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Financial Conflict of Interest in Medical Research: Overview and Analysis of Institutional Controls

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I. INTRODUCTION

The federal regulatory framework governing financial conflicts of interest has substantially influenced policies and practices at the institutional level. Financial conflicts of interest in medical research, where external financial relationships influence or appear to influence an individual's or institution's behavior, create the possibility of compromising research results and the safety of human subjects. Furthermore, public trust of medical research is an important related issue, as financial conflicts draw into question the extent of protection afforded by existing policies, regulations, and practices. Institutional financial conflict policies vary considerably in substance and, most importantly, implementation.

This article examines the general trends of conflict-of-interest policies at institutions across the United States, followed by a closer examination of Harvard Medical School and Stanford School of Medicine—two major academic research institutions operating under distinct approaches to financial conflicts in medical research. In addition to examining existing institutional policies, recently issued government and private organization recommendations for developing workable solutions to the conflict issue are discussed and compared.

II. INSTITUTIONAL VARIATIONS IN FINANCIAL CONFLICT POLICIES

Financial conflict-of-interest policies vary considerably from one institution to another. In general, there are six major elements where institutional financial conflict policies tend to differ. These differences reflect local and institutional attitudes toward financial conflicts, and they impact the very nature of institutional practices.

A. Scope of Financial Conflict Policies

Wide variation exists in the scope of financial conflict policies among institutions, particularly in terms of how institutions choose to define a “financial conflict of inter-

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est.”¹ Some institutions apply federal definitions (e.g., the Public Health Service (PHS) definition) to all research regardless of funding source, while others rely on less stringent definitions.² In addition, financial conflict-of-interest policies vary in terms of whom the policy governs. Some institutions apply a single policy to both faculty and staff, while other institutions have separate policies for each group.³ Interestingly, some institutions either lack—or are unable to easily find and produce—any written policy on financial conflicts.⁴

B. *Disclosure of Financial Interests*

Disclosure of financial conflicts is an area where substantial variation is found among institutions. Differences generally occur in two subcategories: disclosure thresholds and to whom disclosure is required. In terms of the degree of financial interest that triggers disclosure, some institutions set the threshold at \$10,000 (the PHS definition of what constitutes a significant financial interest that should trigger an investigator disclosure to the institution), while others apply looser—or in some cases stricter—thresholds for the disclosure of any financial interest, regardless of amount.⁵ Some institutions distinguish between types of research, applying stricter disclosure thresholds for clinical research and less demanding thresholds for nonclinical research.⁶ In addition, there are differences in the manner in which financial interests are queried. Some institutions require only general information, while others ask for specific information and require documentation in some cases.⁷ Disclosure policies also vary in terms of who is required to disclose to the institution, with some policies requiring disclosure from all faculty members and others requiring disclosure from only those faculty acting as the principal investigator(s) of research.⁸

To whom faculty members are required to disclose their financial interests is the second subcategory where institutional policies tend to differ. In general, federally-funded research is subject to specific disclosure requirements, such as PHS-funded research.⁹ Apart from these federal requirements, institutional disclosure policies are quite varied. The various bodies to which disclosure of financial interests is required may include the institution; institutional review boards (IRBs); conflict-of-interest (COI) committees; in some cases, human research subjects through the informed consent form; or any combination of the above.¹⁰ Other institutions make disclosure decisions on a case-by-case basis.¹¹

¹ See U.S. GENERAL ACCOUNTING OFFICE, BIOMEDICAL RESEARCH: HHS DIRECTION NEEDED TO ADDRESS FINANCIAL CONFLICTS OF INTEREST 11 (2001) [hereinafter GAO REPORT], available at <http://www.gao.gov> (search for GAO Report GAO-02-89) (last visited May 27, 2003).

² See generally S.V. McCrary et al., *A National Survey of Policies on Disclosure of Conflicts of Interests in Biomedical Research*, 343 NEW ENG. J. MED. 1621-26 (2000).

³ See Harvard Medical School, Policy on Conflict of Interest and Commitment, *infra* note 24; Stanford University, Faculty Policy on Conflict of Commitment and Interest, *infra* note 52.

⁴ See McCrary, *supra* note 2, at 1624-25.

⁵ See GAO REPORT, *supra* note 1, at 12-15; McCrary, *supra* note 2, at 1622.

⁶ See GAO REPORT, *supra* note 1, at 13; McCrary, *supra* note 2, at 1622-23.

⁷ See GAO REPORT, *supra* note 1, at 13.

⁸ See generally M.K. Cho et al., *Policies on Faculty Conflicts of Interest at U.S. Universities*, 284 JAMA 2203-08 (2000); B. Lo et al., *Conflict-of-Interest Policies for Investigators in Clinical Trials*, 343 NEW ENG. J. MED. 1616-20 (2000).

⁹ 42 C.F.R. § 50.602. PHS disclosure requirements include investigator disclosure of “significant financial interests” to institutional officials. Institutional officials retain significant discretion in determining which financial interests could affect the design, conduct, or reporting of the research and thus constitute a “conflict-of-interest” that must be disclosed to the funding agency.

¹⁰ See GAO REPORT, *supra* note 1, at 15; see Lo et al., *supra* note 8.

¹¹ See GAO REPORT, *supra* note 1, at 13-15.

C. The Existence and Function of COI Committees

The existence of COI committees is becoming more universal at research institutions, particularly medical research institutions, but their function varies widely between institutions. Some committees have university-wide jurisdiction, overseeing all conflict issues for entire institutions and their various departments.¹² Others have narrower jurisdiction, overseeing conflicts within a particular school or department, such as medical schools.¹³ In addition to jurisdictional issues, the trigger for COI committee review varies. Some institutions involve the COI committee only after department chairs have reviewed the conflict and specifically ask for assistance.¹⁴ Others are charged with reviewing all conflicts from the time of initial disclosure.¹⁵

D. IRB Role in Conflict Determinations

The role of IRBs in financial conflict-of-interest determinations varies considerably. Some IRBs do not consider—nor are they informed of—financial conflicts when reviewing research protocols. Other IRBs are a major part of the process, reviewing disclosure forms and in some cases providing recommendations on management strategies.¹⁶ Some institutional IRBs have the authority to override management strategies proposed by the COI committee, under defined circumstances.¹⁷ In addition, the degree of IRB interaction with COI committees varies among institutions, ranging from no official contact to open communication and collaboration between the two bodies.¹⁸

E. Management Strategies

Management strategies employed to address financial conflicts range from very informal strategies (e.g., disclosure alone or self-monitoring plans) to more formal processes whereby a subcommittee develops a plan and regularly monitors investigator compliance.¹⁹ Some institutions use informal methods to identify investigator disclosure inconsistencies, but none of the surveyed institutions had a formal procedure for verifying whether investigators had fully disclosed.²⁰

F. Financial Conflict-of-Interest Policies Governing Institutions

Despite the lack of any federal requirement for such policies, some institutions have established their own financial conflict-of-interest policies.²¹ For those institutions with existing policies, there is wide variation in terms of what types of transactions are allowed or prohibited, and how those policies are implemented. Many institutions use “firewalls” to separate research/academic endeavors and investment/financial activities; in stark contrast, others encourage interaction between their academic and investment offices.²² In addition, variation can be found in the amount, timing, and involve-

¹² *See id.* at 15.

¹³ *See id.* at 13.

¹⁴ *See id.* at 13-14.

¹⁵ *See id.*

¹⁶ *See id.* at 14-15.

¹⁷ *See id.*

¹⁸ *See id.*

¹⁹ *See id.* at 15-16.

²⁰ *See id.* at 16.

²¹ *See id.* at 18-22.

²² *See id.*

ment of the institution in certain interested transactions involving the transfer of equity with start-up companies.²³

Variations found within the fundamental components of conflict policies are apparent across institutions nationwide. Although these variations illustrate one dimension of the spectrum of conflict policies currently in existence, they do not adequately capture the policies' true impact. A second and more significant element of policy variation occurs, not necessarily within written policies, but in how institutions implement and enforce their written policies.

III. A CLOSER EXAMINATION: HARVARD MEDICAL SCHOOL AND STANFORD UNIVERSITY

While the surveys and reports described above highlight significant variations in financial conflict-of-interest policies at the institutional level, an examination of policy implementation also is required to fully understand each institution's actual approach to financial conflicts. This section focuses on the policies and practices of Harvard Medical School and Stanford School of Medicine—two highly regarded academic research institutions. Harvard Medical School and Stanford University embody different approaches to financial conflict-of-interest issues. Arguably, the size of each institution—in terms of the number of people to whom their respective policies apply—along with their distinct organizational models have impacted each institution's approach. Harvard Medical School operates under a nontraditional model, in that its affiliated hospitals function as independent entities. In contrast, Stanford University operates under a more traditional model in which the hospital and the university function as an integrated whole. Beyond organizational structure, subtle disparities at both the written policy and the practice levels become apparent. Table 1 provides a comparison of Harvard Medical School and Stanford University at the organizational, policy, and practice levels.

A. *Harvard Medical School*

1. *Faculty Conflict Policies*

In March 1990, Harvard Medical School (HMS) instituted a conflict-of-interest policy, and later revised it in 1996.²⁴ Considered by many to be among the strictest in the country, this policy governs medical school faculty conflicts and—owing to the medical school appointment they enjoy—the vast majority of the professional staff at independent teaching hospitals affiliated with Harvard. HMS's conflict policy, "Policy on Conflict of Interest and Commitment," consists of a general policy statement, specific guidelines for conflicts of interest, key definitions, and implementation strategies. It is meant to complement the medical school's principles on industry-sponsored research.²⁵ Importantly, this policy applies to HMS full- and part-time faculty only; nonfaculty, such as HMS staff members, are not subject to these policies, although some are covered by policies of the affiliates.²⁶

Both conflicts of interest and conflicts of commitment are governed by the HMS policy. Generally, HMS is committed to faculty-industry partnerships because the insti-

²³ See *id.* at 20.

²⁴ Harvard Medical School, Policy on Conflicts of Interest and Commitment, available at <http://www.hms.harvard.edu/integrity/conf.html> (last visited May 23, 2003).

²⁵ See Harvard Medical School, Faculty of Medicine Statement on Research Sponsored by Industry, available at <http://www.hms.harvard.edu/integrity/industry.html> (last visited May 23, 2003).

²⁶ See Harvard Medical School, Policy on Conflicts of Interest and Commitment, *supra* note 24.

tution recognizes the mutually beneficial nature of such relationships as well as the potential public benefit resulting from such collaboration.²⁷ The HMS conflict-of-interest policy also recognizes the importance of scientific integrity and public confidence in academic research, and to that end the policy exists to assist faculty in navigating these relationships.

The HMS policy is based on a system of regular faculty disclosures.²⁸ Disclosure of financial interests that may constitute a conflict is an integral part of the institution's approach to financial conflicts. Under the policy, a faculty member has a conflict of interest when that faculty member, his or her family member, or an associated entity possesses a financial interest "in an activity which involves his/her responsibilities as a member of the Faculty of Medicine," including teaching, research, patient care, and administration.²⁹ Financial interest is defined to include stock or ownership interests in a business; income from a business such as consulting fees, salary, forbearances, and royalties derived from the licensing of technology; real or personal property; or any other form of compensation.³⁰

The substance of HMS's policy is found in its Guidelines for Conflicts of Interest,³¹ which establishes guiding principles through the categorization of financial conflicts. Category I consists of two types of conflicts, including those conflicts that generally are not allowed under sections (a) and (b), and those conflicts that generally are allowed after full disclosure, review, approval, and oversight.³² Category II governs conflicts that are ordinarily permissible following the requisite disclosure.³³ Finally, Category III includes those conflicts that are the least problematic and thus allowable (e.g., faculty receipt of royalties from published scholarly works and royalty payments under institutional royalty-sharing policies).³⁴

Most notable about the medical school's conflict-of-interest guidelines are Categories I(a) and I(b). As written, Category I(a) generally does not allow faculty members to participate in clinical research on technology

owned by or contractually obligated to a Business in which the Faculty Member, a member of his/her Family, or an Associated Entity has a consulting relationship, holds a stock or similar ownership interest, or has any other Financial Interest, other than receipt of University- or Hospital-Sponsored Research support or royalties under institutional royalty-sharing policies.³⁵

Under this category, HMS has set the *de minimis* threshold for conflicts at \$20,000 for stock or similar ownership interests in a publicly-traded company, and \$10,000 for consulting arrangements.³⁶ Importantly, these acquisitions must have occurred at arms-length, and thus must not have been acquired as part of the research agreement. Notably, the *de minimis* threshold is not applicable to nonpublicly-traded equity interests.

²⁷ *See id.*

²⁸ *See id.*

²⁹ *See id.*

³⁰ *See* Harvard Medical School, Policy on Conflicts of Interest and Commitment, *supra* note 24, Appendix A: Operating Definitions, available at http://www.hms.harvard.edu/integrity/app_a.html.

³¹ *See* Harvard Medical School, Guidelines for Conflicts of Interest, available at <http://www.hms.harvard.edu/integrity/guide.html> (last visited May 23, 2003).

³² *See id.*

³³ *See id.*

³⁴ *See id.*

³⁵ *See id.*

³⁶ *See id.*

Thus, a faculty member generally would not be allowed to participate in research involving human subjects testing a product the faculty member has licensed to a business, if the faculty member receives, or expects to receive, more than \$20,000 in equity in the business, or \$10,000 from consulting arrangements with the business. If the faculty member's interest is below the *de minimis* threshold and the interest was acquired at arms-length (i.e., acquired before the research came about, or acquired as a gift or inheritance) the faculty member would be allowed to conduct this research. If, however, the same faculty member acquired the interest as part of the research agreement, the *de minimis* threshold will not apply and the faculty member will not be allowed to conduct this research, regardless of the monetary amount involved.

Category I(b) generally does not allow faculty members to receive "University- or Hospital-Sponsored Research support (whether in dollars or in kind) for Clinical Research or research that does not involve human subjects, from a Business in which he/she, a member of his/her family, or an Associated Entity holds a stock or similar ownership interest."³⁷ The same *de minimis* threshold of \$20,000 from Category I(a) applies. Thus, HMS generally would not allow a faculty member to conduct university-sponsored clinical or preclinical research who receives over \$20,000 in equity from the business sponsoring the research.

HMS provides guidance on the implementation of its conflict policy within the policy itself. Specifically, HMS has established a Standing Committee on Conflicts of Interest and Commitment.³⁸ This committee is charged with reviewing the implementation of the conflict-of-interest policy, including reviewing cases and making recommendations to the Dean; developing procedures for the disclosure process; and designing disciplinary actions.³⁹ The Dean is responsible for overseeing implementation of the policy, including dissemination, collection, and review of completed disclosure statements for all HMS faculty.⁴⁰ Significantly, research conducted by HMS faculty through an affiliate hospital or research institution will be subject to the financial conflict policies of that particular institution—policies that tend to be more restrictive than the HMS policy.

Importantly, Category I(a) and (b) activities, as written, leave open the possibility of a faculty member participating in research in which he or she is financially interested. The reality of what is actually allowed, however, is quite different. It is generally understood among HMS faculty that exceptions to Category I(a) and (b) conflicts are seldom, if ever, granted. In fact, it is rare for faculty to request approval of these types of activities. Essentially, Category I(a) and (b) activities are never allowed in practice, thus transforming "Generally Not Allowable" activities with the possibility of an exception into essentially prohibited activities. In practice, then, few of these types of cases are ever reviewed.

2. Harvard University Licensing Policy and Conflict-of-Interest

In 1993, Harvard University issued a policy governing university granting of licenses.⁴¹ The policy applies to all licensing transactions, including Harvard Medical School's licensing activities.⁴² Specifically, it addresses situations where the institution grants a

³⁷ See *id.*

³⁸ See Harvard Medical School, Policy on Conflicts of Interest and Commitment, *supra* note 24, Appendix B, available at http://www.hms.harvard.edu/integrity/app_b.html.

³⁹ See *id.*

⁴⁰ See *id.*

⁴¹ See Harvard Medical School, Technology Licensing Office, Policy Statement Regarding Application of Harvard University's Conflicts of Interest Policies to the Granting of Licenses, available at <http://www.hms.harvard.edu/otl/conflict.html> (last visited May 23, 2003).

⁴² See *id.*

license to a company in which a faculty member or other member of the university has a financial interest. The University Office of Technology and Trademark Licensing (OTTL) and the Harvard Medical School Office for Technology Licensing (OTL) are responsible for implementing this policy, with oversight by the University's Committee on Patents and Copyrights (CPC).⁴³ Notably, in terms of HMS specifically, the licensing policy applies only to the small portion of faculty members whose research goes through the medical school. In reality, the research of most HMS faculty goes through affiliated hospitals and research institutions, each of which has its own policies and technology licensing offices.

Harvard's licensing conflict policy statement gives broad discretion to the OTTL/OTL in determining when a license should be granted to a company in which a faculty member has a "close financial interest."⁴⁴ A "close financial interest" occurs when the faculty member holds equity in the licensee company that constitutes five percent or more of the company; when the license is likely to have a significant impact on the value of the stock; or when the inventor has a long-term, exclusive, or otherwise significant consulting arrangement with the licensee company.⁴⁵ Notably, the CPC retains the authority to deny the granting of a license in which a faculty member has a close financial relationship when it deems such situations are not in the best interest of the university.⁴⁶

3. Institutional Conflicts: Licensed-Derived Stock

Harvard University approved the acceptance of license-derived stock in 1997, and established a policy governing institutional receipt of equity as part of licensing arrangements.⁴⁷ The statement maintains that the university should not hold more than a minority equity position (15%) in any one company and should not hold board positions in companies from which the university has received equity.⁴⁸ In addition, the statement guidelines create a firewall between research and investment activities, and advise against university investment in the formation of any company without the involvement of the Harvard Management Company.⁴⁹ Furthermore, these guidelines require that equity be held and managed by the Harvard Management Company according to procedures that ensure decisions regarding such equity interests are made at arms-length.⁵⁰ All equity arrangements require approval from the Chairman of the CPC.⁵¹ Notably, the majority of sponsored research and associated licensing is conducted under the varying policies of the medical school affiliates.

B. Stanford Medical School

1. Faculty Conflict Policies

Stanford University originally issued its faculty conflict policy in 1994.⁵² Unlike HMS, Stanford School of Medicine (SSOM) does not operate under a conflicts policy specific

⁴³ *See id.*

⁴⁴ *See id.*

⁴⁵ *See id.* The Harvard policy distinguishes between those potential licensees that are emerging companies and those that are existing operating companies. *See id.*

⁴⁶ *See id.*

⁴⁷ *See* Harvard Medical School, Technology Licensing Office, Procedures for Acceptance, Management and Sale of License-Derived Stock, available at <http://www.hms.harvard.edu/otl/equity.html> (last visited May 23, 2003).

⁴⁸ *See id.*

⁴⁹ *See id.*

⁵⁰ *See id.*

⁵¹ *See id.*

⁵² *See* Stanford University, Faculty Policy on Conflicts of Commitment and Interest (RPH 4.1), available at <http://www.stanford.edu/dept/DOR/rph/4-1.html> (last visited May 23, 2003).

to the medical school. Rather, SSOM is governed by Stanford's general conflict policy, as included in the university's Research Policy Handbook (RPH). Stanford's approach to conflict-of-interest arguably is, to some extent, a byproduct of the institution's organizational structure and size—quite different than Harvard's. Stanford University has a more integrated organizational structure in which individual schools, as well as hospitals, operate under the umbrella of the larger institution and institutional policies, rather than as separate entities. Thus, in terms of financial conflicts of interest, disclosure is made to the deans of individual schools, who then report to the dean of research for the entire institution.⁵³

Stanford's conflict policy, "Faculty Policy on Conflict of Commitment and Interest," applies to all faculty members, including SSOM faculty.⁵⁴ A separate, less stringent policy also in the institution's policy handbook governs academic staff.⁵⁵ Like HMS, Stanford's policy addresses both conflicts of commitment and interest, with Stanford's written conflict policy placing greater emphasis on conflicts of commitment, due in part to the institution's view and strong history of consulting activities as a mechanism to fulfill its goal of transferring knowledge to the private sector.⁵⁶

Like HMS, Stanford's conflict policy relies on disclosures. On an annual basis, faculty are required to certify their compliance with the university's conflict policies, as well as to disclose any consulting arrangements, significant financial interests, or participation as a principal investigator for research sponsored by a company in which the faculty member has a financial interest.⁵⁷ Currently, Stanford defines "significant financial interest" to include "ownership interests in an entity amounting to at least one-half percent (0.5%) of the company's equity or at least \$10,000 in ownership interests (except when the ownership is managed by a third party such as a mutual fund)."⁵⁸ For any research activity, however, disclosure of equity held in private companies, regardless of amount, is required.⁵⁹

In addition to annual disclosures, the Stanford conflict policy includes four transactions that will trigger faculty disclosure and then required review by the institution. These include unrestricted gifts; technology licensing arrangements; sponsored research; and procurement of materials or services where the faculty member is employed by, consults for, or possesses a significant financial interest in the involved outside entity.⁶⁰ When any of these events occur, the involved faculty member is required to disclose any related conflict.⁶¹

Clinical research involving financially interested faculty is not explicitly prohibited under the Stanford policy. Rather, Stanford may require the assignment of an independent oversight group to protect the scientific objectivity of the research, while allowing the faculty member to proceed with the research.⁶² An oversight group is assigned to

⁵³ See generally Stanford University, Faculty Policy on Conflicts of Commitment and Interest, *supra* note 52.

⁵⁴ See *id.*

⁵⁵ See Stanford University, Conflict of Commitment and Interest for Academic Staff, *available at* <http://www.stanford.edu/dept/DOR/rph/4-4.html> (last visited May 23, 2003).

⁵⁶ See Stanford University, Outside Consulting Activities by Members of the Academic Council, *available at* <http://www.stanford.edu/dept/DOR/rph/4-3.html> (last visited May 23, 2003).

⁵⁷ See Stanford University, Faculty Policy on Conflicts of Commitment and Interest, *supra* note 52.

⁵⁸ See *id.* Prior to the introduction of the current definition, the threshold for significant financial interest was set at \$100,000.

⁵⁹ See *id.*

⁶⁰ See *id.*

⁶¹ See *id.*

⁶² See *id.*

evaluate and monitor clinical research in the following situations: 1) where a financially interested faculty member is involved in clinical trials evaluating his/her invention; 2) where a company that has been licensed a faculty invention sponsors the trial; 3) where the faculty member's objectivity is questionable; 4) where the trial outcome may be perceived as influencing potential research support; or 5) when the research is referred to other members of the faculty's department.⁶³ Any financial conflict, not just significant financial conflicts, must be disclosed in these circumstances.⁶⁴

Specific to the School of Medicine, faculty members disclose conflicts to a COI committee, whether annually or on an ad hoc basis as required. The COI committee then communicates with the IRB and advises the dean of research for the medical school, who then reports to the dean of research for the university. Theoretically, the dean of research or the COI committee can disapprove of research, regardless of IRB approval. In cases where the IRB rejects research, however, the COI committee or dean of research cannot overrule this decision.

In addition to faculty disclosure to the institution, Stanford faculty are required to disclose all financial conflicts to human subjects participating in clinical trials, through the informed consent document. This practice stems from the University's assumption that disclosure of financial conflicts falls within the requirements of the Common Rule's informed consent provisions.

In practice, Stanford University rejects the "one-size-fits-all" theory, which makes decisions on a case-by-case basis. This mechanism is supported by the University's policy that does not include explicit rules or guidelines, such as those provided by HMS, to categorize the types of relationships or activities that are allowed or prohibited once disclosure has been made. Each individual school dean is required to decide when a conflict of interest exists based on the facts and circumstances of each case. Thus, Stanford's policy theoretically allows for more flexibility on the part of decision-makers to consider extenuating circumstances; in practice, the policy also raises the possibility of less predictability for faculty members proposing research, and less uniformity of decisions across the institution or over time. Central review of such decisions by the Office of the Dean of Research of the university allows for some measure of consistency.

2. *University Investment in Start-Up Companies*

Stanford University has issued a written policy on university investment in start-up companies in which a faculty member also holds an interest.⁶⁵ Specifically, the university will not invest in start-up companies where faculty members on leave hold line management responsibilities, to avoid the potential for real or apparent conflicts.⁶⁶ When faculty involvement is limited to equity holdings or advisory roles, however, Stanford may choose to invest in the start-up.⁶⁷ The policy prohibits the university from being a lead investor or holding equity amounting to more than ten percent of the company.⁶⁸ In addition, Stanford officers may not hold board positions or personal equity interests in the start-up concurrent with the university's holding prior to the company going public.⁶⁹ Furthermore, university investment in start-ups in which fac-

⁶³ See *id.*

⁶⁴ See *id.*

⁶⁵ See University Investments in Start-Up Companies Involving Stanford Faculty, available at <http://www.stanford.edu/dept/DoR/rph/4-5.html> (last visited May 23, 2003).

⁶⁶ See *id.*

⁶⁷ See *id.*

⁶⁸ See *id.*

⁶⁹ See *id.*

ulty have an interest are subject to approval from the Provost and subject to recommendation from the Stanford Management Company.⁷⁰

3. *Institutional Conflicts: Equity Acquisition in Technology Licensing*

Stanford University also has a policy governing institutional acquisition of equity as a form of compensation for the licensing of university-owned technologies.⁷¹ Unlike the Harvard policy, Stanford's policy does not explicitly limit the amount of equity the university may receive from these companies. The policy allows equity acquisition, "subject to a conflict-of-interest review if appropriate."⁷² The Provost is charged with reviewing such matters,⁷³ but the policy does not specify under what conditions a review is considered "appropriate."

C. *Summary*

HMS and Stanford University utilize distinct approaches to financial conflicts of interest. While both academic research institutions address the same general issues surrounding financial conflicts, their policies differ in application and practice: they set different disclosure thresholds, provide faculty with disparate levels of guidance, and require disclosure at different times and under different circumstances. Substantial differences also are apparent in how the policies are implemented. HMS's conflict policy results in the de facto prohibition of certain activities, while the organizational structure of the university necessarily requires the application of affiliated hospitals' and research institutions' varying conflict policies to HMS faculty research. Stanford University's conflict policy necessarily results in case-by-case determinations, as specific guidelines have not been provided. The organizational structure of Stanford provides for a more uniform umbrella policy without the added complexity of policies at individual institutions, but the less structured policy, as implemented, potentially results in less predictability and uniformity of decisions. Disparities between these two major research institutions provide a telling example of the spectrum of policies and practices existing nationwide, thus highlighting the complexity of the issue and the potential value of more uniform standards.

IV. RECOMMENDATIONS OF POLICY ORGANIZATIONS

Conflict-of-interest issues in medical research, particularly financial conflicts, recently have come under increasing scrutiny. Financial relationships in medical research, especially research involving human participants, have been scrutinized most closely in order to comprehend potential negative impacts of certain relationships and, more importantly, to devise solutions. Government, industry, educational institutions, and trade associations have examined financial conflicts of interest and formulated solutions and recommendations. While there is some variation among the policies, there also is considerable agreement. For example, many organizations suggest establishment of a COI committee at research institutions, broader disclosure within the institution, increased communication between IRBs and COI committees, as well as stricter standards for

⁷⁰ See *id.*

⁷¹ See *Equity Acquisition in Technology Licensing and Learning Agreements*, available at <http://www.stanford.edu/dept/DoR/rph/4-6.tml> (last visited May 23, 2003).

⁷² See *id.*

⁷³ See *id.*

research involving human subjects. The recommendations tend to remain quite general, however, stopping short of providing detailed guidance for research institutions. Table 2 provides a summary of the main similarities and differences found among some of these organizational policies.

A. *The Association of American Medical Colleges*

In December 2001, the Association of American Medical Colleges (AAMC) issued a document containing policy and guidelines for investigators engaged in human subject research.⁷⁴ While the policy contains core principles and baseline standards for individual conflicts, conflict at the institutional level is not addressed.⁷⁵ Furthermore, with its exclusive focus on human subject research, the scope of the AAMC report is narrower than that of other reports covering all medical research.

To establish effective institutional control of financial conflicts, the AAMC advocates establishment of a COI committee, primarily responsible for conflict-of-interest issues.⁷⁶ To further that committee's work, the document promotes increased communication and reporting among institutional officials, the COI committee, IRBs, and technology licensing offices,⁷⁷ as well as extensive disclosure of conflicts within the institution.⁷⁸ The policy also addresses the mechanics of policy implementation, and recommends electronic reporting systems; allocation of additional resources to conflict issues; and education and training efforts for faculty, staff, students, and trainees.⁷⁹

Particularly noteworthy about the AAMC's policy is its inclusion of royalty income from patent license or copyright agreements in its definition of "significant financial interests in research." Under this definition, "where the research is directly related to the licensed technology or work," royalty income or the right to receive future royalties constitutes a significant financial interest.⁸⁰

Two principles of the AAMC's recommendations also deserve special attention. First, the AAMC recommends that institutions establish a rebuttable presumption that automatically prohibits an individual from conducting research when that individual has a significant financial interest, regardless of how the research is being funded.⁸¹ Second, the AAMC policy allows "compelling circumstances" to rebut this presumption, although this term is not specifically defined.⁸² The policy recognizes that institutional circumstances vary, and provides elements for COI committees to consider when making such determinations.⁸³

Importantly, this proposed automatic presumption of impropriety draws a bright line for prohibited activities, perhaps easing the identification of those conflicts requiring

⁷⁴ Association of American Medical Colleges, Task Force on Financial Conflicts of Interest in Clinical Research, *Protecting Subjects, Preserving Trust, Promoting Progress—Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subject Research* (released Dec. 2001), available at <http://www.aamc.org/members/coitf/start.htm> (last visited May 23, 2003).

⁷⁵ The authors duly acknowledge the release of a separate document by the AAMC entitled *Protecting Subjects, Preserving Trust, Promoting Progress II: Principles and Recommendations for Oversight of an Institution's Financial Interests In Human Subjects Research*, subsequent to submission of this manuscript.

⁷⁶ See *id.* at 7-9.

⁷⁷ See *id.* at 14-15.

⁷⁸ See *id.* at 18-19.

⁷⁹ See *id.* at 15-16.

⁸⁰ See *id.* at 13.

⁸¹ See *id.* at 20-21.

⁸² See *id.* at 16.

⁸³ See *id.*

further scrutiny. In addition, a loosely defined rebuttal allows for decisions to be made on a case-by-case basis, taking into account unique circumstances. This de facto automatic prohibition and the subsequent need to establish compelling circumstances may prove a substantial administrative burden both to those who seek to conduct industry-funded research in the academic setting and to those who must determine whether to permit such activities.

B. *The Association of American Universities*

In October 2001, the Association of American Universities (AAU) issued a report addressing both individual and institutional conflicts of interest.⁸⁴ For individual conflicts, the report focuses on university-wide management and compliance through annual disclosures (regardless of funding source); transparent policies; and coordination of oversight, management, and compliance efforts.⁸⁵ Significantly, the report recommends handling conflicts on a case-by-case basis, because “[m]any financial interests are not conflicts, and many conflicts can be managed.”⁸⁶ The report also states, however, that research involving human subjects requires greater scrutiny and that conflicts under these circumstances are impermissible in the absence of compelling circumstances that justify an exception.⁸⁷ Finally, the document advocates extensive disclosure; conflicts are to be disclosed to the institution, to federal agencies, to human participants through IRBs, and in publications and oral presentations.⁸⁸

Importantly, the AAU report distinguishes between two types of institutional conflicts of interest: 1) conflicts involving university equity holdings or royalty interests in university faculty research programs, and 2) conflicts involving university officials who make decisions with institution-wide implications.⁸⁹ For both types of conflicts, the report recommends following a three-step approach: 1) always disclose; 2) manage where appropriate; and 3) prohibit when necessary.⁹⁰ Specifically, the report advocates the segregation of financial and research decisionmaking processes, as well as the establishment of clear policies, administrative processes, and a review board to assess conflict issues and to determine how to manage them.⁹¹ The report stops short of more specific guidance in these areas.

C. *The General Accounting Office*

The General Accounting Office (GAO), in its report examining institutional variations in conflict of interest in biomedical research, made two policy recommendations for the Department of Health and Human Services (DHHS).⁹² Specifically, the report recommended that DHHS develop “best practices” guidelines for institutions, delineating guidance for both individual and institutional conflicts of interest to assist institutions in their efforts to manage and reduce potential negative impacts of such conflicts.⁹³ In

⁸⁴ See Association of American Universities, Task Force on Research Accountability, Report on Individual and Institutional Financial Conflict of Interest (released Oct. 2001), available at <http://www.aau.edu/research/conflict.html> (last visited May 23, 2003).

⁸⁵ See *id.* at 2-6.

⁸⁶ *Id.* at 4.

⁸⁷ See *id.*

⁸⁸ See *id.* at 5-6.

⁸⁹ See *id.* at 10.

⁹⁰ See *id.* at 12.

⁹¹ See *id.* at 12-14.

⁹² See GAO REPORT, *supra* note 1.

⁹³ See *id.* at 29.

addition, the GAO suggested that DHHS address institutional conflict policies with greater detail and depth through the development of guidance documents or regulations to ensure research integrity and protection of human research participants.⁹⁴

D. The National Bioethics Advisory Commission

In an extensive review of research involving human subjects, the National Bioethics Advisory Commission (NBAC) addressed financial conflicts of interest, focusing on IRB conflicts of interest.⁹⁵ In addition to its focus on IRBs, the report provided a review and limited recommendations on individual conflicts. NBAC acknowledged that the prohibition of all conflicts is not feasible, stating that IRB review of financial conflicts will not be sufficient because IRBs currently are limited in the type and scope of their reviews.⁹⁶ NBAC recommended that institutions inform IRBs of investigator financial conflicts, to allow IRBs to use such information to determine possible disclosure to human participants.⁹⁷ NBAC also encourages institutions and sponsors to take responsibility for oversight of financial conflicts.⁹⁸

E. The National Institutes of Health

In contrast to NBAC's recommendation, NIH would like to see IRBs assume a lead role in monitoring conflicts of interest.⁹⁹ In a guidance document issued in 2000, NIH estimated that twenty-five percent of IRBs currently deal routinely with financial conflicts of interest.¹⁰⁰ Moreover, in the absence of explicit provisions governing financial conflicts of interest, many patient advocates maintain that the disclosure of such conflicts should fall under the Common Rule's informed consent requirement and within the purview of IRB review. Thus, an investigator's obligation to provide research participants with sufficient information to make an informed judgment about whether to join a study would include providing information about the researcher's own financial interests in the study, if any. Critics argue that patients are not in a position to effectively process complex financial conflict information under such circumstances; instead, they encourage the screening of conflicts at an earlier stage.

NIH also has proposed several approaches to minimize the potentially detrimental effects of financial conflicts of interest on research activities.¹⁰¹ For example, the agency recommends that a research institution's consent form include a statement ensuring compliance with institutional financial conflict policies. In addition, the agency suggests that IRBs be made aware of an institution's financial conflict policy. Finally, NIH recommends that institutions provide IRBs with appropriate procedures for identifying and responding to perceived financial and academic conflicts of interest.¹⁰²

⁹⁴ *See id.*

⁹⁵ *See* NATIONAL BIOETHICS ADVISORY COMMISSION, ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS Vol. I, Ch. 3 (Aug. 2001).

⁹⁶ *See id.* at 59.

⁹⁷ *See id.* at 60.

⁹⁸ *See id.*

⁹⁹ *See* NIH Guidance, Financial Conflicts of Interest and Research Objectivity: Issues for Investigators and Institutional Review Boards (June 5, 2000), available at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-040.html> (last visited May 23, 2003).

¹⁰⁰ *See id.*

¹⁰¹ *See id.*

¹⁰² *See id.*

V. CONCLUSION

Financial conflicts of interest in medical research have received considerable attention recently, due largely to unfortunate occurrences that have illustrated the potential consequences of real or perceived financial conflicts. Variation among institutional conflict policies contributes to the complexity of the issue, creating confusion not only among investigators and sponsors, but also the public. It is apparent from the numerous conflicts recommendations and guidelines recently promulgated that there is some consensus regarding basic standards that should be applied at the institutional level. At the same time, it is equally apparent that other aspects of the issue lack such consensus. Establishment of a workable solution to conflict issues requires balancing a measure of uniformity with adequate institutional discretion—a process that necessarily will involve all stakeholders in the medical technology development process.

TABLE 1

HARVARD MEDICAL SCHOOL AND STANFORD UNIVERSITY:
COMPARISON OF FINANCIAL CONFLICT POLICIES AND PRACTICES

	Harvard Medical School	Stanford University
Organizational Structure	<ul style="list-style-type: none"> ◆ Harvard Medical School (HMS) operates as distinct entity in terms of conflict of interest ◆ Nontraditional 'independent' model where teaching hospitals are separate entities from medical school, resulting in frequent application of non-medical school conflict policies of affiliated hospital or institution 	<ul style="list-style-type: none"> ◆ School of Medicine operates 'under' University umbrella in terms of conflict of interest ◆ Traditional integrated medical school-hospital model with single policy applicable to Stanford School of Medicine (SSOM) faculty research whether conducted through SSOM or the Univ. hospital
Policy Approach	<ul style="list-style-type: none"> ◆ Explicit categorization of financial conflicts into 'allowable,' 'ordinarily allowable,' 'generally allowable,' and 'generally not allowable' categories ◆ Decisions made according to guidelines 	<ul style="list-style-type: none"> ◆ General 'triggering' events result in heightened review ◆ No explicit guidelines categorizing types of conflicts ◆ Decisions made on case-by-case basis
Key Mechanisms and Provisions	<ul style="list-style-type: none"> ◆ Disclosure of <i>financial interests</i> (stock or ownership interests, income such as consulting fees, salary, and royalty derived from the licensing of technology, and any other form of compensation) ◆ Financial conflict exists when faculty member or faculty's family members or associated entities have a financial interest in an activity involving his/her responsibilities as a member of the Faculty of Medicine ◆ <i>De minimis</i> threshold for Category I(a) [financially interested faculty conducting clinical research on technology s/he owns or is contractually obligated to] and (b) [financially interested faculty receiving university or hospital-sponsored support for clinical or nonclinical research] set at \$20,000 for stock in publicly-traded company and \$10,000 for consulting income; all acquisitions must have been made at arms-length ◆ Disclosure made to standing conflict of interest committee; dean reviews 	<ul style="list-style-type: none"> ◆ Annual disclosure and certification of compliance—disclose <i>significant financial interests</i> (equity equal to or greater than .5% of company or over \$10,000 in ownership interests), consulting activities, and faculty w/ Principle Investigator (PI) status in outside research while on leave. ◆ Financial conflict exists when there is a divergence between the faculty's private interests and his/her professional obligations to the University ◆ Clinical research automatically requires heightened review and may require independent oversight group ◆ Equity in any amount held in a private company requires disclosure ◆ Four types of events trigger review: unrestricted gifts, technology licensing arrangements, sponsored research, and materials/services procurement. Disclosure is required, regardless of amount, in these cases. ◆ Disclosure to conflict-of-interest committee; COI committee communicates with IRB and dean of research at medical school; dean of research of the university reviews ◆ Disclosure of faculty financial conflicts to human research subjects

	Harvard Medical School	Stanford University
Key Distinctions	<ul style="list-style-type: none"> ◆ In practice, Category I conflicts prohibited; few of these cases ever reviewed ◆ Distinction between clinical vs. preclinical work ◆ Distinction between income and equity—'income' includes consulting fees, salary, royalty from licensed technology, real or personal property, or any other form of compensation ◆ Royalty payments not considered problematic unless derived from the licensing of technology and outside of institutional royalty-sharing policies 	<ul style="list-style-type: none"> ◆ No explicit prohibitions; in practice, only a few cases being managed at any given time ◆ Distinction between clinical vs. preclinical work ◆ Distinction between income and equity ◆ Royalty payments not explicitly included in "significant financial interest"; yet all technology licensing arrangements trigger review
Institutional Financial Conflict Policies	<ul style="list-style-type: none"> ◆ Allows university investment in start-ups in which faculty has an interest ◆ Allows equity acquisition in technology licensing agreements ◆ Outside policies apply when research conducted through affiliate entity 	<ul style="list-style-type: none"> ◆ Allows university investment in start-ups in which faculty has an interest ◆ Allows equity acquisition in technology licensing agreements

TABLE 2

POLICY ORGANIZATIONS' FINANCIAL CONFLICT OF INTEREST RECOMMENDATIONS

Organization	Title	Released	Addresses...	Key Mechanisms and Provisions
Association of American Medical Colleges	<i>Protecting Subjects, Preserving Trust, Promoting Progress—Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subject Research</i>	Dec. 2001	Individual financial conflicts in human subject research	<ul style="list-style-type: none"> ◆ Establish COI committee ◆ Promote communication between institution, COI committee, IRB, and technology licensing office ◆ Extensive disclosure within the institution ◆ Allocation of more resources to issue ◆ Education/training for faculty, staff, students, and trainees ◆ Establishes a rebuttable presumption ◆ Includes royalties in definition of significant financial interest
Association of American Universities	<i>Report on Individual and Institutional Financial Conflict of Interest</i>	Oct. 2001	Individual and institutional financial conflicts in all medical research	<p>Individual</p> <ul style="list-style-type: none"> ◆ Institution-wide management ◆ Annual disclosures of financial conflicts, regardless of funding source to institution, federal agencies, IRBs, human participants ◆ Coordination of oversight, management, and compliance efforts ◆ Case-by-case decisions ◆ Heightened scrutiny for human subject research = all conflicts impermissible unless compelling circumstances <p>Institutional</p> <ul style="list-style-type: none"> ◆ Distinguish b/w institutional conflicts and institutional officials' conflicts ◆ Always disclose, manage where appropriate, and prohibit when necessary ◆ Create firewalls between financial and research decisions ◆ Establish review board
General Accounting Office	<i>Biomedical Research: HHS Direction Needed to Address Financial Conflicts of Interest</i>	Nov. 2001	Individual and institutional financial conflicts in biomedical research	<ul style="list-style-type: none"> ◆ HHS development of "best practices" guidelines on individual and institutional conflicts ◆ HHS address institutional conflicts in greater detail
National Bioethics Advisory Commission	<i>Ethical and Policy Issues in Research Involving Human Participants</i>	Aug. 2001	Individual financial conflicts in human subject research	<ul style="list-style-type: none"> ◆ Disclosure of individual conflicts to IRB ◆ Disclosure to human subjects determined by IRB ◆ Institutional and sponsor responsibility for oversight ◆ Discourages IRB taking lead role
National Institutes of Health	<i>Guidance—Financial Conflicts of Interest and Research Objectivity: Issues for Investigators and IRBs</i>	June 2000	Individual financial conflicts	<ul style="list-style-type: none"> ◆ IRBs assume lead role in monitoring ◆ Investigator compliance statement in informed consent form

