives for university-industry collaborations, created largely by federal legislation passed in the 1980s, began to produce effects during the 1990s. According to statistics compiled by the National Science Foundation, American research universities are obtaining more of their research and development funds from industry. Research and development expenditures in universities and colleges rose from \$18.8 billion in 1992 to \$27.5 billion in 1999, a 46 percent change. In that same period industry contributions to the research and development budget of the academic institutions rose 60 percent from \$1.3 billion to \$2.1 billion. Industry contributions to the research and development budgets of colleges and universities amounted to 4.1 percent in 1980, 6.8 percent in 1992, and about 8 percent in 2001.

Still, the vast expenditure of university research comes from federal and foundation sources. These figures, however, do not tell the whole story. A smaller percentage of trend-setting research universities have quite a different profile of funding. Over a seven-year period, industry funding at Duke University increased 280 percent while total research and development rose 85 percent. At the University of Texas in Austin there was a 725 percent in-

Table 11-1
Top Ten Industry-Funded Universities in the United States, 1999

<i>Institution</i>	<i>Industry-Funded Research and Development</i>	<i>Percent Change, in Industry- Funded Research Development 1992-99</i>	<i>Total Research and Development</i>	<i>Percent Change, in Total Research and Development 1992-99</i>	<i>Industry-Funded Research and Development as a Proportion of Total</i>
Duke University	121,630,000	280	348,274,000	84.6	34.9
Massachusetts Institute of Technology	75,444,000	51.4	420,306,000	25.9	17.9
Pennsylvania State University	65,698,000	53.9	379,402,000	36.3	17.3
Georgia Institute of Technology	62,752,000	163.9	263,725,000	46.3	23.8
Ohio State University	52,034,000	271.8	322,810,000	58.8	16.1
University of Washington	51,319,000	101.6	482,659,000	54.0	10.6
University of Texas— Austin	39,729,000	725.3	258,122,000	12.9	15.4
University of California— San Francisco	36,830,000	490.8	417,095,000	40.5	8.8
Texas A&M	34,722,000	30.1	402,203,000	31.7	8.6
University of Michigan	34,432,000	37.8	508,619,000	29.4	6.8

SOURCE: National Science Foundation. 1999. *Science and Engineering Indicators—Academic Research and Development Expenditures: FY 1999*. NSF-01-329. Washington, D.C.: National Science Foundation, table B-38.

crease in industry research and development funding while total research and development increased by 13 percent. Also, a review of industry funding as a proportion of total research and development for the top ten industry-funded universities reveals that Duke University heads the list at 35 percent followed by the Georgia Institute of Technology at 24 percent, the Massachusetts Institute of Technology at 18 percent, Pennsylvania State University at 17 percent, and the University of Texas at 15 percent. A decade ago, 15 percent of university research and development coming from industry was considered an upper limit (see table 11-1.) Now, as universities have become more aggressive in seeking private funding sources, it is no longer unusual to see industry-funded research and development exceed 15 percent of their total research and development budget. For example, in 2000 the industry support in the research budgets of Alfred University, the University of Tulsa, Eastern Virginia Medical School, and Lehigh University was 48 percent, 32 percent, 24 percent, and 22 percent, respectively. As university research and development funding begins to reach these levels, it brings with it changes in the culture of scientific research that make academic traditionalists uneasy.

The federal legislation and executive policies that created incentives for private investment in academic research were based on two assumptions. First, American competitiveness in the global marketplace would improve by stimulating technology transfer of discoveries at universities. Second, new efforts to balance the federal budget would mean declining support for university research. Corporations saw an opportunity to shift resources from investments in internal research and development to collaborations with academic institutions. The number of university industry research centers has risen dramatically in the past decade. By 1990 there were close to 1,000 at more than two hundred American universities and colleges, and more than half of the number were established in the 1980s. Meanwhile, during the past two decades, the federal share of support for universities and colleges has declined, accounting for 5.8 percent of the total federal research and development budget, the lowest share since the end of the 1950s. In *Academic Capitalism*, Slaughter and Leslie (1997) observe that "U.S. public research universities are attempting to maximize revenues from external sources as the several state governments decrease their shares of support" (238).

A confluence of events, including the 1980 U.S. Supreme Court Decision on the patenting of living organisms (which opened the door for gene patents); the Bayh-Dole Act (which gave universities the intellectual property rights to federally funded discoveries); and the Human Genome Project (which infused large sums of research dollars into university-industry collaborations), has created a patent frenzy in academia. According to Slaughter and

Leslie, "the Bayh-Dole Act of 1980 signaled the inclusion of universities in profit making" (45). In the twenty-five years from 1974 to 1999, the patent awards among the top-hundred research universities rose from 177 to more than 3,000 (Association of University Technology Managers 2000).

Other indicators of the commercialization of university research can be found in the rise in trade secrets and self-imposed restrictions on the sharing of scientific data. A series of studies reveal these trends in the biomedical sciences. One study, which surveyed more than one hundred faculty members in the forty universities that receive the largest share of federal research in the United States, reported that biotechnology faculty with industry support were four times as likely as other biotechnology faculty to report that trade secrets had resulted from their university research. The number of trade secrets was directly related to the amount of university support (Blumenthal et al. 1986).

A survey of senior executives in life-sciences companies found that the majority of companies supporting academic research require scientists to hold information confidential for more than six months, a period many professional societies view as dangerously long (Blumenthal 1986). In another survey of geneticists, nearly 50 percent responded that their requests for scientific information from other scientists were denied; more than one-third indicated that data withholding is increasing among members of their community (Campbell et al. 2002). Finally, a study of fourteen high-profile science and medical journals revealed that one-third of the articles published in 1992 had at least one lead author with a personal financial interest in the subject matter of the work (Krinsky and Rothenberg 1996).

The intense commercialization of the academy, a phenomenon that is now widely acknowledged, has created a need for new ethical guidelines in universities, government, scientific and medical journals, and professional societies to protect the integrity of science and to secure its trust within the broader society. Litigation and fear of litigation are forcing some changes. In *The Research University in a Time of Discontent*, Jonathan Cole observes, "universities must balance their dedication to a neutral position regarding the outcome of scientific experiments against their efforts to support entrepreneurial efforts of their talented faculty" (Cole, Barber, and Graubard 1994, 32). But the balance point is precisely what is being contested.

There are signals that the pendulum has swung too far, that disclosure will not be accepted as the universal antidote for the condition, and that some restraints are being considered. The ethical limits of research and publication integrity are being tested. Some efforts are underway to reset the academic sector's moral compass. Five major institutional stakeholders are beginning to

respond to the public's concerns about conflicts of interest in science and medicine: the journals, professional societies, governmental agencies, universities, and nonprofit research institutes.

Scientific Publications

Scientific journal editors have become more sensitive to the appearance of conflict of interest by contributors and editorial staffs. During the 1990s many of the leading medical journals adopted conflict of interest policies. Most policies added financial disclosure requirements for authors. Some journals took a tougher stance and sought to prevent authors from contributing editorials or reviews if they had a direct conflict of interest with the subject matter. Medical journals are far ahead of basic science journals in establishing author guidelines on conflict of interest. Issues of ghostwriting, prestige authorship, and authors who do not have full control of their data trouble some journal editors. The International Committee of Medical Journal Editors took a bold step in recommending that their member journals require a signed statement affirming that the author alone has made the decision to publish the data and that the individuals listed as authors have made a worthy contribution to the article.

Compliance with the conflict of interest policies of academic journals is based on the honor system. Most journals do not have the personnel or the time to assess the level of compliance. When a colleague and I published a study of the rates of author disclosure in nearly two hundred peer-reviewed journals with conflict of interest policies, a number of editors were surprised that their journals did not have a single disclosure of personal financial interest for the entire test year (Krimsky and Rothenberg 2001). In the current climate of academic commerce, it seemed unlikely that so many authors had nothing to disclose. This raises the question of compliance when a policy has no sanctions against violators.

Except for a small number of internationally acclaimed journals that do well economically, many operate under tight financial constraints. Electronic access to journals has reduced subscribers to hard copies, putting some journals in even greater economic peril. If editors place too much emphasis on author conflicts of interest, they may lose potential contributors who would rather publish in a journal that doesn't require disclosure of their personal income or equity holdings. Journals are making some effort to respond to the rising tide of scientific conflict of interest, but they cannot do it alone. A few journals proscribe authors with conflicts of interest from publishing editorials or reviews; most can only offer their readers voluntary disclosure. To be fully

effective, the response to author conflict of interest must be systematic and include all players in the research community.

Professional Societies

Several professional associations in science and medicine have begun to develop policies on conflicts of interest. The American Medical Association (AMA) has been a leader in addressing the problems of conflicts of interest since 1990. As the largest medical association for American physicians, the AMA has published several principles and supporting opinions that establish its code of ethics. Its *Principles of Medical Ethics*, revised in 1980, includes its primary guidelines from which all other codes and recommendations derive. Among the guide's seven basic principles, there is no reference to conflicts of interest. In 1990, the AMA adopted six principles under the heading "Fundamental Elements of the Patient-Physician Relationship." One states: "Patients are also entitled . . . to be advised of potential conflicts of interest that their physicians might have and to secure independent professional opinions" (American Medical Association 2000-01, xiii). The AMA's *Code of Medical Ethics* is a compilation of opinions based on the interpretation of its adopted principles and reports applied to numerous specific cases. In the section devoted to biomedical research, it states: "Avoidance of real or perceived conflicts of interest in clinical research is imperative if the medical community is to ensure objectivity and maintain individual and institutional integrity" (69). It also states that medical researchers receiving funding from a company "cannot ethically buy or sell the company's stock until the involvement ends" and that clinical investigators are obligated to disclose their financial conflicts of interests in all published results including letters (69-70). Because these are solely guidelines, we have no basis for knowing what percentage of the AMA membership complies with its principles.

Other professional societies have issued policy directives on conflicts of interest, particularly those groups that are involved with human-subject research. The American Society of Gene Therapy, which adopted a statement titled *Financial Conflicts of Interest in Clinical Research* in 2000, set its standards higher than the federal guidelines: "all investigators and team members directly responsible for patient selection, the informed consent process and/or clinical management in a trial must not have equity, stock options or comparable arrangements in companies sponsoring the trial" (American Society of Gene Therapy 2000, 1).

The Association of American Medical Colleges (AAMC) is the professional group representing 125 accredited U.S. medical schools, covering also

four hundred teaching hospitals and approximately 90,000 medical school faculties. The AAMC's views on conflicts of interest were issued in its 1990 publication, *Guidelines for Dealing with Faculty Conflicts of Commitment and Conflicts of Interest in Research*. Like many of its sibling university associations, the AAMC supports the basic principles behind the partnership between industry and academia as "essential to preserve medical progress and to continue to improve the health of our citizenry" (Association of American Medical Colleges 2001, 3). But it also asserts that "the mere appearance of a conflict between financial interests and professional responsibilities may weaken public confidence in the researcher's objectivity" (3). How do organizations reconcile the view that some relationships, such as industry-university collaborations, are essential but that they have an *appearance* that weakens the public's trust?

Maintaining that human-subject research requires an especially high standard of moral integrity, the AAMC applies the regulatory concept of "rebuttable presumption" to establish the burden of proof. "Institutional policies should establish the rebuttable presumption that an individual who holds a significant financial interest in research involving human subjects may not conduct such research" (7). Moreover, the AAMC maintains that the principle—namely, "the rebuttable presumption against significant financial interest in human subjects research"—should apply whether the funding is public or private (7).

Under the AAMC's ethical code on conflict of interest, the institution may provide compelling evidence (presumably to itself since the code is voluntary) that, even with significant financial interests, the investigator may be permitted to conduct the research. This hearkens back to the federal ethics guidelines for advisory committees, where the first principle is to prevent scientists with conflicts of interest from participating and the second principle is to permit waivers for the scientists with conflicts of interest when there are "compelling circumstances." The approach taken by the AAMC is to establish a high standard but to leave plenty of latitude for exceptions. Like the federal agencies, the AAMC states: "when the individual holding such interests is uniquely qualified by virtue of expertise and experience and the research could not otherwise be conducted as safely or effectively without that individual, he or she should be permitted the opportunity to rebut the presumption against financial interests by demonstrating these facts to the satisfaction of an institution's conflict of interest committee" (7).

Just how effective will institutional conflict of interest committees be in the face of large grants and contracts and researchers with weighty résumés? Many question the effectiveness of institutional oversight groups against im-

perial faculty. But there is progress: the AAMC recommends that institutions report conflict of interest information to the university's institutional review board (IRB), a federally mandated body. The IRB is responsible for approving human-subject protocols, and some are already taking on the additional responsibility of making judgments about conflicts of interest.

We continue to hear the argument that the management of conflict of interest and human-subject protection should be kept distinct. But after the death of Jesse Gelsinger in a failed human gene therapy experiment at the University of Pennsylvania, there has been more discussion about folding conflicts of interest into informed consent. Lawsuits filed on behalf of victims who died in clinical trials have argued that failure to disclose a conflict of interest or to prevent a conflict of interest introduce additional risks to the patient, which should be either prevented or disclosed.

The Association of American Universities (AAU) established a special task force on research accountability to produce a report and issue recommendations on individual and institutional financial conflict of interest. The task force was co-chaired by Steven B. Sample and L. Dennis Smith, the presidents of the University of Southern California and the University of Nebraska at Lincoln, respectively. Also included in the task force were the presidents of the University of Iowa, Princeton University, and Columbia University. The association published the task force's findings in October 2001. After reviewing the available information, the task force concluded that, "although the definitive data about the prevalence of conflict of interest is lacking, academic-industry relationships are clearly increasing, and with them, the risk of conflicts of interest compromising the integrity of research conducted in academia continues to rise" (Association of American Universities 2001, 2). While generally favoring an institutional, case-by-case approach to conflicts of interest among university faculty, the task force issued a special warning for situations involving human subjects and presented a zero tolerance recommendation: "Since research involving humans creates risks that non-human research does not, any related financial interest in research involving humans should generally not be allowable" (4).

But like the AAMC, the task force tempered its zero tolerance recommendation by leaving open the opportunity for exceptions: "If compelling circumstances justify an exception to this general rule, the research should be subject to more stringent management measures" (4). Both the AAU and the AAMC positions ask the universities to avoid, whenever possible, financial interests in human trials, to be able to defend trials if necessary, and to apply the ethical rules regardless of the source of funds. In addition, both believe that the IRBs should be involved in reviewing or monitoring conflicts of interests. The

AAU asserts rather confidently that the institutional IRB has jurisdiction over whether a particular financial interest should be managed or disclosed to the human subjects. This jurisdiction is not, however, in the legislation and charter of the IRBs; and many IRBs are not equipped to handle these types of questions. The AAU task force recommends a double layer of protection against financial conflicts in human subject experiments. The first layer of review would be made by the institutional conflict of interest committee. Its recommendation would then be passed on to the IRB, which also makes an independent determination. According to the AAU task force, "in such a system, neither the IRB nor the conflict of interest committee would be able to override the other's management requirements if the result would be to lessen the stringency of the management requirements. Either one could prohibit the research from proceeding, unless the financial conflict was removed or mitigated" (6).

The AAU task force report provides the strongest safeguards to date proposed by any review committee on managing conflicts of interest involving human subjects. The recommendations are designed, however, to keep the government's role to a bare minimum, to avoid further federal regulations, to foster the principle of self-governance, to keep flexibility within the institutions, and to establish ethical principles that extend beyond current federal regulations. For example, the government has not issued any restrictions on institutional financial conflict of interest, while the AAU task force reported that this type of conflict of interest "strikes to the heart of the integrity of the institution and the public's confidence in that integrity" (10). The major categories of institutional financial conflicts of interest include those involving university equity holdings or royalty arrangements and their effect on research programs and those involving university officials with personal financial interests in faculty companies or trustees whose firms could supply the university with goods or services. What is at stake?

In the task force's words, "institutional conflicts can reduce a university's role as an objective arbiter of knowledge on behalf of the public" (12). There are warnings and general guidelines for the institution but no clear prohibitions. For institutional conflicts of interest, the AAU task force cites three principles: always disclose, manage the conflicts in most cases, and prohibit the activity when necessary to protect the public interest or the interest of the university.

But how reasonable is it to expect that universities will choose the higher moral ground of public interest when the institution's bottom line or acquiescence to its big donors is at stake? In the past ten years several of the large professional societies have begun to address the serious erosion of academic

integrity for both the individual and institutional conflicts of interest that have become endemic to the university culture. The specialized medical groups have not been as responsive. A 2000 study by the Office of the Inspector General of the Department of Health and Human Services of twenty-one medical association guidelines found that only two associations (the American College of Emergency Medicine, and the American Psychiatric Association) had codes of ethics with explicit reference to physicians' disclosure of financial conflicts of interest to their patients/subjects (Brown 2000). The federal government's policy actions have been slow and cautious. There have been some incremental changes in response to the demands for more accountability.

Federal Agency Conflict of Interest Policies

Beginning in the late 1990s, in the wake of high-profile scandals and internal investigations, federal agencies began to tighten up their conflict of interest policies. The trend has been toward greater transparency, more comprehensive disclosures of financial relationships to funding and regulatory agencies, and protection of the self-management of conflicts of interest by grantee institutions. The interest of government is twofold. It wants to project an image of fairness and objectivity in policy decisions. And it wants to assure the general public that money going into research, especially clinical research, is not tainted by the real or perceived bias of scientists with a financial interest in the subject matter of their research.

The U.S. General Accounting Office (GAO), an investigative arm of government, reviewed the selection of external advisers on Environmental Protection Agency (EPA) panels in its June 2001 report. The GAO found that conflicts of interest were not identified and mitigated in a timely manner and that the public was not adequately informed about the points of view represented on the EPA's influential panels of experts (General Accounting Office 2001). By June 2002, the EPA drafted new guidelines with changes in how it would deal with conflict of interest.

The EPA's scientific advisory board consists of a staff and about one hundred experts in various fields of science. When advisory panels are chosen to review an area of science that informs a policy, the panel is formed of members of the board with additional experts chosen at large. According to provisions of the Ethics in Government Act of 1978, the board's staff screens panel candidates for conflicts of interest and the appearance of partiality.

The new policy has several changes that will be more attentive to conflicts of interest and afford the public more involvement in the process through which individuals are recommended to serve on expert panels. According to

the new policies and procedures, "If a conflict exists between a panel candidate's private financial interests and activities and public responsibilities as a panel member, or even if there is the appearance of partiality, as defined by federal ethics regulations, the [board staff members] will, as a rule, seek to obtain the needed expertise from another individual" (U.S. Environmental Protection Agency 2002, A4). Previously, prospective panel members filled out conflict of interest forms annually. Under the current standards, they file a form each time they are recommended to serve on a scientific advisory board panel. The forms that must be filed by panel members are more detailed. Each prospective panel member is asked to write in narrative form any relationship he or she has that could be perceived as a conflict of interest. If a conflict of interest is identified, staff members must consult with the chair of the board's executive committee. Moreover, the public is given the opportunity to protest against potential panel candidates on grounds of bias. While the EPA has the legal authority to waive the conflict of interest of a potential panel member, by making the process more transparent to the public, the agency will have to think more seriously about exercising its waiver authority because it requires documentation.

The Public Health Service and the National Science Foundation issued conflict of interest regulations in 1995 for all recipients of grants from those agencies. This was a significant step toward establishing a reporting mechanism and a responsible party for managing conflicts of interest within each institution that receives federal grants. The government has not introduced a system for evaluating compliance. Federal guidelines set the standard for disclosure for researchers at equity ownership in companies exceeding 5 percent or aggregate payments received from companies in excess of \$10,000 per year. Neither agency's guidelines prohibit any activity or research relationship but let the individual institutions manage what they interpret as a "significant conflict of interest."

As of 1997, under its *Guidelines for the Conduct of Research in the Intramural Research Program*, the National Institutes of Health (NIH) had a full disclosure policy for its scientists. This policy requires NIH employees to file a statement on all of their relevant financial interests (including those of the scientist's immediate family) to any funding agencies to which they submit grant applications, to peer review panels, and to meeting organizers before presentation of results. Finally, they must disclose their financial interests to journal editors when they submit publications and communications, written and oral. The requirement that intramural scientists have to disclose all personal financial interests to journal editors does not translate to extramural research (grants to academic scientists). Government grants do not impose a require-

ment that academic grantees publish their results in journals that have conflict of interest policies. Such a requirement would undoubtedly create an incentive for more journals to adopt such policies.

Because of the public sensitivity to conflicts of interest in clinical trials and the national priority to protect the integrity of experiments with human subjects, the U.S. Food and Drug Administration (FDA) became a lightning rod for criticism of clinical investigators who had commercial agendas. The FDA published a rule in February 1998, which became effective the following year, requiring disclosure of financial interests of clinical investigators that "could affect the reliability of data submitted to the FDA" by applicants for research support (U.S. Food and Drug Administration 1998, 5233). The FDA rule requires that anyone who submits a marketing application for any drug, biological product, or device must also submit information about the financial interests of any clinical investigator who made a significant contribution to the demonstration of safety. Failure to file the information could result in the FDA's refusal to file the marketing application.

The FDA also requires certification from the applicant that no financial arrangements with a clinical investigator have been made in which the outcome of a study could affect the compensation. In other words, companies should not be giving investigators payments in stock options or special rewards for drugs that "work." Investigators should have no proprietary interest in the tested product and the investigator should not have a significant equity interest in the sponsor of the study. Thus, the FDA has adopted a few prohibitions of the most egregious conflicts of interests. For others, it requires financial disclosure, presumably so the agency can factor in conflict of interest in assessing the reliability of the data.

In May 2000, Department of Health and Human Services secretary Donna E. Shalala outlined her intention to issue additional guidance to clarify its regulations on conflicts of interest. One of her goals was to get the National Institutes of Health and the FDA to work together "to develop new policies for the broader biomedical research community, which will require, for example, that any researchers' financial interest in a clinical trial be disclosed to potential participants" (U.S. Department of Health and Human Services 2000a, n.p.). One of the first initiatives of the secretary was to get IRBs to address conflicts of interests for investigators and institutions. Shalala wrote that the department will "undertake an extensive public consultation to identify new or improved means to manage financial conflicts of interest that could threaten the safety of research subjects or the objectivity of the research itself" (41073).

It was the intention of the secretary to seek new legislation to enable the FDA to issue civil penalties against violations of conflict of interest disclosure.

Shalala hoped to close the loop between conflict of interest, human-subject protection, and IRBs. The failure to disclose a conflict of interest was viewed as either an increased risk or an increased perceived risk to a potential human volunteer. The department issued a draft interim guidance document in January 2001. Strictly speaking, a guidance document is not a regulation, but commentators viewed it as another layer of federal controls on research centers and universities. It said explicitly: "[the department] is offering this guidance to assist Institutions, Clinical Investigators, and IRBs in their deliberations concerning potential and real conflicts of interest, and to facilitate disclosure, where appropriate, in consent forms" (U.S. Department of Health and Human Services 2001, 1). The draft guidance document proposed that the IRBs should be involved in identifying and managing both individual and institutional conflicts of interest and that consent forms for clinical trials should contain the sources of funding of the clinical investigators. A number of commentators were critical of the ill-defined concept of "institutional conflict of interest" and questioned whether IRBs could make decisions based on this concept. Would human volunteers act differently if they learned that clinical researchers or their institution had a financial stake in the outcome of the experiment? Would it be more difficult to recruit volunteers for such studies? Would the IRBs, already overworked in many cases, be able to handle this added responsibility? These were some of the concerns raised by professional societies to the department's draft interim guidance document.

A second draft of the guidance document on financial relationships in research involving human subjects was issued on 31 March 2003. The new draft defines a conflicting financial interest as one that "will or may be reasonably expected to create a bias" (U.S. Department of Health and Human Services 2003, 15457). While an advancement over the purely subjective definition in the prior draft, this definition is limited by linking conflict of interest to the "effect of a relationship" rather than to the "relationship itself." If, during sentencing of a convicted felon, a judge discloses his financial interest in a for-profit prison, we would not need an outcome measure of the effect of such a relationship to declare a conflict of interest. The new draft guidance document stops short of making any clear determinations about what relationships should be prohibited, leaving that decision to individual institutions. The earlier guidance asserts that, in clinical trials, when conflicts of interest cannot be eliminated, they should be disclosed in the consent document. The latest guidance recommends that the investigator *consider* whether to disclose the financial interest to the human subject—a weakening of the transparency concept.

Notwithstanding the initiatives taken by the Public Health Service and the FDA to manage conflicts of interest, according to the Office of Human

Research Protection, "there is currently no uniform comprehensive approach to consideration of potential financial conflicts of interest in human research" (U.S. Department of Health and Human Services 2001, 1). As of 2002, the actions of the federal agencies, by and large, still embrace the belief that data speak for themselves and that good science, not financial interests, determines the reliability of data. The government has taken no formal initiative to address institutional conflicts of interest, notwithstanding the fact that, increasingly, universities are investing in companies funded by faculty members. The responses taken by the FDA and the National Institutes of Health are largely public relations efforts responding to a climate that demands political correctness but does not get to the core of the problem, which is the increasingly commercial face of American universities.

Academic Institutions

American universities are still learning about faculty conflicts of interest. And with respect to institutional conflicts of interest, without a federal mandate or national guidelines, each university is going it alone. The most significant changes have arisen in response to federal mandates that a research university receiving National Science Foundation or National Institutes of Health funding must establish a conflict of interest management plan. Beyond that mandate, some universities are introducing the topic of conflicts of interest in relationship to training programs on scientific integrity designed for doctoral students and clinical investigators.

The research on university conflict of interest policies thus far shows a lack of specificity and wide variation in the content and the management of the policies. For example, a survey examined the conflict of interest policies of one hundred institutions with high levels of National Institutes of Health funding in 1998 and found that 55 percent of the policies required disclosure from all faculty while 45 percent required them only from the principal investigators. A relatively small number (19 percent) of the policies set explicit limits on faculty financial interests in corporate-sponsored research; a mere 12 percent contained language on what type of delay in publication was permissible, while 4 percent had taken the step to prohibit student involvement in work sponsored by a company for which the faculty had a personal financial interest. The study cited the need for uniform guidelines across academia: "Wide variation in management of conflicts of interest among institutions may cause unnecessary confusion among potential industrial partners or competition among universities for corporate sponsorship that could erode academic standards" (Cho et al. 2000, 2208).

In the aftermath of Jesse Gelsinger's death, significant attention at university medical schools has focused on clinical trials and conflicts of interest. The Department of Health and Human Services held hearings on this matter. A study published in 2000 analyzed policies governing conflicts of interest at ten medical schools in the United States that received the largest amount of research funding from the National Institutes of Health. Five of the schools had disclosure policies that exceeded the federal guidelines. Six required disclosure to the IRB as well as to the assigned administrator on conflict of interest policies. Four had stricter requirements for researchers conducting clinical trials than the federal government did (Lo, Wolf, and Berkeley 2000).

Another survey yielding 250 responses from medical schools and research institutions found that 9 percent had policies that exceeded federal guidelines. This indicates that the direction of the moral compass of the universities is favoring more stringent conflict of interest policies to protect the values and integrity of the university than the de minimus standards of the federal government (McCrary et al. 2000). Having learned from the experiences of their peers, university administrators are more cautious with regard to industry contracts containing restrictive covenants giving the sponsor control over data or publication. Two decades ago, Yale University's president Bart Giamatti (1982) wrote, "As an indispensable condition to arrangements for cooperative research with industry . . . the university will not accept restrictions, inhibition, or infringement upon a member of the faculty's free inquiry or capacity orally to communicate the results of his or her research . . . the university will not accept any restriction of written publication, save the most minor delay to enable a sponsor to apply for a patent or a license" (1280). When the faculty member is both the investigator and the corporate head, then the decision to delay publication is not an external control on the university but a part of the academic norm to maximize economic value before communicating the results of science research. The norm of trade secrecy arises as much from within the university as from outside. Delaying publication or denying data to other researchers can have adverse social consequences if they delay potential therapeutic uses or restrict the development of a technique or new product.

Independent Research Institutes

Many leading research institutes receive the majority of their funding from government sources. Typically, they also have ties to universities where researchers have academic appointments. One of these institutions, which has been the target of ongoing investigations by government agencies and inves-

tigative journalists, is the Seattle-based Fred Hutchinson Cancer Research Center, a tax-supported nonprofit with ties to the University of Washington. Scientists at "the Hutch," as it is known by locals, were financially involved with companies that financed their research. Since its founding in the 1970s, an estimated twenty scientists working at the Hutch have left to start companies with equity value of more than \$18 billion. A series of stories in the *Seattle Times* under the headline "Uninformed Consent" (11 and 15 March 2001) brought these conflicts of interest to the attention of the general public. For many years, physicians at the Hutch were not required to tell patients when they had private financial interests in drugs or medical products. Clinical investigators could supervise clinical trials while they had substantial equity in a company that had a financial interest in the trial's outcome. The *Seattle Times* focused its report on two experiments: one involving a bone marrow transplant protocol, which was carried out between 1981 and 1993; the other a series of experimental treatments for breast cancer, which took place between 1991 and 1998. According to the report, an unusually high number of deaths accompanied these experimental treatments.

A physician at the Hutch, who served on the institution's IRB, contacted federal authorities about what he alleged were egregious conflicts of interest at his institution. The whistleblower was quoted in the *Seattle Times*, 12 March: "In essence, financial conflict of interest led to highly unethical human experimentation, which resulted in at least two dozen patient deaths. Oversight committees were misled, lied to and kept uninformed while in an atmosphere of fear and intimidation." According to records received by the investigative journalists, in addition to the clinical investigators, the Hutch itself had a financial stake in the experiments. Ironically, the board of trustees of the Hutch adopted a conflict of interest policy in 1983 that banned employees from participating in research in which they or their family members had an economic interest of any type. But the policy was not enforced in the cases investigated. Some scientists claimed they did not even know about the policy.

As an outgrowth of the federal investigations and media attention, the Hutch introduced a new conflict of interest policy in May 2002 that markedly restricts a clinical researcher from participating in human-subject research if it is sponsored by or designed to test a product or service of a for-profit entity in which the researcher (or his or her family) has a prohibited financial interest, which includes ownership interest of any amount or any nature in that for-profit entity. This new, rather complex policy signals a move toward the reform of conflict of interest policies among many leading research institutes and medical centers. Nevertheless, the conflict of interest disclosures at these institutes and centers are internal to the institutions and are thus gen-

erally shielded from the Freedom of Information Act. Without public disclosure, failure to implement conflict of interest procedures cannot easily be detected unless there is litigation.

Conclusion

The ethics of entrepreneurial research and conflict of interest are still being debated. There are many remaining contested issues:

- Should scientists with a personal financial interest in the subject of federally funded research disclose those interests to the funding agencies or simply to their home institutions? Should clinical scientists who have a commercial interest in drugs, medical procedures, or equipment be required to disclose those interests to human subjects who are invited to participate in a clinical trial? Should the IRBs rule on conflict of interest?
- Should scientists who have equity in a company or who are principals in a company be permitted to accept research grants from the company through their university?
- Should authors with financial interests in the subject matter of their publications be required by journals to disclose those interests? Should they be prohibited from contributing review articles and editorials?
- Should scientific books reviewed in journals be required to disclose the funding sources of the research they discuss?
- Should journals refuse review articles, editorials, and book reviews by authors with a conflict of interest?
- Should government agencies prohibit membership on scientific advisory panels when scientists have a conflict of interest?

Thus far, much of the response to faculty conflict of interest has focused on disclosure. The Department of Health and Human Services has set a priority for addressing conflicts of interest in clinical trials and has issued a draft guidance document that establishes a role for the IRBs in reviewing the competing interests of clinical investigators. The problem of institutional conflicts of interest has not received attention at the federal level and is rarely discussed among other science communities. While journals are beginning to issue policies that require disclosure, compliance by authors may not be high. And university approaches to managing conflicts of interest vary widely.

In the current state of affairs, both institutional and investigator conflicts

of interest in basic science and medical research are addressed through a patchwork of voluntary guidelines. An alternative approach would be to apply the concept of *fiduciary responsibility*, a term with strong precedent in the legal community, to academic research and medical sectors. One of the guiding principles underlying that responsibility is that those who produce knowledge in nonprofit institutions that are largely publicly funded, and those stakeholders who have a financial interest in that knowledge, must be kept separate and distinct. The separation of roles within certain professions that serve a public good such as the judiciary or financial auditors is what prevents even the appearance of conflicts of interest.

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Buying In or Selling Out?

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