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Curing Conflicts of Interest in Clinical Research: Impossible Dreams and Harsh Realities

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CURING CONFLICTS OF INTEREST IN CLINICAL RESEARCH: IMPOSSIBLE DREAMS AND HARSH REALITIES

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"Conflicts of interest are of concern because of their potential effect on the quality, outcome, and dissemination of research, as well as their effects on the public's perception of and trust in researchers and universities."

"Academic medical institutions are themselves growing increasingly beholden to industry."

"Patients died prematurely in two failed clinical trials... experiments using drugs in which the center and its doctors had a financial interest."

These three quotes from recent high profile articles on conflicts of interest present but the tip of the proverbial iceberg. Even as we laud numerous medical advances—better drugs, devices and procedures—there are nagging concerns that alleged research successes are tainted by the quest for dollars, prestige, and power. Making the issue more pressing is the fact that an increasing number of research subjects are involved, and arguably at risk, in clinical trials. Making the issue more public is the bright light of media attention focused on clinical trials beset with conflicts of interest.

Conflicts of interest in medicine, and more particularly in clinical research, cover a wide range of activities, practices, and even accepted norms. For example, in the context of non-experimental health care services, the American public is increasingly concerned that managed care organizations are subverting physician judgment with financial incentives and rewards for doing less for the hapless patient. Studies demonstrate that physician prescriptive practices are significantly affected by dollars and other benefits provided to them by the

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4. Volunteer subjects increased from 502,000 in 1995 to over 700,000 in 1999—a 39% increase. See Tom Abate, Maybe Conflicts of Interests Are Searing Clinical Trial Patients: Report that Blames Negative Media also Cites Complaint Surge, S.F. CHRON., Apr. 30, 2001, at D1.
pharmaceutical industry. In the research context, our consciousness has been brutally raised by high profile media exposures of blatant conflicts of interest, allegedly responsible for the deaths of research subjects, and harmful prolongation of unsuccessful research trials. Most of these high profile cases have focused on financial conflicts of interest. These financial conflicts include not only dependence on industry sources for ongoing support of clinical research, but also additional "downstream" revenue which may motivate individual researchers and the academic research centers alike. Alas, financial conflicts of interests are only one category of conflict compromising research integrity.

This article will explore conflicts of interest in the context of clinical research, focusing on the incentives and practices that foster such conflicts. Part I will briefly define and categorize the revenue streams at play in clinical research—both contemporaneous with the clinical trial, and the downstream, long-term gains available to the researcher and research university. Part II will discuss how these entangled revenue streams result in financial and non-financial conflicts of interest that affect the nature and balance of the research enterprise and potentially endanger patients and human subjects. Part III will summarize current conflicts of interest regulations and policies, including methods for addressing and preventing conflicts of interest. Finally, Part IV will suggest some reforms to the current conflict of interest management strategies, with the concession that, absent a major culture shift in research institutions and existing law, conflicts of interest will continue to undermine confidence in the integrity of the research enterprise.

I. FUNDING OF CLINICAL RESEARCH: THE ONCE AND FUTURE DOLLAR

Although lack of funding is frequently decried as a barrier to research, little empirical evidence supports this hypothesis. Clinical research is simultaneously financed by several contemporaneous, intertwined funding streams. It is not unusual for federal grant dollars, private industry support, third-party payments, and direct patient payment to all be in play in a given clinical research project. In addition to these present-day funding streams, there is also future revenue potential for both the research university and the researcher in the form of equity

7. See Wilson & Heath, supra note 3; Donna Shalala, Protecting Research Subjects—What Must Be Done, 343 NEW ENG. J. MED. 808, 808 (2000).
8. The Institute of Medicine (IOM) has done a thorough study of this issue and found that this belief is based more on perception than reality. See NAT'L ACAD. OF SCIENCES, INST. OF MED., EXTENDING MEDICARE REIMBURSEMENT IN CLINICAL TRIALS (Henry J. Aaron & Hellen Gelband eds., 2000) [hereinafter MEDICARE REIMBURSEMENT IN CLINICAL TRIALS], available at http://www.nap.edu/catalog/9742.html.
interests, royalties, and licensing fees from enterprises and products derived from the research.

A. Financing of Clinical Research: Present Day Funding Streams

Researchers and universities finance the costs of clinical research from several different sources. These include classical federal grant funding, contribution from private sponsors such as pharmaceutical, medical device and biotechnology firms, reimbursement from third party payers, and direct payments from the patient/subject.

1. Federal Funding

Following World War II, the federal government heavily subsidized biomedical research. The massive investment resulted in what has become known as the “golden age” of research. Although federal research support investment has been tempered by private industry sponsorship in recent years, federal funding is still one of the mainstays for financing clinical research.

On the individual front, researchers and clinicians develop and test new drugs, devices, and procedures in research funded by federal grants. Typically, this is in the form of salary support, usually phrased as a percentage of total work effort. This compensation is funneled through the institutional employer—

9. The National Institutes of Health (NIH), its companion institutes, and various bureaus fund a broad scope of research, including cancer (National Cancer Institute (NCI)), heart disease (National Heart, Lung and Blood Institute), and mental health and substance abuse (Alcohol, Drug Abuse and Mental Health Administration (ADAMHA)). See INST. OF MED., FUNDING HEALTH SCIENCES RESEARCH: A STRATEGY TO RESTORE BALANCE 37-39 (Floyd E. Bloom & Mark A. Randolph eds., 1990) [hereinafter FUNDING HEALTH SCIENCES RESEARCH]. In addition, numerous other federal entities sponsor medical research and clinical trials, including the National Science Foundation (NSF), Centers for Disease Control (CDC), the Department of Veteran’s Affairs, National Aeronautics and Space Administration (NASA), and the Department of Defense. Id. at 38-47. Approximately two-thirds of federally sponsored research is conducted in academic institutions, whereas only about a quarter is conducted in government-owned laboratories, such as those on NIH’s Bethesda campus. See id. at 35. This decentralization is viewed as one of the key reasons for America’s research eminence. See id. at 35-36. See also Harold Varmus, Scientific Lecture—Biomedical Research Enters the Steady State, 333 NEW ENG. J. MED. 811, 812 (1995).

10. Despite its prominence, federal funding of research is relatively short-lived. Prior to World War II, health research was financed primarily by industry, academic institutions, and private philanthropy. See FUNDING HEALTH SCIENCES RESEARCH, supra note 9, at 32-34. However, in the aftermath of the War, the federal government poured money and resources into medical research. Id. See also Varmus, supra note 9, at 811-12.

usually the university or the academic medical center. In the case of research clinicians, this salary support will apply to their income as employees of the university or academic medical center. It is likely only one of the several income streams enjoyed by the researcher.

The academic medical center will benefit financially from clinical research through compensation by the government grantor for the costs it incurs for the trial. These generally are skimmed off the top of the grant award as so-called "indirect costs" of the institution. It is not unusual for academic medical center and university indirect costs to consume half of the grant award. In addition, the academic medical center will benefit from federal grant awards by being able to recapture salary of researchers who are supported by the grant. Most academic researchers, although dependent on "soft money," do have the safety net of a guaranteed salary from the university or medical center. Thus, when a grantee receives a percentage of salary support from the grant, the institution will also indirectly benefit by being freed from this percentage of the salary expense.

2. Private Sponsor Funding

Although the federal government has been the primary source of funding for clinical research in the past, it has been superseded by private industry in the last decade. There is a pronounced trend toward a greater percentage of research being funded by the private sector. One study has shown that 28% of life sciences faculty received private sponsor funding. In 1986, the private sector funded 42% of health care research and development. By 1995, the private sector's allocation of research dollars had risen to 52%. This equated to a three-fold increase, from approximately $6 billion to $19 billion. Thus, although

12. See, e.g. FUNDING HEALTH SCIENCES RESEARCH, supra note 9 (grants are disbursed by federal agencies to the institutional employers which, in turn, compensate the researcher).
13. Id.
15. See also Peter S. Arno & Michael H. Davis, Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed Upon Patents Deriving in Whole or in Part from Federally Funded Research, 75 TUL. L. REV. 631, 636 (2001).
17. See Neumann & Sandberg, supra note 14, at 112. See also Arno & Davis, supra note 15, at 636-37.
18. Neumann & Sandberg, supra note 14, at 111.
19. Id.
20. Id. at 112.
federal funding of research has incrementally increased over time, the private funding has increased exponentially.

Research clinicians receive compensation from the sponsor for their work on the clinical trial. This may be in the form of salary support, honoraria, or even in some cases, per-head payment for recruitment of human subjects. The researcher may also serve as the spokesperson for the new innovation. In return for this activity, the researcher may receive additional compensation for presenting the new technology or treatment at academic and industry meetings and conferences. Although this spokesperson role may be consistent with the spirit of scientific exchange and academia, it may also serve a marketing function. The latter is more likely as the product is nearing the end of the regulatory approval process and is entering, or has entered, the commercial marketplace. As such, it becomes a source of downstream financial gain.

3. Third Party Payers Funding Clinical Research

In the case of clinical research, the cost may be further defrayed by seeking payment from a third party payer. Both the physician researcher and the academic medical center will typically seek additional reimbursement from third party payers.

While we once saw health care payers as insurers, the health insurer payer of yesteryear has been supplanted by the self-insuring employer using a managed care organization to administer the employee health benefit plan. The other big payers, of course, are the federal and, to a lesser degree, state governments who finance the Medicare and Medicaid programs.

Health plans, whether public or private, seek to avoid paying for unproven or speculative treatments. At the time Medicare was enacted in 1965, one of the standards borrowed from the private health insurance market was the requirement that care must be medically necessary and reasonable in order to be

21. See Elizabeth Boyd & Lisa A. Bero, Assessing Faculty Financial Relationships With Industry, 284 JAMA 2209, 2209 (2000). Fourteen percent of researchers reported that they had equity in the private sponsor. Id. Thirty-four percent reported arrangements involving speaking engagements and honoraria of $250 - $20,000 per year. Id. Thirty-three percent involved a paid consulting arrangement on either an occasional or regular basis. Id. Thirty-two percent involved paid board or advisory board positions. Id. See also Kurt Eichenwald & Gina Kolata, Drug Trials Hide Conflicts for Doctors, N.Y. TIMES, May 16, 1999, at A1; DEPT. HEALTH & HUMAN SERVS., RECRUITING HUMAN SUBJECTS: SAMPLE GUIDELINES FOR PRACTICE, PUB. NO. OEl-01-97-196, 8-11 (2000) [hereinafter RECRUITING HUMAN SUBJECTS].

22. Pharmaceutical and other private sponsors pay physicians for their work in a clinical trial at a substantially higher rate than do government grantors; for example, for oncology research, physicians get a median payment of $750 per patient from the National Cancer Institute, as compared to $2,500 per patient for industry sponsored trials. See MEDICARE REIMBURSEMENT IN CLINICAL TRIALS, supra note 8, at 41-42.

23. See id. at 30.
covered and reimbursed by Medicare. Therapies and technologies that are "investigational" or "experimental" are not eligible for coverage. Although this coverage policy is frequently articulated by Medicare, Medicaid, and private third party payers, there is considerable uncertainty as to how concretely this exclusion is administered and maintained, even in the setting of regular treatment.

Despite a few targeted national coverage policies excluding coverage for certain procedures, Medicare has been surprisingly forthcoming with support for costs of clinical research. In 1996, when an audit revealed that most of the audited hospitals had billed Medicare for care rendered in connection with implantable medical devices, the Health Care Financing Administration (HCFA) chose to enter into an agreement with the Food and Drug Administration (FDA) and cover a large percentage of investigational devices. Indeed, the investigational devices that fall into this covered category include 96% of the devices in ongoing clinical trials.

In June, 2000, then-President Clinton issued an executive memorandum directing the Secretary of Health and Human Services to "explicitly authorize [Medicare] payment for routine patient care costs . . . and costs due to medical complications associated with participation in clinical trials." Pursuant to that memorandum, HCFA issued a national coverage decision in September, 2000 authorizing coverage of the routine costs of qualifying clinical trials, including costs of diagnosis and treatment resulting from complications arising from

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25. This provision was explicitly spelled out in 1977. Experimental or Investigational Items or Services, Part IA Intermediary Letter, Medicare & Medicaid Guide (CCH) ¶ 28,152 (Jan. 1, 1977).
27. See MEDICARE REIMBURSEMENT IN CLINICAL TRIALS, supra note 8, at 32.
28. See id. at 33.
29. See id. at 34.
30. Memorandum on Increasing Participation of Medicare Beneficiaries in Clinical Trials, 36 WEEKLY COMP. PRES. DOC. 1311 (June 7, 2000). Routine costs in clinical trials include:
   * Items or services that are typically provided absent a clinical trial (e.g., conventional care);
   * Items or services required solely for the provision of the investigational item or service (e.g., administration of a noncovered chemotherapeutic agent, the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and
   * Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service—in particular, for the diagnosis or treatment of complications.

participation in the trial. Routine costs include all items and services normally covered by Medicare and provided to subjects in either the experimental or control arm of the trial. The coverage does not extend to the investigational item or service itself, items or services related to data collection and analysis that are not integral to the clinical management of the patient, and anything customarily furnished by research sponsors free of charge to subjects.

With respect to private payers, whether an employer-provided health plan or an individually purchased plan, there is a long tradition of excluding "experimental" or "investigational" services and items. These exclusions, typically found in the policy contract, have been the subject of frequent and vigorous litigation. On balance, these exclusions have proven feeble in courts of law. They have also resulted in public relations disasters when used to deny care to a pitiable beneficiary. In recent years, payers, particularly the private payers—typically employee health plans administered by managed care organizations—have opted to cover the cost of these unproven therapies rather than engage in costly court and media battles.

In fact, in recent years, there has been willingness on the part of third party payers to assume the costs of clinical research, especially the routine services associated with such research. For example, the American Association of Health Plans encourages its health plans to reimburse the routine costs of care associated with National Institutes of Health (NIH) sponsored trials.
large private health plans cover costs of patient care in cancer research trials conducted under the National Cancer Institute (NCI).\textsuperscript{40}

Even absent the payers' increasing willingness to fund the routine patient costs of clinical research, the fact is that isolating costs associated with research from costs not associated with research is administratively difficult and costly.\textsuperscript{41} Because of this difficulty, both Medicare and private payers have actually been paying for a large proportion of research-related costs long before they affirmed their willingness to do so.\textsuperscript{42}

Indeed, according to a recent study published by the Institute of Medicine (IOM), coverage and reimbursement of medical services—especially routine services—associated with clinical trials is common.\textsuperscript{43} The IOM sought to verify this "widespread understanding" with a study commissioned by the Lewin Group, a health policy consulting firm.\textsuperscript{44} In the Lewin Group study, clinical trial investigators reported routine patient claims generated in clinical trials are routinely submitted and paid by plans.\textsuperscript{45} This finding was sustained across a variety of research areas. In fact, oncologists indicated claims would be routinely submitted for nearly all the routine services used in the course of the clinical trial.\textsuperscript{46} Similarly, cardiologists reported they commonly bill insurers for routine patient costs in clinical trials, although not necessarily for protocol-specific procedure costs.\textsuperscript{47} It appears a lack of clarity about what constitutes standard therapy versus research makes it difficult for both provider and payer to discern what is covered and reimbursable.\textsuperscript{48}

4. Patient "Out-of-Pocket" Payment

In some instances, the patient/subject will pay out-of-pocket for care and services received in the course of clinical research. This generally occurs in protocols in which a new experimental procedure is being offered. New procedures are typically not funded by federal agencies and there is frequently no new drug or device involved that might be under sponsorship by private


\textsuperscript{41} See id. at 42-43.

\textsuperscript{42} See \textit{id.}

\textsuperscript{43} See \textit{id.}

\textsuperscript{44} See \textit{id.} at 38-40.

\textsuperscript{45} See \textit{id.} at 39-43.

\textsuperscript{46} \textit{Id.} at 39-40.

\textsuperscript{47} See \textit{id.} at 40-41.

\textsuperscript{48} See \textit{id.} at 42.
industry. Alternatively, the new drug or device may be provided in concert with an experimental procedure that is not covered by third party payers or part of the federal grant or industry sponsorship.

Perhaps the most timely example of this would be the use of autologous bone marrow or stem cell transplant for breast cancer. This procedure has been the subject of countless suits brought by patients seeking health plan coverage. Although highly touted as “cutting edge” therapy by the research and oncology community, it remained of unproven value by scientific standards for many years. Health plans, including Medicare, balked at covering the procedure, and patients desiring the procedure frequently had to cover the cost themselves; a cost typically well in excess of $100,000. Ironically, this cutting edge, much sought after therapy, has recently been discredited and shown to be no better, and perhaps worse, than conventional breast cancer treatments.

B. Downstream Gains: Future Products, Patents and Profits

In addition to the multiple contemporaneous streams of revenue available to the individual researchers and the academic medical center, both stand to earn additional dollars through equity ownerships, licensing fees, and royalties derived from the sale of drugs, devices, and biologics. Often, it is these downstream bonuses that result in allegations of financial conflicts of interest.

Although the “golden era” of federal funding energized post-war biomedical research, there was growing concern that not enough benefit was realized from the relatively massive expenditures. Government officials and scientists alike argued that potentially useful information was sequestered in laboratories and not fully exploited to benefit the public with new biomedical products. Much information and scientific discovery remained at the “bench science” level. Once developed by government money, the technology was trapped in a “maze” of federal bureaucracy that presented barriers to further development and marketing by either the university or the private sector.

49. See generally MEDICARE REIMBURSEMENT IN CLINICAL TRIALS, supra note 8.
50. See generally id.
53. See Witt & Gostin, supra note 52, at 547-48.
54. See Ducker, supra note 11, at 460. The post-war growth in federal funding was accompanied by an ever increasing number of federal agencies which regulated the research. Id. In some cases, as many as 26 separate agencies could assert title to research inventions resulting in a “Byzantine” regulatory structure. Id.
Congress sought to break down these perceived barriers to progress by enacting legislation that would leverage federal investments in research while simultaneously providing incentives to researchers and their universities. It accomplished this by passing a series of laws designed to facilitate the transition from research to commercial products. These laws provide the opportunity for both the research university/institution as well as the researcher to share in the ownership and profits of the ultimate commercial product.

During the first several decades of federal funding, the federal government adhered to the position that research funded by federal dollars was, in effect, public property with the title firmly held by the government. The opportunity to license research inventions was available to private industry, but this opportunity was burdened with such high transaction costs that private industry was unenthused and/or foreclosed from pursuing further development. In addition, the fact of public access further diminished incentives for commercial exploitation of the research—after all, the exploiter was unable to restrict others from using the same unrestricted substrate. Indeed, fewer than five percent of the 28,000 patents held by the government had been licensed in 1979. Much of the scientific research and development done under the aegis of federal funding languished unused and undeveloped with respect to the commercial market. Concern was growing that resources devoted to biomedical research were delivering neither public benefit, nor a revenue stream that could be plowed back into the research enterprise.

In 1980, Congress passed the Stevenson-Wydler Technology Act which sought to improve utilization of technologies created as a result of federal funding. This Act essentially signaled the switch to a “cooperative model” by requiring federal laboratories to develop technology-transferring capacity. As a result of this Act, all federal laboratories established Offices of Research and Technology Transfer.

The Stevenson-Wydler Act was paired with the Bayh-Dole Act, also passed in 1980, which opened up patenting and licensing opportunities for research universities and researchers. The Bayh-Dole Act allowed universities and other non-profit organizations to retain title to inventions and products discovered as

55. See Dueker, supra note 11, at 461.
56. See id. See also Arno & Davis, supra note 15, at 640.
57. See Dueker, supra note 11, at 460. See also Arno & Davis, supra note 15, at 640.
58. See Arno & Davis, supra note 15, at 640.
59. See id. at 657.
60. See id. at 640.
a result of federal funding and grants. Private and non-government laboratories quickly established technology transfer offices and expertise in order to avail themselves of these new opportunities.

The Bayh-Dole Act also allowed federal agencies to grant licenses to private organizations to allow development of products from the research performed in federal laboratories, such as NIH. This licensing capacity was enhanced by allowing the agency to grant exclusive licenses allowing the licensee significant marketing advantages. However, the federal government retained "march-in-rights" so it could, if need be, access an exclusively licensed technology, either on the basis of public health and safety concerns, or if the licensee failed to use and disseminate the invention.

Augmenting the Bayh-Dole and Stevenson-Wydler Acts is the Federal Technology Transfer Act of 1986. This Act allows federal agencies to enter into joint venture Cooperative Research and Development Agreements (CRADA) with private research facilities. CRADAs provide an opportunity for the government to partner with private industry by contributing personnel, facilities, and equipment to a research endeavor while the private entity provides funding and other resources. The end result of these joint ventures is that the private entity will have first access to licensing opportunities. Once again, the federal government retains the right to use the product and subvert an exclusive license under a "march-in" provision.

1. Institutional Benefits Resulting From Technology Transfer

The technology transfer statutes have proven to be major boons to research universities as well as to private laboratories. Entrepreneurial private laboratories began to flourish, being able to offset high start-up costs by engaging

66. See Dueker, supra note 11, at 476.
67. See id. at 462-63.
68. See Arno & Davis, supra note 15, at 647; Brody, supra note 52.
69. See Dueker, supra note 11, at 463-64; see also Mary Eberle, March-in Rights Under the Bayh-Dole Act: Public Access to Federally Funded Research, 3 MARQ. INTEL. PROP. L. REV. 155, 159-60 (1999). There has yet to be a case in which the government has exercised the march-in provision. See id. at 160.
71. Golden, supra note 62, at 121.
72. See id.
73. See Eberle, supra note 69, at 155.
74. See id.; See also Arno & Davis, supra note 15, at 660-61.
75. See Peter D. Blumberg, Comment, From "Publish or Perish" to "Profit or Perish": Revenues From University Technology Transfer and the §501(c)(3) Tax Exemption, 145 U. PA. L. REV. 89, 94-95 (1996).
in joint ventures with university laboratories. This phenomenon has been particularly marked in the biotechnology industry which is dominated by small firms that often engage in a complex web of collaborations with research universities.

Beset with decreasing allocations from state legislatures and increasing operational costs, research universities have found income from technology transfer a veritable lifesaver. Moreover, this revenue stream is essentially tax free as most universities are organized under section 501(c)(3) of the tax code which exempts corporations dedicated primarily to scientific and educational activities. This tax exemption is not iron-clad as unrelated business income (UBIT) derived from trade or business not integral to the university's scientific or educational mission is vulnerable. However, income from biomedical and scientific research typically is considered firmly rooted in university's scientific research mission. The dollar gains realized by universities from the shift to a "cooperative model" have been substantial. For example, a 1980 agreement between a German pharmaceutical firm and Harvard University's Massachusetts General Hospital provided the hospital with $70 million in exchange for an exclusive license for technologies developed by one renowned researcher. This was an early example of the money that could be made from technology transfer. In 1980, royalty payments to universities totaled a modest one million dollars; by 1994, nonprofit universities netted over $265 million in royalty payments. Research universities are increasingly party to many entrepreneurial agreements which provide them with steady streams of opportunity and dollars.

One typical mechanism is a "faculty start-up company" involving a research scientist, the university and a pharmaceutical industry sponsor. In such arrangements, the scientist is urged to recognize promising discoveries early and partner with the university to protect the intellectual property and its potential financial rewards. Both the scientist and the university will have equity in the

76. See Golden, supra note 62, at 116.
77. See id. at 117-19.
78. See Blumberg, supra note 75, at 94-95.
79. See id. at 102-03.
80. See generally IIT Research Inst. v. United States, 9 Cl. Ct. 13 (1985) (setting forth a three part test for defining UBIT in the context of a tax exempt scientific institution). IIT's scientific research was deemed to have been carried on in the public interest, to have been disseminated to the public through publication of results and done under the aegis of government. Id.
81. See Blumberg, supra note 75, at 94-95. Indeed some scholars question whether universities are treated too leniently with respect to profits from scientific inventions. See id.
82. See Peter J. Harrington, Faculty Conflicts of Interest in an Age of Academic Entrepreneurialism: An Analysis of the Problem, the Law and Selected University Policies, 27 J.C. & U.L. 775, 778 (2001).
83. See Blumberg, supra note 75, at 94.
84. See Harrington, supra note 82, at 780.
85. See id. at 779-80.
start-up enterprise. This new partnership will seek to license the new technology to an industry player who will then develop the technology into a marketable product. The potential profits from such ventures have resulted in universities seeking to focus their research efforts on applied research rather than basic "bench" research.

Universities have also sought to gain from research discoveries and technologies by patenting and marketing the inventions themselves. There is a marked concentration of patents in the life sciences, especially in biomedical areas. This concentration is not mirrored by U.S. patents in general. In the aftermath of the Bayh-Dole Act, the number of academic institutions receiving patents increased rapidly in the 1980s from about 75 early in the decade to double that by 1989 and nearly 175 by 1997. The expansion in the number of institutions receiving patents was paired with even more growth in the number of patent awards to universities; increasing from 589 in 1985 to 3151 in 1998. Academic patents now account for five percent of all new U.S.-origin patent awards, up from less than half a percent in 1980.

Universities have effected this increase in patent accumulation by investing in and expanding their technology transfer programs and negotiating an ever-increasing number of licensing and royalty agreements. In keeping with the life

86. See Harrington, supra note 82, at 780.
87. See id.
89. The number of academic patents has risen tenfold since the early 1970s. See 1 NAT'L SCI. BD., SCIENCE AND ENGINEERING INDICATORS 2000 6-56 (2000) [hereinafter NAT'L SCI. BD. REPORT], available at http://www.nsf.gov/sbe/srs/scind00/start.htm. The 3,151 patents awarded in 1998 represented about 5% of U.S. owned patents, up from 0.5% in the earlier period. Id.
90. The National Science Board has documented two trends in academic patenting. Id. at 6-57. First, there is a heavy concentration in areas connected with the life sciences. Id. "Patents in a mere three technology areas or "utility classes"—all with presumed biomedical relevance—accounted for 41 percent of the academic total [for 1998], up from a mere 13% through 1980." Id. "Second, the growth in the number of academic patents was accompanied by a decrease in the number of utility classes in which they fall." Id. "Academic patents are concentrated in far fewer application areas than are all U.S. patents." Id.
91. See NAT'L SCI. BD. REPORT, supra note 89, at 6-56.
92. See id. Indeed, "the number of academic patents has risen tenfold, from about 250 annually in the early 1970s to more than 3,100 in 1998." Id. The Association of University Technology Managers, which also tracks academic patents, places the 1998 number at greater than 4,800. See Cho, supra note 1, at 2203.
93. NAT'L SCI. BD. REPORT, supra note 89, at 6-56. The vast majority (89%) of these academic patents are held by large research universities. Id.
94. A 1992 survey by the U.S. General Accounting Office based on 35 universities found that they had substantially expanded their technology transfer programs during the 1980s. See UNIVERSITY RESEARCH: CONTROLLING INAPPROPRIATE ACCESS TO FEDERALLY FUNDED
sciences/biomedical trend, typical licensees are pharmaceutical, biotechnology, and medical businesses. University income from patents and licensing reached $483 million in 1997—a six-fold increase from the 1989-1990 income of $82 million. The National Science Board has noted that all indicators show an accelerating use of patenting and technology transfer by universities.

Moreover, several leading academic medical centers have embarked upon ventures designed to transform them into research networks able to compete with the commercial drug trial sector. The purpose of these ventures is to regain market share lost to for-profit entrepreneurs and contract research organizations. These networks bring together academic researchers and practitioners to facilitate clinical trials. This is but one more example of the increasingly entrepreneurial activity by research universities.

2. Individual Researchers’ Stake in Technology Transfer

In addition to the institutional benefits, individual researchers also profit from the transfer of technology. As noted above, faculty researchers are active participants in the technology transfer process from its inception. Indeed, it is the individual research scientist who often triggers the cascade of entrepreneurial activity with respect to a new discovery or technology.

The concept of the faculty member deriving additional outside income is well entrenched. Studies predating the current wave of technology transfer activity have found that nine out of ten university faculty members earn supplemental income in addition to their faculty salaries. This outside income is a significant addition to, and may even surpass, the “primary” income as a faculty member.

In the aftermath of the Bayh-Dole Act, prototypical start-up ventures such as those described above are set up by the university in collaboration with the individual research scientist. Both parties have an equity interest in the new company from its inception. Assuming the venture comes to fruition and the company proceeds to the further development, regulatory approval, and marketing of a commercially valuable product, the research scientist will have to

95. See NAT’L SCI. BD. REPORT, supra note 89, at 6-57.
96. The number of new patents, license disclosures, applications filed, startup firms formed, and base of revenue-generating licenses and options all grew at rapid rates, especially in the late 1990s. See id. at 6-56, 6-57.
98. See id.
99. See supra notes 84-88 and accompanying text.
100. See Harrington, supra note 82, at 780.
101. See id. at 781; see generally DOLLARS AND SCHOLARS (Robert H. Linnell ed., 1982).
102. Such outside earnings typically are equal to 30% of the scientist’s baseline salary. See Harrington, supra note 82, at 781.
decide whether his primary work focus will be his academic research position or his position in the new company. In order to maintain the former, he will be required to limit his involvement in the new company. He will most likely serve as a part-time scientific advisor or consultant to the company. This will, of course, provide him with an income stream from the new company. The research scientist’s equity interest in the new company is over and above his consulting or part-time advisor salary. This equity interest will allow him to share in the value of the company and its profits. Such an initial equity position may be short-lived as it is often the goal of the initial start-up company to be purchased by a larger pharmaceutical or medical device manufacturer. Both the research scientist and university may then receive cash or stock in the successor firm.

With respect to research scientists in government laboratories, the Federal Technology Transfer Act offers opportunities to augment personal income over and above baseline salary. Under the Act, government agencies are required to share the royalties earned through a CRADA with the research scientist who discovered the technology. The research scientist is supposed to receive no less than 15% of the royalties. In the case of a successful venture, these royalty payments will substantially buttress or even outpace the scientist’s baseline salary. Some scholars argue the relative magnitude of royalty payments could seduce scientists into increased secrecy, foster biased results, and cause a “fixation” on commercial gain.

In addition, agencies operating large research laboratories are required to have a program providing cash awards to innovative scientists contributing to technology transfer. This fosters and furthers the “star” system in research and academia, providing not only additional income to the research scientist, but

103. See Harrington, supra note 82, at 780.
104. Id.
105. Id.
106. For example, see discussion of the researchers equity interest in Genovo and Genetic Systems Inc. and their progeny. See infra Part II.
107. See id.
111. Nearly all full-time faculty earn income from outside sources. See Harrington, supra note 82, at 781. Typically, these outside earnings will be equal to 30% of the scientist’s baseline salary. Id.
112. See Steven A. Rosenberg, Street in Medical Research, 334 NEW ENG. J. MED. 392, 393 (1996); Kurt, supra note 110, at 384.
113. See Kurt, supra note 110, at 383.
also enhancing the reputation and power of the scientist within the institution or agency and with his peers. This cash award facet of technology transfer has the capacity to corrupt as well as motivate the researcher. The researcher may seek to be a productive "star" rather than focusing on the advance of science. This is especially true if the internal reward system of the university is also keyed to financial yield rather than intellectual prowess.\footnote{114}

In sum, universities are increasingly interested in applications-oriented research that has the promise of producing revenue and/or building lucrative liaisons with private industry.\footnote{115} The profit from these ventures offers much needed revenue to replace the dwindling state legislative allotments to higher education.\footnote{116} The effect of the Bayh-Dole and the Federal Technology Transfer Act has indeed been to accelerate the transfer of scientific discoveries into useful products and medical practice.\footnote{117} The risk of this shift in focus is that research will become increasingly privatized and particularized to the detriment of the academy's traditional focus on independent thought and intellectual freedom.\footnote{118} The bottom-line question is whether the academic search for truth will be replaced by the quest for a quick buck.\footnote{119}

\section*{II. CONFLICTS: COLLISIONS OF CARETAKING, COMPENSATION, AND COMMITMENT}

In the context of clinical research, the most troubling and fundamental conflicts of interest arise when the research scientist is also a treating physician conducting the clinical trial. In such cases, this double role creates an ever-present conflict of interest, or at least the perception thereof.\footnote{120}

\begin{footnotes}
\item 114. See Blumberg, \textit{supra} note 75, at 136.
\item 115. See Amo \& Davis, \textit{supra} note 15, at 668.
\item 116. During the late 1980s and 1990s, policy makers deprioritized higher education, favoring instead other pressing needs such as medical care, social welfare, benefits for the elderly, primary education, and crime prevention. See F. King Alexander, \textit{The Changing Face of Accountability: Monitoring and Assessing Institutional Performance in Higher Education}, 71 J. HIGHER EDUC. 411, 417 (2000). This trend was accentuated by increasing calls for tax cuts. See id. As a result, universities face annual and continuing uncertainty with respect to state allotted funding and have an increasingly fragile political support base. See Susan H. Frost et al., \textit{State Policy and the Public Research University: A Case Study of Manifest and Latent Tensions}, 68 J. HIGHER EDUC. 363 (1997).
\item 117. See David Korn, \textit{Conflicts of Interest in Biomedical Research}, 284 JAMA 2234, 2235 (2001).
\item 118. See Shimm \& Spece, \textit{supra} note 88, at 370.
\item 119. See id.
\item 120. See Kurt Eichenwald \& Gina Kolata, \textit{When Physicians Doubt as Entrepreneurs}, N.Y. TIMES, Nov. 30, 1999, at A1; \textit{Recruiting Human Subjects}, \textit{supra} note 21, at 11-12. Indeed one can argue that the physician/researcher serves at least six parties with interests—the patient, the institution, the sponsor, the scientific community, the public, and himself. See Edward J. Huth, \textit{Conflicts of Interest in Industry-Funded Clinical Research}, in \textit{CONFLICTS OF INTEREST IN CLINICAL PRACTICE AND RESEARCH} 389, 390 (Roy G. Spece, Jr. et al. eds., 1996).
\end{footnotes}
researcher/physician is subject to conflicting loyalties—the classic duty of care to the patient and the simultaneous loyalty and fiduciary duty to the research enterprise—in which he may have an equity interest or other potential downstream gain. The fear is the lure of profit will corrupt scientific integrity and prompt researchers to withhold or minimize the risks of the trial.121

The gravity of such conflicts has been recently reinforced by the death of several research subjects, notably the death of Jesse Gelsinger, an eighteen year old subject enrolled in a Phase I study of genetic therapy.122 This young man was afflicted with ornithine transcarbamylase (OTC) deficiency.123 This is an inherited disorder resulting in an inability to properly process nitrogen in food proteins due to failure of the liver to produce a specific enzyme.124 In its most common form it causes death in affected newborn males.125 However, Gelsinger was afflicted with a less severe form in which stringent dietary restrictions could keep the disease effects at bay.126 He sought to participate in a Phase I clinical trial at the University of Pennsylvania in which a viral vector containing a correct copy of the needed gene would be injected directly into the liver.127 The goal was that once introduced into liver cells, the gene would function to code for the missing enzyme.128 Accepted as a human subject, he underwent the procedure and almost immediately developed multiple organ failure and died a few days later.129

This Phase I trial sought only to establish the safety of the therapy, not to test for the efficacy of the treatment in correcting the disorder.130 In such Phase I

123. UNIV. OF PENNSYLVANIA HEALTH SYSTEMS, INST. FOR HUMAN GENE THERAPY, STATEMENT ON THE DEATH OF JESSE GELSINGER [hereinafter STATEMENT ON THE DEATH OF JESSE GELSINGER], at http://www.med.upenn.edu/ihgt/jesse.html.
124. Id.
125. Id.
127. UNIV. OF PENNSYLVANIA HEALTH SYSTEMS, INST. FOR HUMAN GENE THERAPY, PRELIMINARY FINDINGS REPORTED ON THE DEATH OF JESSE GELSINGER [hereinafter PRELIMINARY FINDINGS ON THE DEATH OF JESSE GELSINGER], at http://www.med.upenn.edu/ihgt/findings.html.
129. See PRELIMINARY FINDINGS ON THE DEATH OF JESSE GELSINGER, supra note 127. See also STATEMENT ON THE DEATH OF JESSE GELSINGER, supra note 123.
130. See Julian Savulescu, Harm, Ethics Committees and the Gene Therapy Death, 27 J. MED. ETHICS
trials, there typically is no benefit to the subject, and it is fairly clear that Mr. Gelsinger was apprised of this fact. However, his survivors allege he did not fully understand that no improvement of his condition could be expected. They further allege that he was not apprised of the risk of death, the fact that animals who had received this therapy had died, and that the few other human subjects had also had adverse reactions. Moreover, neither Mr. Gelsinger nor his family knew the physician researchers, medical center, and university had financial interests in the trial, and more particularly in the small biotechnology company providing the viral vector. In fact, one of the principal investigators held a 30% equity position in Genovo, the biotechnology firm supplying the viral vector—an equity interest that would ultimately net the researcher over $13 million dollars when it was sold to a larger firm.

This case piqued the interest of bioethicists, scientists, and the government. In short order, the FDA investigated the case and found numerous violations of the study protocol and flaws in the informed consent document. Shortly thereafter, the University of Pennsylvania’s human gene therapy program was suspended. A malpractice suit brought against the researchers and all the institutions involved in the trial was settled shortly after it was filed. Further fueling the conflict of interest debate were revelations regarding cancer research clinical trials conducted by the Fred Hutchinson Cancer Center, one of the preeminent cancer centers in the country. Two separate trials conducted in the 1980s and 1990s have recently come under scrutiny.

One of these trials, labeled “Protocol 126,” involved bone marrow transplants used to treat patients with leukemia. Rather than providing these patients with an allogeneic transplant from a matched donor that, while risky, was the standard...
therapy, the patient/subject group in Protocol 126 was given matched donor marrow that had been treated with a monoclonal antibody that would arguably decrease rejection and enhance engraftment of the donor marrow.\textsuperscript{141} The theory was that pretreated marrow would cut down on the incidence of graft-versus-host disease (GVHD), a dreaded complication of bone marrow transplants.\textsuperscript{142}

The protocol was initially submitted to the Human Subjects Committee in December of 1980, just one month before the researchers received stock and consulting positions with the start-up company, Genetic Systems, which produced and provided the monoclonal antibody.\textsuperscript{143} Early investment prospectuses touted the connection of the fledgling company with eminent researchers and ties with the Fred Hutchinson Cancer Hospital.\textsuperscript{144} By 1983, the stock had increased in value dramatically, and one of the researchers had accepted a vice presidency at Genetic Systems.\textsuperscript{145} The clinical trial was not enjoying similarly positive results. In fact, many, if not most of the subjects, did not have successful engraftment of the donor marrow.\textsuperscript{146} This risk was not disclosed on the informed consent documents used in enrolling additional subjects.\textsuperscript{147} As the years wore on, other studies found better methods for treating GVHD.\textsuperscript{148} This too was not included in the informed consent documents.\textsuperscript{149} It was not until shortly before the experiment was terminated in 1993 that the consent forms were altered to reflect the known risks—and even then, the risks were arguably minimized.\textsuperscript{150}

\begin{footnotes}
\item[141.] See Wilson & Heath, supra note 3.
\item[143.] See Wilson & Heath, supra note 3. In January of 1981, Genetic System gave key investigators stock and consulting fees. See The Blood Cancer Experiment: What Happened, at http://seattletimes.nwsource.com/uninformed_consent/bloodcancer/timeline_day1.html (last visited July 1, 2001). That same month, Protocol 126 was submitted to the Human Subjects Committee and rejected on the grounds that it poses too great a leap from animal to human research especially with respect to questions of graft rejection and cancer relapse. Id. In March, Genetic Systems Inc. signed a 20-year deal with the Fred Hutchinson Center for commercial rights to some Protocol 126 substances in return for which the Center received cash and royalties and an affiliated center received stock. Id. In April, a revised Protocol 126 was approved by the Human Subjects Committee with the proviso that the patient consent form outline the risks and alternatives. Id.
\item[145.] See Wilson & Heath, supra note 3.
\item[146.] See id.
\item[147.] See id.
\item[148.] See id.
\item[149.] See id.
\end{footnotes}
Attempts of members on the Human Subjects Committee to halt or limit the research were rebuffed by the researchers who were very powerful “stars” within the institution.\textsuperscript{151} The researchers and the cancer center note that Protocol 126 was instituted in the early 1980s at a time when standards for conflicts of interest were less developed.\textsuperscript{152} Moreover, the federal oversight agency, the Office for the Protection from Research Risks (the predecessor to the Office of Human Research Protections), did investigate this case and ultimately found no wrongdoing on the part of the researchers or the institution.\textsuperscript{153}

During the many years of the Protocol 126 trial, the fledgling Genetic Systems company was purchased, sold, and reconstituted several times.\textsuperscript{154} The value of the investigators’ stock is about $15 million.\textsuperscript{155} The Fred Hutchinson Cancer Center reportedly has company stock worth about $2.5 million.\textsuperscript{156}

The other trial, labeled “Protocol 681,” involved treatment of late stage breast cancer.\textsuperscript{157} A new drug, Pentoxifylline, allegedly protected vital organs during high-dose chemotherapy.\textsuperscript{158} However, this new drug did not work as planned.

\begin{footnotesize}
\begin{enumerate}
\item[151.] See letter from Dr. Henry Kaplan, IRB Chairman, Fred Hutchinson Cancer Research Center, to Dr. E. Donnall Thomas, Associate Director for Clinical Research, Fred Hutchinson Cancer Research Center (Sept. 28, 1983) (Dr. Henry Kaplan’s First Letter to Dr. Thomas Questioning Safety of Antibodies and Conflicts of Interest); letter from Dr. E. Donnall Thomas, Associate Director for Clinical Research, Fred Hutchinson Cancer Research Center (Oct. 14, 1983) (Dr. Thomas’ Reply Denying Conflicts and Warning the IRB not to Impede Research); memorandum from Dr. Henry Kaplan, IRB Chairman, Fred Hutchinson Cancer Research Center, to Dr. Robert Day, Director, Fred Hutchinson Cancer Research Center (Nov. 30, 1983) (Dr. Kaplan’s Letter to Dr. Robert Day Asking for Independent Scientific Review); memorandum from Dr. Robert Day, Director, Fred Hutchinson Cancer Research Center, to Dr. Fred Applebaum et al., Associate Professor of Medicine, Division of Oncology, Fred Hutchinson Cancer Research Center (Feb. 23, 1984) (Dr. Day’s Reply Refusing an Independent Review but Removing Healthiest Patients); letter from Dr. Henry Kaplan, IRB Chairman, Fred Hutchinson Cancer Research Center, to Dr. Robert Day, Director, Fred Hutchinson Cancer Research Center (Dec. 17, 1984) (Dr. Kaplan’s Third Letter “Once Again” Objecting to Risks and Financial Conflicts of Interest, Dec. 17, 1984); letter from Dr Fred Applebaum, Associate Professor of Medicine, Division of Oncology, Fred Hutchinson Cancer Research Center (Dec. 20, 1984) (Dr. Fred Applebaum Tells Dr. Kaplan to Stop Complaining About Financial Conflicts of Interest), available at http://seattletimes.nwsource.com/uninformed_consent/documents.html (last visited July 1, 2001).
\item[152.] See Hutch Responds, Research Center Responds to Times Stories, at http://seattletimes.nwsource.com/uninformed_consent/hutchresponds.html (last visited July 1, 2001).
\item[153.] See id.; see also E-mail Showing Federal Officials Deciding “Nothing Wrong” with Undisclosed Financial Interests and Federal Investigator Kamal Mittal’s Analysis, Questions, and Recommendation of Actions, at http://seattletimes.nwsource.com/uninformed_consent/documents.html (last visited July 1, 2001).
\item[154.] See Wilson & Heath, supra note 3.
\item[155.] See id.
\item[156.] See id.
\item[157.] Duff Wilson & David Heath, With a Year or Two to Live, Woman Joined Test in Which she was Mislead, and Died, SEATTLE TIMES, Mar. 13, 2001, at A1.
\item[158.] See Wilson & Heath, supra note 157.
\end{enumerate}
\end{footnotesize}
and soon was abandoned by European researchers.\textsuperscript{159} Two proponents of Pentoxifylline, working at Fred Hutchinson, spun off a small company to produce other versions of the drug.\textsuperscript{160} Fred Hutchinson received stock and licensing fees in this enterprise.\textsuperscript{161} Others, including one of the powerful researchers in Protocol 126, also received stock.\textsuperscript{162} The Protocol 681 experiment continued through 1998 despite growing evidence that the drug did not work and, indeed, resulted in adverse outcomes, including death.\textsuperscript{163} The spin-off company, Cell Therapeutics, misrepresenting the results of Protocol 681, moved on to develop other drugs.\textsuperscript{164} Today the company is reportedly worth $485 million.\textsuperscript{165}

These conflict of interest scandals in gene therapy and cutting edge cancer therapies have fueled increased scrutiny by the media and policy makers. Congressional hearings are currently calling for greater federal involvement in biomedical research as well as greater oversight of the behavior and privileges of researchers.\textsuperscript{166} In addition, many institutions and professional organizations are reevaluating their procedures and policies on conflict of interest.

\textbf{A. Financial Conflicts of Interest}

The promise of downstream profits from equity holdings, royalties, and profit sharing offers significant incentives to researchers. As a result, researchers will seek to develop their intellectual property, usually in collaboration with the university or a CRADA.\textsuperscript{167} This is, of course, an intended outcome of the Bayh-Dole Act and the Federal Technology Transfer Act.\textsuperscript{168}

Growing numbers of researchers report personal financial ties to industry sponsors. These ties are diverse and nuanced, ranging from the short-term

\begin{itemize}
\item \textsuperscript{159} See Wilson & Heath, \textit{supra} note 157.
\item \textsuperscript{160} See id.
\item \textsuperscript{161} See id.
\item \textsuperscript{162} See id.
\item \textsuperscript{163} See Reply of Doctor's Notes Showing that Four Women Died From the Experimental Treatment; Two of Four Patients in Previous Breast Cancer Study Were Killed by the Chemotherapy; The Protocol Explains that Two of Four Patients in One Study and Three of Six in Another Were Killed by the High-dose Chemotherapy that Kathryn Hamilton Would Take, at \url{http://seattletimes.nwsource.com/uninformed_consent/documents.html} (last visited July 1, 2001).
\item \textsuperscript{164} See In Trying to Raise Capital from Investors, CTI Touted Amazing Results for a Drug Combination that it had Already Concluded Didn't Work, at \url{http://seattletimes.nwsource.com/uninformed_consent/documents.html} (last visited July 1, 2001).
\item \textsuperscript{166} See Kom, \textit{supra} note 117, at 2234.
\item \textsuperscript{167} See Shimm & Spece, \textit{supra} note 88, at 370. \textit{See also} Golden, \textit{supra} note 62, at 142-54 (discussing the motivation of the "inventor" class).
\item \textsuperscript{168} See Kom, \textit{supra} note 117, at 2235.
\end{itemize}
commitments to attend a single meeting or provide one-time consulting, to more substantive commitments as long-term members of advisory boards holding stock in the company. The International Committee of Medical Journal Editors (ICMJE) has identified the most common and troubling of financial conflicts, citing employment, consultancies, stock ownership, honoraria, and expert witness work, either on the part of the research scientist or an immediate family member. One study of 800 biotechnology faculty members revealed that 47% serve as consultants to industry, almost 25% received industry sponsored grants, and 8% had an equity interest in their industry sponsor. Another study analyzing 789 articles in medical journals found that 34% of the authors had a financial interest in the subject matter they were studying and writing about.

Faculty start-up ventures and other equity arrangements raise conflict of interest issues for both the university and the individual. The individual researcher will likely continue to do research in the same area of technology and study. This university-based research will likely be funded by federal grants. The question will then arise as to whether the university-based research is furthering science, or rather, furthering the aims and development of the new company's products and interests. The line between the two is likely to be blurry and both the university and the research scientist lack credibility as arbiters for clarification.

These financial conflicts of interest are an unintended, albeit predictable, outcome of technology transfer policy. However, financial conflicts are not the only problem. The increasingly entrepreneurial approach to science has produced a change in the culture of biomedical research. The zeal to protect intellectual property discourages the free and open exchange of information that is so fundamental to intellectual discourse and scientific advancement. Such non-financial conflicts and "conflicts of commitment" are at least as, if not more, deleterious than the financial conflicts.

169. See Boyd & Bero, supra note 21, at 2212-13.
171. See Arno & Davis, supra note 15, at 668-69. In this study 30% of those who had industry funding admitted that the funding had influenced their research and choice of topics. See id.
173. See Harrington, supra note 82, at 780.
175. See Harrington, supra note 82, at 787. Non-financial conflicts encompass the questions of conflicts between dedication to scientific integrity and dedication to the non-monetary measures of prestige, such as publications, academic promotion, professional honors, reputation, and access to power. Id. Conflicts of commitment arise as the researchers distribution of effort and time is deflected from the academic research and teaching mission to the industry enterprise. See id.
B. "Other" Currencies: Non-Financial Conflicts of Interest

In addition to the tangible benefits that the university research center and researcher receives from equity holdings, licensing fees, and royalties, there are a host of intangible benefits associated with successful technology transfer. Academic biomedical research has numerous pressures and conflicts. Many, and perhaps the most compelling, conflicts are not financial in nature. Rather, these non-financial conflicts arise out of ambition for academic advancement, zeal to discover better treatments, need for a sustained, stable stream of research funding, pursuit of publications, and desire for accolades from peers.\textsuperscript{176}

There is significant emotional and professional satisfaction from having research result in practical application and public acclaim.\textsuperscript{177} From the perspective of medical altruism, many researchers treating patients are committed to providing state of the art care.\textsuperscript{178} The problem is that the perception of what constitutes the "state of the art" may be colored by the researchers' aims. Researchers tend to be passionate and committed to their research hypothesis and may believe it does offer the best hope for alleviation of pain and suffering, even though the preliminary research results are not confirmatory.\textsuperscript{179} These non-financial conflicts and pressures may create a powerful bias towards positive results, even absent any financial incentives.\textsuperscript{180}

Researchers and their universities benefit from successful research from a prestige standpoint. Academic prestige is measured in terms of publications. There is a strong incentive on the part of researchers to publish in order to further their own academic careers and futures.\textsuperscript{181} The research university shares in, and fosters, this professional and cultural norm. Provocative, high profile projects and positive results bring rewards of promotion and further research funding.\textsuperscript{182} Publications lead to a national reputation, academic tenure and promotion, and an increased national profile for the researcher and the university.\textsuperscript{183}

\begin{itemize}
  \item \textsuperscript{176} See Korn, supra note 117, at 2234.
  \item \textsuperscript{177} See Blumberg, supra note 75, at 101.
  \item \textsuperscript{178} For example, one well-known researcher in genetics who founded seven biotechnology firms while a professor at Harvard, has stated that his primary motivation was not money, but rather "the joy of conceiving ideas and reducing them to practical reality to make a difference in people's lives." See Stolberg, supra note 121.
  \item \textsuperscript{179} See Korn, supra note 117, at 2234
  \item \textsuperscript{180} See id.
  \item \textsuperscript{182} See Kenneth J. Rothman, \textit{Conflict of Interest: The New McCarthyism in Science}, 269 JAMA 2782, 2783 (1993).
  \item \textsuperscript{183} See Blumberg, supra note 75, at 120-21.
\end{itemize}
There is reason for concern because even in more mundane areas of research than the high profile gene therapy and cancer research cases detailed above, skewing of study design, the study itself, and research results due to industry financial support still exist. From a study design perspective, the sponsor may formulate the research plan to produce desired results. Results may be biased towards the desired conclusion, either as a result of study design or biased data interpretations. One study surveying publications reporting clinical trial results found there was an inexplicable correlation between positive results and the presence of pharmaceutical manufacturer funding of the trial. In another study, involving a class of cardiac drugs, clinical researchers with financial support from the drug manufacturer were more likely to report favorable results. More recently, a study reviewing clinical trials involving new “break-through” cancer drugs found that studies funded by pharmaceutical companies were nearly eight times less likely to come to an unfavorable qualitative conclusion as similar studies funded by non-profit entities. These studies scream bias and throw considerable doubt on the integrity and credibility of the research.

In yet another variation on this theme, researchers may withhold timely publication of results to protect their pending patent application or to put off reporting unfavorable results. In one recent study, 19.8% of respondents reported they had delayed publication to allow for patent application, to protect a scientific lead, to slow dissemination of negative results, to allow time for the renegotiation of an intellectual property agreement, or to resolve an intellectual

186. See Richard A. Davidson, Source of Funding and Outcomes of Clinical Trials, 1 J. GEN. INTERNAL MED. 155 (1986).
188. See Mark Friedberg et al., Evaluation of Conflict of Interest in Economic Analyses of New Drugs Used in Oncology, 282 JAMA 1453, 1455 (1999).
189. See International Committee of Medical Journal Editors, supra note 170.
190. See Ducker, supra note 11, at 473.
property dispute. Given the crucial importance of publications to the academic career, it is particularly telling and concerning that, despite the importance of publications, studies have demonstrated that researchers will delay publication in order to firm up patent applications and industry liaisons. Curiously, such delaying tactics are more common among faculty members of higher rank who are more productive in terms of scholarship.

Researchers also seek peer recognition and respect. This need extends far beyond the need for publications to ensure tenure and academic promotion. The rewards of publicity may be more pivotal than personal financial gain. For example, in the Gelsinger case, the conflicted researcher was reportedly offended by the allegation that dollars swayed his judgment. He indicated that what was material to him was not financial gain, but rather academic recognition and honors. The sought after "prize may be Nobel as well as financial." This "glory" factor can be a powerful motivator. In yet another recent research scandal, a researcher who had falsified data to attest to the merit of a controversial, but very lucrative therapy for breast cancer, stated he had engaged in the fraud "out of a foolish desire to make the presentation more acceptable to an audience." In short, in order to obtain the affirmation and respect of expert peers, he was willing to present fraudulent data that would tell them what they wanted to hear and simultaneously appeal to victims of breast cancer seeking a magic bullet.

In addition to the obvious concerns these skewed or delayed studies raise with respect to scientific integrity, biased research results open the door for harm to patients extending far beyond those subjects involved in the clinical trial. These results may lead to erroneous conclusions about the safety or the efficacy of new drugs and devices. The erroneous data and conclusions will be used to win FDA approval for the product. They will also be used by researchers working on the next generation of research, creating a domino effect of error. Once

191. See David Blumenthal et al., Withholding Research Results in Academic Life Sciences, 277 JAMA 1224, 1226 (1997).
192. See id. at 1227-28.
193. See Rothman, supra note 182, at 2783.
195. Id.
197. See King, supra note 194.
disseminated in the market, end user physicians and patients will pay the price for bad science in dollars, poor outcomes, and adverse events.

Non-financial conflicts of interest may be more powerful influences on faculty behavior than the financial conflicts. Oversight of such non-financial conflicts of interest has traditionally been left to the academic professions and the community. If indeed, these non-financial conflicts are at least as compelling to the researcher, this approach may be questionable, if not foolhardy. De facto appointment of the peer community as watchdog over non-financial conflicts cannot be warranted if the academic culture in the institution cannot be depended upon for diligence in responsibly addressing such conflicts.

III. CURRENT METHODS OF ADDRESSING FINANCIAL CONFLICTS OF INTEREST

Although conflicts of interest have been a lurking danger for many years, they have only been addressed by law and institutional policy relatively recently. Now, there are a variety of federal regulations and guidelines, institutional policies, and professional association recommendations regarding conflicts of interest. Most recently, the Office for Human Research Protections (OHRP) has issued draft interim guidance on “Financial Relationships in Clinical Research.” In issuing the draft guidance, the OHRP noted there is no recognized “best practice” with respect to handling conflict of interest questions. These draft guidelines were designed to stimulate consensus on a greater level of protection for human subjects. Unfortunately, there is little consensus among the many entities that have weighed in on the issue to date.

A. Laws and Regulations Addressing Conflict of Interest

At present there are no federal laws or regulations that are prescriptive regarding the types of financial interests that may be held by clinical

200. See Korn, supra note 117, at 2234.
201. See id. at 2234-35.
202. See id. at 2235.
203. See id. at 2234.
206. See OHRP DRAFT GUIDANCE, supra note 204.
207. See id.
researchers. 208. Both the FDA and the Public Health Service (PHS) have issued regulations addressing conflicts of interest, but they are vague and inconsistent. 209

The FDA has had regulations in place since 1998 requiring investigators to have no financial interests 210 in the product and technologies they are testing, with the exception of those disclosed and deemed allowable under the federal regulations. 211 Any such allowable compensation cannot be tied to the outcome or results of the study. 212 Payment by the sponsor to the investigator or the institution cannot exceed $25,000 in excess of the documented costs of conducting the research or clinical trial. 213 Under the FDA regulations, this disclosure must be made during the time the study is being conducted and within one year after it has been completed. 214 This disclosure is the responsibility of the investigator and must be made directly to the FDA. 215

Under the PHS regulations, institutions receiving federal grant funds must maintain a written, enforced policy on conflict of interest. 216 This policy must provide for institutional review of significant financial interests of investigators before the research is commenced. 217

"Significant financial interests" means anything of monetary value, including but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights). 218 The term does not include:

1. Salary, royalties, or other remuneration from the applicant institution;
2. Any ownership interests in the institution . . . ;
3. Income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities;

208. See OHRP DRAFT GUIDANCE, supra note 204.
209. "Differences in the requirements are causing problems for researchers as the line between privately funded trials, regulated by FDA, and federally funded human research, overseen by PHS, continues to blur." Conflict-of-Interest Inconsistencies Cause Problems for Firms, WASH. DRUG LETTER, July 16, 2001, available at 2001 WL 820588.

212. 21 C.F.R. § 54.4(a)(3)(i) (2001). 213. See FDA GUIDANCE, supra note 211. There is also a requirement that financial interests exceeding $50,000 in any publicly held company must be disclosed. See id.
214. 21 C.F.R. § 54.4(b) (2001).
215. See id.
217. See id.
(4) Income from service on advisory committees or review panels for public or nonprofit entities;
(5) An equity interest that when aggregated for the Investigator and the Investigator's spouse and dependent children, meets both of the following tests: Does not exceed $10,000 in value as determined through reference to public prices or other reasonable measures of fair market value, and does not represent more than a five percent ownership interest in any single entity; or
(6) Salary, royalties or other payments that when aggregated for the Investigator and the Investigator's spouse and dependent children over the next twelve months, are not expected to exceed $10,000.219

The PHS regulations are unclear in terms of specific guidance to the institution, containing only an undefined requirement that the institution take "reasonable steps" to manage conflicts.220

Both the FDA and the PHS regulations focus heavily on disclosure. However, differences in government regulations addressing conflicts produce a baseline level of confusion. The PHS regulations require disclosure of the conflict to the research institution.221 In contrast, the FDA regulations require disclosure to the FDA.222 The reporting threshold for financial conflict of interest under the FDA regulations is $25,000, while under the Public Health Service, which applies to all NIH grants, the threshold is $10,000.223 Further complicating this issue is the fact that the royalty payments authorized under the Federal Technology Transfer Act, which are also a form of equity, have only a 15% dollar cap.224

It is unclear in both sets of regulations how wide the scope of the disclosure should be; is it sufficient to disclose the conflict to the university and/or government agency, and is there a duty to disclose the conflict to subjects and patients in the formal consenting process? The federal regulations applying to research consent do not require such disclosure.225 There is an entirely different ethic and flavor to informed consent in the context of research. In research, informed consent focuses on emphasizing the unknowns of the experiment and on the fact the subject cannot necessarily expect benefit. In addition, a rigorous disclosure of risks is required.226 In traditional informed consent transactions, the goal is to disclose all of the known material information to the patient to aid

220. See Arno & Davis, supra note 15, at 673.
222. See 21 C.F.R. pt. 54. See also OHRP DRAFT GUIDANCE, supra note 204.
223. See 42 C.F.R. § 50.603(5); see also 21 C.F.R. pt. 54.
224. See Arno & Davis, supra note 15, at 673. Indeed, this inconsistency produced sufficient unease that the Office of Government Ethics was obliged to issue an advisory opinion that royalty payments under a CRADA do not constitute a prohibited financial interest. See Kurt, supra note 111, at 383.
225. See OHRP DRAFT GUIDANCE, supra note 204.
them in making the most beneficial choice they can.227 The common law standard requiring disclosure of all facts that would be deemed “material” to the patient’s or subject’s decision-making would likely require disclosure of a financial conflict.228

In the aftermath of the Gelsinger case, Donna Shalala, then Secretary of the Department of Health and Human Services, called for increased oversight of conflicts of interest.229 To that end, she appointed a twelve member National Human Research Protections Advisory Committee, designed to serve as the principal advisory body to the department on issues pertaining to human subjects protection and responsible conduct of human research.230 The Secretary also reconstituted the Office for the Protection from Research Risks (OPRR) as the new Office for Human Research Protections (OHRP), empowering it to lead efforts for protecting human subjects in biomedical and behavioral research.231

In January 2001, OHRP issued Draft Interim Guidelines designed to “help IRBs [Institutional Review Boards], Clinical Investigators, and Institutions in carrying out their responsibilities to protect human subjects.”232 These guidelines addressed the respective roles of institutions, clinical investigators, IRBs, and IRB members and staff.233 While not modifying existing law and regulation, the guidance does provide clues as to likely future trends.234 The guidance advocates strongly for communication of conflict of interest information to Human

227. See Canterbury v. Spence, 464 F.2d 772, 790-91 (D.C. Cir. 1972) (requiring the physician to disclose information that a reasonable person would consider material in deciding whether or not to undergo the treatment; the information is to be considered from the patient’s, not the physician’s, perspective).

228. See e.g., Moore v. Regents of the Univ. of California, 793 P.2d 479 (Cal. 1990) (holding that physician required to disclose his financial interests related to research that will be done on cellular material removed from patient during surgery).

229. See Shalala, supra note 7. Secretary Shalala announced several steps she was putting in place to effect this increased oversight. Id. The NIH and FDA were charged with providing increased education and training for researchers, research administrators, and IRBs. Id. She also called for the issuance of more rigorous, more specific guidelines on informed consent, and increased monitoring reports. Id. She announced a plan to pursue legislation to levy civil monetary penalties for violations of informed consent and other research standards. Id. Finally, she called for clarification of regulations relating to conflicts of interest and renamed and expanded the Office for Protection from Research Risks. See id.


232. See OHRP DRAFT GUIDANCE, supra note 204.

233. Id.

234. See generally id.
Subjects Committees so that they can consider how much of the information should be disclosed to subjects in the informed consent document.\textsuperscript{235} OHRP stressed the importance of Human Subjects Committees in management of conflict of interest and noted that it is imperative that IRB members and staff are carefully vetted for any conflicts they may have as well.\textsuperscript{236} The guidance specifically states that research institutions are increasingly corporate partners with private sponsors and "should not lose sight of . . . their own conflicts."\textsuperscript{237} The guidance stops short of advocating a "prohibition" approach, but argues for enhanced disclosure and assiduous management of conflicts.\textsuperscript{238}

In addition, the OHRP draft guidelines stress the need for disclosure beyond the institution to the patient/subject and advocate inclusion of this information in the informed consent process.\textsuperscript{239} The FDA has expressed disagreement with this view, arguing that appropriate management of the conflict would eliminate the need for disclosure to the subject.\textsuperscript{240} Patients' rights activists argue that the patient or subject should be fully apprised of financial conflicts of interest during the consent process and that regulations should be revamped to reflect this requirement.\textsuperscript{241} They advocate mandatory, enforced disclosure of both investigator and institutional conflicts before the patient or subject begins the treatment.\textsuperscript{242}

Clinical investigators counter that providing complete information may be detrimental to the overall goals of informed consent.\textsuperscript{243} Patients may be unable to understand and assimilate the information sufficiently to draw their own conclusions as to the propriety of the conflict.\textsuperscript{244} Moreover, the complex informed consent document might chill participation in trials and lead to a perception that the conflict is more central than it actually is.\textsuperscript{245}

Moreover, there may be occasions when the patient/subject would be disadvantaged by having a conflicted investigator excluded from involvement in

\textsuperscript{235} See OHRP DRAFT GUIDANCE, supra note 204.
\textsuperscript{236} See id.
\textsuperscript{237} Id.
\textsuperscript{238} See generally id.
\textsuperscript{239} See id.
\textsuperscript{242} Id.
\textsuperscript{244} See generally id.
\textsuperscript{245} See id.
It may be that the conflicted scientist is the most qualified and knowledgeable person to conduct the trial. Indeed some argue that such concrete exclusion rules have already produced such anomalies. For example, the IOM does not allow anyone who has ever served on an advisory committee to author an IOM report on vaccine safety. This policy seeks to ensure that the IOM reports are unbiased and impartial. However, it may also mean that most of the experts and renowned specialists are excluded in favor of others who are less knowledgeable, less equipped, and less passionate about the subject matter.

There are also questions and concerns as to the optimal time for collection of information about conflicts of interest. For example, the recently issued draft guidance from the Office of Human Research Protections calls for collection and documentation of conflict information early in the trial, while the FDA requires a less stringent time frame.

Given the confusion and unanswered questions produced by the conflicting regulations and guidance, it is no wonder institutions that generally bear the burden for managing financial conflicts of interest exhibit similar disarray with respect to conflict of interest policies. Moreover, like the federal regulation, most institutions are silent with respect to nonfinancial conflicts of interest. Less quantifiable, this important class of conflicts is in an abyss with respect to recognition, much less management.

B. Institutional Policies on Conflict: Disclosure vs. Prohibition

Under the PHS regulations and the recently issued OHRP Draft Interim Guidance, the onus for "managing" conflicts falls upon the research institution. Once a conflict is disclosed, the institution must manage the conflict, determine what actions should be taken to reduce or eliminate the conflict, and impose any restrictions or modifications deemed necessary to ensure that the conflict does not bias the design, conduct, or reporting of the research project. Accordingly, research institutions have promulgated institutional

246. See WASH. DRUG LETTER, supra note 243.
247. See id.
249. Id.
251. See e.g., 42 C.F.R. §§ 50.601-50.607 (2000); OHRP DRAFT GUIDANCE, supra note 204.
252. See 42 C.F.R. § 50.605.
Examples of conditions or restrictions that might be imposed to manage conflicts of interest include, but are not limited to:
(1) Public disclosure of significant financial interests;
(2) Monitoring of research by independent reviewers;
(3) Modification of the research plan;
policies that attempt to satisfy the limited federal regulations while simultaneously conforming to their institutional cultures. The result is a patchwork of policies with little consensus.

Several studies have recently reviewed institutional conflict of interest policies. The most notable of these reviewed 89 conflict of interest policies from leading research universities.233 There was little commonality among the policies. Fifty-five percent of the 89 conflict of interest policies reviewed required disclosures from all faculty, while 45% required disclosure only on the part of the principal investigator.254 The majority (88%) required disclosure about the financial interests of family members of the pertinent faculty member.255

The dollar thresholds for disclosure were frequently more stringent than the existing PHS federal threshold of $10,000.256 However, the authors noted that this variable dollar threshold could be interpreted differently based on the institutional culture and values as well as the nature of the conflict.257 All of the policies dealt with financial conflicts of interest, but only a subset addressed other types of conflicts.258 Most of the policies described prohibited activities in a general sense rather than honing in on clinical research related taboos.259 The most common prohibition applied to researchers having financial interests in companies sponsoring their research.260 Only 19% of the reviewed policies had provisions specifically addressing clinical research.261 These provisions addressed limits on equity holdings in sponsors, disclosure of financial interests in published work, required disclosure of conflicts to the human subjects committee, and more stringent provisions for clinical versus non-clinical research.262

Another study, in which the ten top medical schools were surveyed in terms of research funding, also found variability among conflict of interest policies.263

(4) Disqualification from participation in all or a portion of the research funded by the PHS;
(5) Divestiture of significant financial interests; or
(6) Severance of relationships that create actual or potential conflicts.

42 C.F.R. § 50.605. In addition to the types of conflicting financial interests described in this paragraph that must be managed, reduced, or eliminated, an institution may require the management of other conflicting financial interests, as the institution deems appropriate. See id.

253. See Cho, supra note 1, at 2205.
254. See id.
255. Id.
256. See Boyd & Bero, supra note 21, at 2214.
257. Id.
258. See Cho, supra note 1, at 2205.
259. See id.
260. See id.
261. See id. at 2206.
262. See id.
263. See Bernard Lo et al., Conflict-of-Interest Policies for Investigators in Clinical Trials, 343 NEW
Although all ten universities required that faculty members disclose financial interests to university officials, they varied in terms of the dollar threshold for disclosure. 264 Only four of the ten universities extended the disclosure rule to the entire research team, rather than just a cohort of the team. 265

There are increasing questions as to whether or not disclosure, even an expanded level of disclosure, is sufficient to adequately protect human subjects. Disclosure is but one of the models for managing conflicts of interest. It is criticized for being susceptible to loopholes and inconsistency. 266 Increasingly, it is being viewed as “too cheap and easy” a method for addressing conflicts. 267

The other model is that of prohibition—a zero tolerance of financial conflict of interest. The prohibition model is criticized as having a chilling effect on research and development of new therapies and treatment. 268 A few institutions, notably Harvard Medical School, have embraced a more prohibition-oriented model with respect to clinical research. 269 These institutions argue that, in the case of clinical research, financial conflicts of interest may undermine clinical judgment. 270 Equally concerning to Harvard and other proponents of more stringent conflict policies is the public perception that research which is biased has led to erosion of patient trust in medicine and the research enterprise. 271

Several leaders in medicine support a prohibition policy. 272 They argue that disclosure merely “passes the buck” to the hapless subject/patient who is ill-equipped to assess its importance in the equation of impending care. 273 At the most extreme, prohibition would be extended to all financial ties with sponsors, including speaking fees, consulting fees, sponsor-paid travel, and require that industry support be placed in general research support funds. 274 Under the prohibition model, investigators with financial interests would be forestalled from

ENG. J. MED. 1616, 1616 (2000).

264. See Lo, supra note 263, at 1617.

265. Id.


270. Harvard’s more stringent policy was adopted after a much publicized scandal involving a physician at Massachusetts Eye and Ear Hospitals. See Bass, supra note 269. See also Stolberg, supra note 121 (describing a similar prohibition-style policy at the University of California at San Diego).

271. See Korn, supra note 117, at 2235.

272. See Angell, supra note 2, at 1518.

273. See WASH. DRUG LETTER, supra note 243.

274. See Angell, supra note 2, at 1517.
having authority over study design, data collection, and results interpretation, and sponsors would be forbidden from editorial involvement or pre-publication review of studies.\textsuperscript{275} Less draconian versions of prohibition would allow clinical investigators to be supported by a private sponsor, so long as the investigator had no stock, stock options, or decision-making position in the sponsoring company.\textsuperscript{276}

In justifying prohibition, adherents note that university-based investigators should be held to a higher standard than researchers working in commercial venues, because of their role in training and mentoring the next generation of scientists.\textsuperscript{277} This movement toward prohibition appears to be gaining favor. Advocates argue that the only way to solve conflict is to remove it completely by refusing to allow researchers to have a financial stake in the therapies they are researching.\textsuperscript{278}

IV. REDRESSING CONFLICTS: PALLIATING AN UNRESOLVABLE PROBLEM

In the wake of renewed attention to conflicts and the publication of the OHRP draft guidance, it is becoming increasingly clear that there is no easy solution to the complex issues of conflicts of interest. Researchers and reformers alike are essentially boxed into a corner by virtue of incentives of the Bayh-Dole and other technology transfer acts. Moreover, after two decades, technology transfer has forever changed the culture of biomedical research. At best, policymakers and regulators will be able to palliate conflict of interest problems, not eradicate them.

The primary purpose of the federal technology transfer laws was to stimulate innovation and facilitate the transfer of academic science into useful, marketable products.\textsuperscript{279} This purpose has been achieved. There has been a marked increase in patenting and licensing activity by research universities and their researchers.\textsuperscript{280} This test has created a “positive feedback loop” that both stimulates and rewards research that has practical application. On the other hand, the secondary goal of supporting research and decreasing the federal burden for the cost of research has not been met. Royalties recouped by the federal government equal only about one percent of federal research funding.\textsuperscript{281} Although private sponsorship has increased sharply, relative to government funding of research, the federal

\textsuperscript{275} See Pink Sheet, supra note 270.
\textsuperscript{276} See Lo, supra note 263, at 1619.
\textsuperscript{277} See id.
\textsuperscript{279} See Arno & Davis, supra note 15, at 643.
\textsuperscript{281} See Arno & Davis, supra note 15, at 639-40.
dollars devoted to research have continued their unabated trajectory of increase.\textsuperscript{282}

Technology transfer is a two-edged sword in that the growing dependency of researchers, and particularly research universities, on revenue from such transfers, sets the stage for virtually unavoidable conflicts of interest.\textsuperscript{283} Even were a policy of complete prohibition of conflicting financial interests politically palatable, it would probably be economically and practically impossible. As a result, the best that can be hoped for is consistent, enforceable policy and regulation. This will be easier to fashion for individual researchers than for research institutions.

The conflict issues for researchers involved in clinical research using human subjects are the most risky and require the most stringent management. Here the researcher will be caught between his two worlds of research scientist and physician. In such cases, a financial or non-financial conflict of interest is particularly charged. Regardless of whether the researcher believes that his judgment is being corrupted by the conflict, knowledge of the conflict would be material to the reasonable patient and should be disclosed.\textsuperscript{284}

However, disclosure of financial conflicts in the context of informed consent is fraught with difficulty. The patient may have difficulty understanding the conflict and ascertaining its importance. The provider/researcher may be unwilling or unable to adequately explain the issues, and indeed may be a poor emissary for such a mission. More importantly though, knowledge of the conflict may undermine the provider/patient relationship and deter enrollment of human subjects and chill the research altogether. So in the case of clinical research, the individual researcher may be in a "Catch-22." If he has a financial interest in the research, he must disclose it to the institution and to the patient/subject. But disclosure may derail the patient's trust in the physician/researcher and the research itself, even if the researcher believes that the conflict is not affecting his clinical judgment.

In such cases, the policy of prohibition is the most sensible approach. If the researcher has, and wishes to maintain, a financial interest in the research, he should withdraw from care of the subjects and data collection. Moreover the researcher's involvement in study design and interpretation should also be


\textsuperscript{283} See generally Kom, supra note 117.

\textsuperscript{284} This concept of materiality is well entrenched in medical malpractice law. In recent years, the breadth of information that must be disclosed has generally expanded. The case of Moore v. Regents of the Univ. of Cal. specifically dealt with financial conflicts of interest in the context of research. See supra note 228. The Supreme Court of California held that when a researcher has an ulterior financial interest, he must disclose that to the patient. See generally id. In Moore, the physician/researcher treating the plaintiff for leukemia planned to use cells culled from the patient's excised spleen in research that allegedly had great commercial promise. \textit{Id}. This financial interest should have been disclosed to the patient. \textit{Id}. 
curtailed, or at least be subject to impartial cross-checking. Such confirmation would not be a departure from good scientific practice in any case. A policy of prohibition in this scenario is not only protective of the human subjects, it also protects the researcher from inadvertently or overtly biasing the research, protects the university from liability, and protects the integrity of the scientific research enterprise. In such a situation, the researcher could maintain his financial interest, so long as he is sufficiently separated from administering the trial and caring for the subjects.

In rare cases, there may be "compelling and necessary" reasons why such a prohibition approach is not in the best interests of the patient and the research enterprise. For example, suppose that the scientific invention in the trial is designed to treat a clinically unique subset of patients with a relatively rare disease. The researcher may be the most qualified, even the only qualified expert in both the disorder and the invention. In such a case, a conflict of interest might be managed by having an oversight committee or non-conflicted investigator integrally involved in the clinical trial with the express purpose of safeguarding against bias in the study design, informed consent process, and data collection, analysis, and reporting. Such situations would be exceedingly rare.

Where the researcher is involved in the trial from an arms length and not directly involved in the clinical care of the patient/subject, the goal should be appropriate disclosure and management of financial conflicts. For this to occur with any consistency, there needs to be some harmonization of the laws and regulations applicable to financial conflicts of interest. Management should include an ongoing evaluation of the conflict as it relates to the progress and stage of the research. At the early basic bench level of the research, a conflict may be less important and meaningful than it is at a later stage of the research and development of the product. As the product becomes more commercially viable and the potential risks to human subjects and patients greater, the management of the conflict will need to become more rigorous and exacting.

However, even with a measured, sliding scale management approach, there are conflicts that are recalcitrant to management. These include the macro-level issue of choice of research topic, and hypothesis. Individual researchers may find themselves encouraged by their superiors, their research institutions, their private industry sponsors, and the American dream to pursue research that has some relationship to foreseeable commercial promise. They may perceive that choosing an area of research not susceptible to technology transfer will not only affect their financial future, but also their options for career advancement. In many cases, the influence of this type of conflict may not even be part of the researcher's conscious thought process, but rather due to the pervasiveness of

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286. Id.
the institutional and professional culture.\textsuperscript{287} As a result, creative thought and innovation will be stifled, with the goal of commercial worth taking precedence over intellectual ingenuity.

Institutional conflicts present a particularly ironic scenario. Although institutions are charged with managing conflicts, they themselves have a vested financial interest in maintaining and increasing their revenues from successful technology transfer. Even without articulated policy, universities and research institutions may push researchers toward research that will yield money-making products.\textsuperscript{288} The institution or research university may be swayed by non-financial conflicts as well. For example, in several research scandals, the conflict issue involved the leading, most celebrated research clinician in the institution.\textsuperscript{289}

Given their inherent culture and power structure, the research institution may be unable to appreciate that their management efforts are differentially applied, managing perceived "stars" with a lighter hand.

The OHRP Draft Interim Guidance seeks to mitigate this by investing greater power in the Human Subjects Committees and IRBs to review conflicts.\textsuperscript{290} However, these committees, despite their mission to protect human subjects, are not immune to institutional pressures. For example, in a conflict of interest scandal at the University of Minnesota involving the illegal sale of an anti-rejection transplant drug, investigation revealed that powerful clinical faculty in the medical school had, among other violations, failed to comply with FDA regulations and scoffed at IRB authority.\textsuperscript{291} Human Subjects Committees and IRBs are frequently understaffed and lack institutional power. They may be in a poor position to deal with conflicts of interest, especially with respect to its implications beyond informed consent.

One way in which institutional financial conflicts have been addressed is to take advantage of the diversified nature of many larger research institutions by divorcing the management of investments and equity interests from the clinical research endeavor.\textsuperscript{292} For example, at the University of Washington, management of such investments is handled by offices and structures outside of

\textsuperscript{287} Even the most scrupulous professional may be unable to avoid skewing results or making claims that are not fully substantiated by the research—whether purposefully or subconsciously. Reg Gale, \textit{Doctors' Disclosure Dilemma: Untold Ties to Biotech Firms}, NEWSDAY, June 15, 2001, at A7.

\textsuperscript{288} See Kowalczyk, supra note 269.

\textsuperscript{289} See Wilson & Heath, \textit{supra} note 3; Christopher Anderson, \textit{Scandal Sears Minnesota Medical School}, 262 SCIENCE 1812, 1812 (1993).

\textsuperscript{290} See OHRP DRAFT GUIDANCE, \textit{supra} note 204. \textit{See also Jesse A. Goldner, Dealing with Conflicts of Interest in Biomedical Research: IRB Oversight as the Next Best Solution to the Abolitionist Approach}, 28 J.L. MED. ETHICS 379, 398 (2000).

\textsuperscript{291} See Anderson, \textit{supra} note 289, at 1812.

research academia.\textsuperscript{293} This provides some insulation for university administrators who may have some involvement in decisions relating to clinical trials and their management. Another growing trend is the installation of regulatory compliance officers, often reporting directly to the President or Dean, that serve as secondary, impartial surveyors of institutional practice with respect to research.\textsuperscript{294} It remains to be seen whether such watchdogs can themselves remain and be perceived as immune to institutional pressures.

Even with financial safeguards, the non-financial institutional conflicts of interest are still present. Institutional culture has been changed by the value placed on research leading to successful technology transfer. Corollary to this is a valid concern that traditional academic and scholarly values of seeking truth, rewarding intellectual curiosity, and freedom of expression and thought will be sacrificed.

The harsh reality is that conflicts of interest, both financial and non-financial are now deeply embedded in the fabric of biomedical research. As a result, the traditional boundaries and values differential between the market and the ivory tower of academia are blurred, if not completely obliterated. The public-private partnership borne of technology transfer has accelerated the funding and progress of biomedical and clinical research. But it has also exacted a toll on research integrity, academic freedom, and the scientific soul that will be impossible to retrieve.

\textsuperscript{293} Letter from Parks, \textit{supra} note 292.
\textsuperscript{294} See \textit{generally} Lo, \textit{supra} note 263.