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

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Executive Summary

Financial conflict of interest has emerged as a major challenge to the increasingly collaborative environment in which medical research is conducted. While the potential benefits of collaboration with for-profit entities are great, financial conflicts of interest, where external financial relationships influence or appear to influence an individual's or institution's attitude or behavior, threaten to compromise medical research results in the case of pre-clinical or clinical research, and potentially place human subjects at risk. Perhaps most importantly, financial conflicts, whether real or perceived, tend to erode the public's trust in important medical research endeavors. Regulation of these conflicts generally occurs at two levels, federal and institutional. As outlined in the preceding white paper, federal controls in the form of numerous regulations issued by several agencies, address disparate goals and needs through varying mechanisms, which are diffuse by nature. Institutional controls, influenced by varying local conditions, institutional values, and state laws represent local approaches to the financial conflict issue.

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Reflecting these local and institutional influences, control of financial conflict-of-interest at the institutional level varies considerably nationwide. General areas of variation found among academic research institutions include: (1) the scope of financial conflict policies; (2) disclosure rules, including financial interest thresholds dictating disclosure and to whom disclosure is required; (3) the existence and function of conflict-of-interest committees; (4) the extent of IRB participation in conflict determinations; (5) conflict management strategies; and (6) the existence of policies governing institutional financial conflicts, in contrast to personal conflicts. In addition to these general differences, institutional policies differ in the manner in which they distinguish between different types of financial instruments (income, equity, and royalty payments) and types of research (basic, clinical). These differing institutional standards have the potential to generate confusion among investigators and sponsors, as well as public mistrust in the protection afforded by existing rules and regulations, particularly when a financial conflict is linked to an untoward patient outcome.

Confounding the existing variation found in institutional written policies are institutional practices, in terms of the way institutions interpret their written policies and the manner in which the policies are implemented and enforced. On their face, many of the written policies appear similar, but it is the manner in which they are enforced that determines their true impact.

A closer examination of Harvard Medical School (HMS) and Stanford University, two well-regarded medical research institutions, provides a particularly useful illustration of the degree of variation found in financial conflict-of-interest policies, procedures, and more importantly, practices. HMS's conflict policies are considered by many authorities to be among the most rigorous and conservative in the United States. Harvard's written policies, which include explicit guidance and rely heavily on disclosure, categorize financial conflicts, offering faculty some measure of predictability while also appearing to allow for some case-by-case discretion. However, in practice HMS's conflict policies are somewhat stricter than their written policy communicates. Importantly, due to the University's organizational structure, faculty members are frequently required to comply with separate financial conflict policies specific to affiliated hospitals, policies that tend to vary from HMS's policies. In addition to faculty conflict policies, HMS has issued policy statements

governing institutional activities, including the granting of licenses to companies in which a faculty member has a financial relationship and institutional receipt of license-derived equity. Again, due to its organizational structure, the specific policies of affiliated entities addressing licensing activities may govern particular HMS faculty research activities that take place at that affiliate.

Stanford University has embraced a less structured, yet more centralized approach to financial conflicts. Stanford policy rejects the "one size fits all" approach, allowing for greater flexibility, yet raising the possibility of less predictability and uniformity of decisions. The University's disclosure threshold for significant financial interests is set at 0.5% equity of a public company and \$10,000 in ownership interests. Any interest in a privately held company or research involving human subjects requires disclosure. In addition, four defined transactions including unrestricted gifts, technology licensing arrangements, sponsored research, and procurement of materials or services where the faculty member consults for or possesses a significant financial interest in the outside entity, trigger heightened review. While financially interested faculty members are not prohibited categorically from conducting research involving human subjects, review is required to determine whether compelling circumstances exist that justify such involvement. In these cases, Stanford requires the assignment of an independent oversight group to protect the scientific objectivity of the research. Like Harvard, Stanford has a written policy on university investment in start-up companies in which a faculty member has a financial interest as well as a policy governing acquisition of equity in licensing agreements. Notably, due to its integrated organizational structure and conflict policies, Stanford medical faculty are rarely subject to "outside" conflict policies of affiliated hospitals, as is often the case with HMS faculty research conducted through affiliated hospitals or institutions.

Government, industry, academic organizations, and trade associations have explored institutional policies governing the financial conflicts issue and formulated potential solutions and approaches. Although sharing common themes, these proposals differ at the more detailed level. Among the shared themes from these reports are the establishment of conflict-of-interest committees, broad disclosure within the institution, communication between institutional review boards (IRBs) and conflict committees, and stricter standards for research involving human subjects. The various reports include:

- The Association of American Medical Colleges (AAMC). Released in December 2001, this policy focuses exclusively on individual conflict in human research and shares many of the broader recommendations found in other policies. Beyond these similarities, the AAMC recommends establishment of a rebuttable presumption against interested individuals with a significant financial interest. Although left undefined, the AAMC policy allows a showing of “compelling circumstances” to rebut this presumption. The AAMC policy also recommends that more resources be devoted to conflict issues as well as education and training for faculty, staff, students, and trainees.
- The Association of American Universities (AAU). An October 2001 policy statement addresses individual and institutional conflicts in all types of medical research, advocating institution-wide management, transparent policies, and coordination of oversight, management, and compliance efforts. The AAU policy counsels for extensive disclosure of conflicts to institutions, federal agencies, and human research participants through IRBs. The section of policy governing institutional conflicts stops short of specific guidance, instead providing a general recommendation to always disclose, manage where appropriate, and prohibit when necessary.
- The General Accounting Office (GAO). The GAO, in its report examining institutional variation in conflict policies, calls upon HHS to develop “best practice” guidelines and address institutional conflict policies further through guidance documents or regulations.
- The National Bioethics Advisory Commission (NBAC). In an extensive review of research involving human subjects, the NBAC focuses on IRB involvement with conflict-of-interest determinations and management. The document encourages institutions and research sponsors to take responsibility for conflict-of-interest oversight, maintaining that IRBs are currently limited in the type and scope of their reviews.
- The National Institutes of Health (NIH). In a guidance document issued in 2000, NIH suggests IRBs assume a lead role in monitoring conflicts of interest, a position in stark contrast to that of NBAC. In addition, NIH proposes inclusion of conflict statements in the informed consent document.

The ultimate effect of these recent policy recommendations, while well-considered and well-intentioned, is uncertain. Though many institutions will undoubtedly strive to adhere to these new recommendations, their relative lack of specificity will make compliance difficult and likely uneven. Without additional guidance from government regulation and thought leaders, particularly in the academic community, and without sharing examples of the handling of real cases, these latest attempts to ensure effective conflict regulation may merely serve to increase existing policy variation among institutions.

I. Introduction

The federal regulatory framework governing financial conflicts of interest, as outlined in the preceding CIMIT white paper, “Financial Conflict of Interest in Medical Research:

Overview and Analysis of Federal and State Controls,” 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 paper 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 University, 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, impacting the very nature of institutional practices.

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 interest.”¹ Some institutions apply federal definitions, such as 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 financial conflict 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

Disclosure of Financial Interests – Disclosure of financial conflicts is an area where substantial variation is found among institutions. Differences generally occur in two sub-categories: disclosure thresholds and to whom disclosure is required. In terms of the degree of financial interest triggering disclosure, some institutions set the threshold at \$10,000, the Public Health Service (PHS) definition of what constitutes a significant financial interest triggering investigator disclosure to the institution, while others apply looser, or in some cases stricter, thresholds requiring 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 non-clinical 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, in some cases, require documentation.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 of research.⁸

To whom faculty members are required to disclose their financial interests is the second sub-category 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, IRBs, conflict-of-interest (COI) committees, and 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

The Existence and Function of COI Committees – The existence of COI committees is becoming more universal at research institutions, particularly medical research institutions. However, their function within institutions 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

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

Management Strategies – Management strategies employed to address financial conflicts vary, from very informal strategies such as disclosure alone or self-monitoring plans, to more formal processes whereby a subcommittee develops a plan and regularly monitors investigator compliance.¹⁹ However, while some institutions use informal methods to identify investigator disclosure inconsistencies, none of the surveyed institutions had a formal procedure for verifying whether investigators had fully disclosed.²⁰

Financial Conflict-of-Interest Policies Governing Institutions - Despite the lack of any federal requirement for such policies, some institutions have instituted institutional 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 they are implemented. Many institutions use “firewalls” to separate research/academic endeavors and investment/financial activities, while in stark contrast, others encourage interaction between their academic and investment offices.²² In addition, variation can be found in the amount, timing, and involvement 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. These variations, while illustrating one dimension of the spectrum of conflict policies currently in existence, do not adequately capture their 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 above surveys and reports highlight significant variations in financial conflict-of-interest policies at the institutional level, an examination of policy implementation is also 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 University, 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 non-traditional model, as its affiliated hospitals function as independent entities. In contrast, Stanford University operates under the more traditional model, with the hospital and the University functioning as an integrated whole. Beyond organizational structure, subtle disparities at the written policy level and at the practice level 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 instituted a conflict-of-interest policy, later revised 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, and 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. Non-faculty, such as HMS staff members are not subject to these policies, though 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, as the institution recognizes the mutually beneficial nature of such relationships as well as the potential public benefit resulting from such collaboration.²⁷ However, the HMS policy also recognizes the importance of scientific integrity and public confidence in academic research. To that end, HMS's conflict-of-interest 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 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 the "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 are generally not allowed under sections (a) and (b), and those conflicts that are generally 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, such as 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 minimus 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 minimus threshold is not applicable to non-publicly traded equity interests. Thus, a faculty member would generally 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 minimus 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 minimus 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 which 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 minimus threshold of \$20,000 from Category I (a) applies. Thus, HMS would generally not allow a faculty member to conduct university-sponsored clinical or pre-clinical 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. However, the reality of what is actually allowed 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, transforming “Generally Not Allowable” activities with the possibility of an exception into essentially prohibited activities. As such, in practice, 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 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 under oversight by the University’s Committee on Patents and Copyrights (CPC).⁴³ Notably, in terms of Harvard Medical School specifically, the licensing policy only applies 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 5% 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, advising 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 Committee on Patents and Copyrights.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 Harvard Medical School, Stanford School of Medicine (SSOM) does not operate under a conflicts policy specific to the medical school. Rather, SSOM is governed by Stanford's general conflict policy included in the University's Research Policy Handbook (RPH). Stanford's approach to conflict-of-interest is arguably, to some extent, a byproduct of the institution's organizational structure and size, quite different than that found at Harvard. Stanford University has a more integrated organizational structure, where 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 found 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 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 However, for any research activity, 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 thus, heightened 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 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; (5) or, 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 conflict-of-interest 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 conflict of interest committee can disapprove of research, regardless of IRB approval. However, in cases where the IRB rejects research, 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, with decisions made 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 Harvard Medical School, categorizing 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, yet in practice, also raises the possibility of less predictability for faculty members proposing research, and less uniformity of decisions across the institution or over time in a given period. 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 However, when faculty involvement is limited to equity holdings or advisory roles, 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 over 10% 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 faculty 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 However, the policy does not specify under what conditions a review is considered "appropriate."

C. Summary

Harvard Medical School and Stanford University embody 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, setting different disclosure thresholds, providing faculty with disparate levels of guidance, and requiring disclosure at different times and under different circumstances. Substantial differences are also 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 hospital's 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. While the organizational structure of Stanford provides for a more uniform umbrella policy without the added complexity of policies at individual institutions, as implemented, the less structured policy 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 currently existing nationwide, 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, have recently come under increasing scrutiny. Financial relationships in medical research, especially research involving human participants, have been most closely scrutinized so as to understand the 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 between the various policies, there is also considerable agreement. For example, many organizations suggest establishment of a conflict-of-interest committee at research institutions, broader disclosure within the institution, increased communication between IRBs and COI committees, as well as stricter standards for research involving human subjects. However, the recommendations tend to remain quite general, stopping short of providing detailed guidance for research institutions.

Table 2 provides a summary of the main similarities and differences found among 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. 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 conflict-of-interest committee, primarily responsible for conflict-of-interest issues.⁷⁵ To further that committee's work, the document promotes increased communication and reporting among institutional officials, the COI committee, IRBs and technology licensing offices,⁷⁶ as well as extensive disclosure of conflicts within the institution.⁷⁷ The policy also addresses the mechanics of policy implementation, recommending electronic reporting systems, the allocation of additional resources to conflict issues, and education and training efforts for faculty, staff, students, and trainees.⁷⁸

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.⁷⁹

Two principles of the AAMC's recommendations also deserve special attention. First, the AAMC recommends that institutions establish a rebuttable presumption automatically prohibiting an individual from conducting research when that individual has a significant financial interest, regardless of how the research is being funded.⁸⁰ Second, the AAMC policy allows "compelling circumstances" to rebut this presumption, though this term is not specifically defined.⁸¹ Rather, the policy recognizes that institutional circumstances vary, and provides elements for COI committees to consider when making such determinations.⁸²

Importantly, this proposed automatic presumption of impropriety draws a bright line for prohibited activities, perhaps easing the identification of those conflicts requiring 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. However, 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 those who must make the determinations of 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.⁸³ 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.⁸⁴ Significantly, the report recommends handling conflicts on a case-by-case basis as, "[m]any financial interests are not conflicts, and many conflicts can be managed."⁸⁵ However, the report also states 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.⁸⁶ Finally, the document advocates extensive disclosure, with conflicts disclosed to the institution, federal agencies, human participants through IRBs, and in publications and oral presentations.⁸⁷

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.⁸⁸ 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.⁸⁹ Specifically, the report advocates for the segregation of financial and research decision-making processes, the establishment of clear policies, administrative processes, and a review board to assess conflict issues and make determinations as to how to manage them.⁹⁰ However, the report stops short of more specific guidance in these areas.

C. The General Accounting Office

The General Accounting Office, in its report examining institutional variations in conflict of interest in biomedical research, concluded with two policy recommendations for the Department of Health and Human Services.⁹¹ Specifically, the report recommends that the Department of Health and Human Services 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.⁹² In addition, the GAO suggests the Department 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.⁹³

D. The National Bioethics Advisory Commission

In an extensive review of research involving human subjects, the National Bioethics Advisory Commission (NBAC) addresses financial conflicts of interest, focusing on IRB conflicts of interest.⁹⁴ In addition to its focus on IRBs, the report provides a review and limited recommendations on individual conflicts. NBAC acknowledges that the prohibition of all conflicts is not feasible, stating that IRB review of financial conflicts will not be sufficient, as IRBs are currently limited in the type and scope of their reviews.⁹⁵ NBAC recommends that institutions inform IRBs of investigator financial conflicts to allow IRBs to use such information to determine possible disclosure to human participants.⁹⁶ However, NBAC also encourages institutions and sponsors to take responsibility for oversight of financial conflicts.⁹⁷

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.⁹⁸ In a guidance document issued in 2000, NIH estimates that 25% of IRBs currently deal routinely with financial conflicts of interest.⁹⁹ 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 encouraging the screening of conflicts at an earlier stage.

NIH has also proposed several approaches to minimizing the potentially detrimental effects of financial conflicts of interest on research activities.¹⁰⁰ 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 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.¹⁰¹

V. Conclusion

Financial conflicts of interest in medical research has 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 with 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 will necessarily 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 ◆ Non-traditional ‘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 ◆ De minimus 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 non-clinical 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 ◆ 4 types of events trigger heightened 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
Key Distinctions	<ul style="list-style-type: none"> ◆ In practice, Category I conflicts prohibited; few of these cases ever reviewed ◆ Distinction between clinical vs. pre-clinical 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. pre-clinical work ◆ Distinction between income and equity distinction - yet, ‘income’ not clearly defined ◆ Royalty payments not explicitly included in “significant financial interest”; yet all technology licensing arrangements trigger heightened 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

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¹ See United States General Accounting Office, 2001. *Biomedical Research: HHS Direction Needed to Address Financial Conflicts of Interest*. Washington, D.C.: General Accounting Office, at 11.

² See generally SV McCrary et al., *A National Survey of Policies on Disclosure of Conflicts of Interests in Biomedical Research*, NEW ENG. J. MED. 343(22): 1621-1626.

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

⁴ See, McCrary, *supra* note 2 at 1624-1625.

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

⁶ See GAO Report at 13; see McCrary, *supra* note 2 at 1622-1623.

⁷ See GAO Report at 13.

⁸ See generally MK Cho et al., *Policies on faculty Conflicts of Interest at U.S. Universities*, JAMA 284(17): 2203-2208; see generally B Lo et al., *Conflict-of-Interest Policies for Investigators in Clinical Trials*, NEJM 343(22): 1616-1620.

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 *id.* at 13-15.

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.*

²³ See *id.* at 20.

²⁴ Harvard Medical School, Policy on Conflict of Interest and Commitment, *available at* <<http://www.hms.harvard.edu/integrity/conf.html>>.

²⁵ See Harvard Medical School, Faculty of Medicine Statement on Research Sponsored by Industry, *available at*

<<http://www.hms.harvard.edu/integrity/industry.html>>.

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

²⁷ See *id.*

²⁸ See *id.*

²⁹ See *id.*

³⁰ See Harvard Medical School, Policy on Conflicts of Interest and Commitment – 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>>.

³² See *id.*

³³ See *id.*

³⁴ See *id.*

³⁵ See *id.*

³⁶ See *id.*

³⁷ See *id.*

³⁸ See Harvard Medical School, Policy on Conflicts of Interest and Commitment - 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>>.

⁴² See *id.*

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>>.

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>.

⁵³ See generally Stanford University Faculty Policy, *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>.

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>.

⁵⁷ See Stanford University Faculty Policy, *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.*

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>.

⁶⁶ See *id.*

⁶⁷ See *id.*

⁶⁸ See *id.*

⁶⁹ See *id.*

⁷⁰ See *id.*

⁷¹ See Equity Acquisition in Technology Licensing and Learning Agreements, available at <http://www.stanford.edu/dept/DoR/rph/4-6.html>.

⁷² See *id.*

⁷³ See *id.*

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 December 2001, available at <http://www.aamc.org/members/coitf/start.htm>.

⁷⁵ See *id.* at 7-9.

⁷⁶ See *id.* at 14-15.

⁷⁷ See *id.* at 18-19.

⁷⁸ See *id.* at 15-16.

⁷⁹ See *id.* at 13.

⁸⁰ See *id.* at 20-21.

⁸¹ See *id.* at 16.

⁸² See *id.*

⁸³ See Association of American Universities, Task Force on Research Accountability, *Report on*

Individual and Institutional Financial Conflict of Interest. Released October 2001, available at <http://www.aau.edu/research/conflict/html>.

⁸⁴ See *id.* at 2-6.

⁸⁵ *Id.* at 4.

⁸⁶ See *id.*

⁸⁷ See *id.* at 5-6.

⁸⁸ See *id.* at 10.

⁸⁹ See *id.* at 12.

⁹⁰ See *id.* at 12-14.

⁹¹ See United States General Accounting Office. 2001. *Biomedical Research: HHS Direction Needed to Address Financial Conflicts of Interest*. Washington, D.C.: General Accounting Office (2001).

⁹² See *id.* at 29.

⁹³ See *id.*

⁹⁴ See National Bioethics Advisory Commission, *Ethical and Policy Issues in Research Involving Human Participants*, Volume I, Chapter 3; Bethesda, Maryland. August 2001.

⁹⁵ See *id.* at 59.

⁹⁶ See *id.* at 60.

⁹⁷ See *id.*

⁹⁸ See NIH Guidance, "Financial Conflicts of Interest and Research Objectivity: Issues for Investigators and Institutional Review Boards," June 5, 2000.

⁹⁹ See *id.*

¹⁰⁰ See *id.*

¹⁰¹ See *id.*