

Protecting Subjects, Preserving Trust, Promoting Progress II:

Principles and Recommendations for Oversight of
an Institution's Financial Interests in Human
Subjects Research

Task Force on Financial Conflicts of Interest
in Clinical Research

October 2002

All true universities, whether public or private, are public trusts designed to advance knowledge by safeguarding the free inquiry of impartial teachers and scholars. Their independence is essential because the university provides knowledge not only to its students, but also to the public agency in need of expert guidance and the general society in need of greater knowledge; and . . . these latter clients have a stake in disinterested professional opinion, stated without fear or favor, which the institution is morally required to respect.

*American Association of University Professors,
Declaration of principles (1915)*.*

* 1 Bull. Am. Assoc. Univ. Professors 40 (Spring 1954).

Protecting Subjects, Preserving Trust, Promoting Progress II:

Principles and Recommendations for Oversight of
an Institution's Financial Interests in Human
Subjects Research

Task Force on Financial Conflicts of Interest
in Clinical Research

October 2002



AAMC Task Force on Financial Conflicts of Interest In Clinical Research

Task Force Chair

William Danforth, M.D.
Chancellor Emeritus and Vice-Chairman, Board of Trustees,
Washington University at St. Louis

John Thomas Bigger, M.D.
Professor of Medicine and
Pharmacology
Columbia University

Frank Davidoff, M.D.
Editor
Annals of Internal Medicine

Martin J. Delaney
Founding Director
Project Inform

Susan Dentzer
NewsHour with Jim Lehrer

Susan H. Ehringhaus, Esq.
Vice Chancellor and General Counsel
University of North Carolina at Chapel
Hill

Ginger Graham
Group Chairman
Guidant Corporation

Susan Hellmann, M.D., M.P.H.
Chief Medical Officer
Genentech

Jeffrey Kahn, Ph.D., M.P.H.
Director
Center for Bioethics
University of Minnesota

Marvin Kalb
Executive Director, Washington Office
Joan Shorenstein Center for the Press,
Politics and Public Policy
John F. Kennedy School of Government

Russel E. Kaufman, M.D.
Vice Dean
Education and Academic Affairs
Duke University School of Medicine

Robert P. Kelch, M.D.
Dean
University of Iowa College of Medicine

Mark R. Laret
Chief Executive Officer
University of California, San Francisco
Medical Center

Joan S. Leonard, Esq.
Vice President and General Counsel
Howard Hughes Medical Institute

Ronald Levy, M.D.
Robert K. and Helen K. Summy
Professor in the School of Medicine
Stanford University

Constance E. Lieber
President
NARSAD

Joseph B. Martin, M.D., Ph.D.
Dean, Faculty of Medicine
Harvard Medical School

Edward D. Miller, M.D.
Dean, Johns Hopkins School of
Medicine
CEO, Johns Hopkins Medicine

Thomas H. Murray, Ph.D.
President and Chief Executive Officer
The Hastings Center

Charles P. O'Brien, M.D., Ph.D.
Chief of Psychiatry
Philadelphia Veterans Affairs Medical
Center
Kenneth Appel Professor and Vice-
Chair of Psychiatry
University of Pennsylvania

Hon. John E. Porter, Esq.
Partner
Hogan and Hartson, L.L.P.

Roger Porter, M.D.
Vice President Clinical Research and
Development
Wyeth-Ayerst Research

Paul G. Ramsey, M.D.
Vice President for Medical Affairs and
Dean of the School of Medicine
University of Washington

Dorothy K. Robinson, Esq.
Vice President and General Counsel
Yale University

Frances M. Visco, Esq.
President
The National Breast Cancer Coalition

Savio Woo, Ph.D.
Director and Professor
Institute for Gene Therapy
Mount Sinai School of Medicine

Alastair J.J. Wood, M.D.
Assistant Vice Chancellor for Research
Professor of Medicine
Professor of Pharmacology
Vanderbilt University School of Medicine

AAU Liason

Richard J. Turman
Director of Federal Relations
The Association of American
Universities
1200 New York Avenue, NW, Suite 550

AAMC Staff

David Korn, M.D.
Senior Vice President
Association of American Medical
Colleges
Division of Biomedical and Health
Sciences Research

Jennifer Kulynych, J.D., Ph.D.
Director and Regulatory Counsel
Association of American Medical
Colleges
Division of Biomedical and Health
Sciences Research

The work of the Task Force was supported in part by a grant from the Howard Hughes Medical Institute.

Introduction: New Recommendations To Address an Emerging Concern

Academic institutions are privileged to serve as a public trust for the advancement, preservation, and dissemination of knowledge. These institutions have diverse obligations: to students, faculty, and staff; to legislators and regulators; to donors and benefactors; and to society at large. When meeting these obligations in the ordinary course of business, institutions must and do reconcile competing interests.¹ In so doing, institutions recognize widely that policies must be made and decisions taken in a manner that is free of the taint of improper bias or conflict of interest.

Increasingly, academic institutions that conduct research also invest in -- and accept the philanthropy of -- commercial research sponsors. Regulators, legislators, journalists, and patient advocates have now begun to question whether such financial relationships may give rise to "institutional" conflicts of interest that could threaten research integrity and, especially troubling, potentially pose risks to human research subjects. Concern has arisen that existing institutional processes for resolving competing interests may be insufficient when the institution has a financial interest in the outcome of research and the safety and welfare of human subjects are at stake.

Although perceived risks to human subjects have received the greatest attention thus far, the growing perception that research institutions may have financial conflicts of interest also threatens to weaken public support for research. In an era of tremendous public investment in academic research, legislators and policymakers and others justifiably expect heightened public accountability from research institutions.

In a 2001 report to Congress, the General Accounting Office addressed concerns about institutional financial interests in research, noting that equity ownership or other investment in a research sponsor "may color [an institution's] review, approval, or monitoring of research conducted under its auspices or its allocation of equipment, facilities, and staff for research."² The GAO called upon the U.S. Department of Health and Human Services to promulgate new regulations or to issue guidance to address institutional conflicts of interest.

The AAMC's Task Force on Financial Conflicts of Interest in Clinical Research believes that an institution holding certain financial interests related to its human subjects

¹ For example, an institution may adopt policies that require board members to disclose any financial or other personal interests in companies that transact business with the institution.

² U.S. General Accounting Office, *Biomedical Research: HHS Direction Needed to Address Financial Conflicts of Interest* (GAO-02-89) (November 2001) at 7 [hereafter "GAO Report"].

research³ may face a conflict of interest when that institution employs the individuals who review, supervise, and conduct the research. This is especially troubling because the regulation of federally sponsored university research is centered on the principles of institutional integrity in the conduct of that research and responsibility and accountability for its oversight. Because the safety and welfare of research subjects and the objectivity of the research could be -- or could appear to be -- compromised whenever an institution holds a significant financial interest that could be affected by the outcome, the Task Force offers the principles and the recommended processes described in this report as a means to address an institution's competing fiduciary responsibilities and ethical obligations in the context of human subjects research.

As an initial response to a problem of remarkable complexity, this report does not provide an exhaustive list of potentially troubling financial interests; nor does it prescribe a comprehensive scheme for the oversight of all institutional relationships with commercial research sponsors. Instead, the report offers a conceptual framework for assessing institutional conflicts of interest and a set of specific recommendations for the oversight of certain financial interests in human subjects research that, in the view of the AAMC's Task Force, are especially problematic and must therefore receive close scrutiny.

The Task Force recognizes that the Association of American Universities, in its role as the representative of the leaders of major research universities, has issued recommendations on institutional conflicts of interest and continues to develop policies applicable to an institution's financial interests in research of any type. The AAMC's Task Force believes that its own recommendations, which apply specifically to financial interests in human subjects research, complement and further develop the general recommendations issued by the AAU in its 2001 Report on Individual and Institutional Financial Conflict of Interest.⁴

I. A Framework for Assessing Institutional Conflicts of Interest in Human Subjects Research

An institution may have a conflict of interest in human subjects research whenever the financial interests of the institution, or of an institutional official acting within his or

³ "Human subjects research" includes all research meeting the definition of "research" performed with "human subjects" as these terms are defined in federal regulations at 45 C.F.R. Part 46 and 21 C.F.R. Part 56, without regard to the source of the research funding or whether the research is otherwise subject to federal regulation. In the event that the federal definitions of "human subject" or "research" are modified through rulemaking, any such revisions shall apply for the purpose of this guidance.

⁴ Association of American Universities, Task Force on Research Accountability, Report on Individual and Institutional Financial Conflict of Interest (Oct. 2001). Among the AAU's recommendations were the following: that institutions segregate decisionmaking about financial and research activities so they are separately and independently managed, and that institutions establish a review group to evaluate possible conflicts arising from the financial interests of the institution and its officials.

her authority on behalf of the institution, might affect -- or reasonably appear to affect -- institutional processes for the conduct, review, or oversight of human subjects research.

An institution conducting human subjects research may face a conflict among multiple duties or interests. Among these are a duty to protect human subjects, a duty to ensure the integrity of research and its compliance with applicable law and regulation, and the institution's legitimate interest in its own financial health and the economic viability of its academic and research missions. Institutional policies should affirm that the welfare of human subjects and the integrity of research will not be compromised -- or appear to be compromised -- by competing institutional interests or obligations.

Such compromise is possible when an institution fails to separate fully and reliably the responsibility for the administrative oversight of human subjects research from the responsibility for the management of certain financial interests. Institutions should ensure that the responsibility for human subjects research does not overlap or coincide with the responsibility for those institutional financial interests that may be directly affected by the outcome of the research. Individuals with authority for the immediate oversight of human subjects research, such as deans, chairs, department and laboratory heads, and IRB chairs, should not have responsibility for the management of an institution's investments or technology transfer program.⁵

As a fundamental principle, institutions should ensure that in practice, the functions and administrative responsibilities related to human subjects research are separate from those related to investment management and technology licensing.

The GAO noted in its 2001 report on financial conflicts of interest that several of the five major research institutions that it examined did attempt to separate financial and research functions, either by segregating technology transfer offices organizationally from the administration of research or by erecting "firewalls" between the management of institutional investments and academic affairs.⁶ The AAMC's Task Force believes that institutions may achieve credible separation of function when technology transfer is segregated from human subjects research administration and when institutional financial interests, such as the endowment and other investments, are managed externally, through legally

⁵ The Task Force recognizes that at some level of senior institutional administration -- whether the office of president, vice president, or provost -- responsibilities for oversight of these functions will necessarily converge.

⁶ GAO Report, *supra* note 2, at 4.

separate organizations.⁷ When such financial interests are managed within the institution, separation of function is more challenging and requires policies and procedures for ensuring the strict segregation of all human subjects research and investment management responsibilities.⁸ Ultimately, however, each institution must determine how best to segregate human subjects research and investment management functions fully and reliably within the context of its own organization and governance structure.

Implicit in the principle of separation of function is an acknowledgement that in general, circumstances in which investment and research responsibilities are formally and effectively separate do not foster institutional conflict of interest. Importantly, however, circumstances exist in which separation of function is not sufficient to avoid the appearance of institutional conflict of interest. As described in Section III, even when separation of function has been achieved, certain financial relationships with commercial sponsors should be examined closely for the presence of institutional conflict of interest. Institutions should, as a matter of prudence, establish mechanisms for formally reviewing such financial relationships and assessing the nature and extent of any conflict of interest. Moreover, where such relationships exist, institutions should presume that absent compelling circumstances and careful management of the conflict, the human subjects research in question should not be conducted at, or under the auspices of, the conflicted institution.

II. Institutional Officials

At times the institution's officers and administrators may face a conflict between a primary and professional duty-- serving the institution -- and a secondary, personal interest, namely, the possibility of individual financial gain. Personal financial interests are ordinarily governed by an institution's policies on individual conflicts of interest.

In some cases, however, an official's position may convey an authority that is so pervasive or a responsibility for research programs or administration that is so direct⁹ that a conflict between the individual's financial interests and the institution's human subjects research should also be considered an "institutional conflict of interest."

⁷ With regard to institutional investments, the Task Force distinguishes between the functions of oversight and management, and uses the term "management" to refer to day-to-day decisions about investing in individual securities, funds, etc. The Task Force recognizes that the institution's board or other governing body will typically oversee the selection of investment managers and the evaluation of manager performance.

⁸ Moses and Martin (2001) have suggested that institutions create a separate entity to hold and manage individual and institutional equity interests in research sponsors. The investment company would be overseen by a board with "wide representation," including representatives from outside the university. Hamilton Moses and Joseph B. Martin, *Academic Relationships With Industry: A New Model for Biomedical Research*, 2001 JAMA 285, 933.

⁹ An institutional official with direct responsibility for research has the capacity, by virtue of his or her position, to reasonably affect or appear to affect the conduct, review, or oversight of current or proposed research at the institution.

Such an individual might be, for example, the dean of research, but might also be the head of a laboratory or institute or the director of a division or department in which the research is conducted, depending upon the organizational structure of the institution and the autonomy of investigators within the administrative unit.

Consequently, when an individual has the authority to make decisions that affect or reasonably appear to affect the conduct, review, or oversight of human subjects research at the institution,¹⁰ while at the same time holding a significant financial interest in the investigational product or the research sponsor (with reference to the valuation thresholds in the 2001 AAMC guidelines on individual financial interests) an institutional conflict of interest may exist. In such cases, the individual should disclose all relevant circumstances to a superior, and if any conflicts of interest cannot be eliminated through recusal, or managed effectively via a strategy approved by the appropriate institutional committee, the research should not be conducted within or under the auspices of the institution.¹¹

Beyond compliance with policies and procedures, institutional officials must foster what has been described as a "culture of conscience" in the research enterprise.¹² Exercising their authority within the institution, officials should insist upon rigorous enforcement of conflict of interest policies. Leading by personal example, officers and administrators should demonstrate to the academic community and to the public that compliance with these policies, including full disclosure of financial conflicts of interest, is an imperative reflecting core institutional values.

III. Circumstances That *Ipsa Facto* May Create - or Appear to Create - Institutional Conflict of Interest (ICOI) in Human Subjects Research and Must Therefore Receive Close Scrutiny

It is the view of the Task Force that certain financial relationships between institutions and commercial sponsors of human subjects research may present -- or appear to

¹⁰ For example, the official may have the authority to make supervisory decisions about the institution's or administrative unit's research program, or promotion and tenure decisions regarding research faculty. Institutions may also wish to consider how best to dissuade senior faculty with significant financial interests in research sponsors from transferring pro forma responsibility for a research protocol to a junior colleague, in an attempt to avoid disclosure and oversight of financial conflicts of interest.

¹¹ The Task Force recognizes that some institutions have established policies governing potential conflicts of interest arising from the personal financial interests of institutional officials. If an official lacks the authority to make decisions that will affect or appear to affect the conduct, review, or oversight of research, that official's financial interests should be evaluated and, if necessary, managed or eliminated as required by an institution's applicable policies on individual conflict of interest.

¹² Charles Marwick, New Head of Federal Office Clear on Protecting Human Research Participants, 2002 JAMA 284, 1501, 1502.

present -- a conflict of interest, even though an institution has fully separated all of its research and investment functions. Such circumstances warrant the highest degree of scrutiny in every instance in which they occur.

Accordingly, when one or more of the following circumstances exist, the institution should conduct a specific, fact-driven inquiry into whether the particular financial relationship may affect or reasonably appear to affect human subjects research conducted at or under the auspices of the institution:

- A. When the institution is entitled to receive royalties from the sale of the investigational product that is the subject of the research;
- B. When, through its technology licensing activities or investments related to such activities, the institution has obtained an equity interest or an entitlement to equity of any value (including options or warrants) in a *non-publicly traded* sponsor of human subjects research at the institution;
- C. When, through technology licensing activities or investments related to such activities, the institution has obtained an ownership interest or an entitlement to equity (including options or warrants) of greater than \$100,000 in value (when valued in reference to current public prices, or, where applicable, using accepted valuation methods), in a *publicly-traded* sponsor of human subjects research at the institution;¹³ [see fn] or
- D. When, with regard to a specific research project to be conducted at or under the auspices of the institution, institutional officials with direct responsibility for human subjects research (see Section II) hold a significant financial interest in the commercial research sponsor or the investigational product. “Significant financial interest” is defined for this purpose as one or more of the following:
 1. An equity interest or entitlement to equity (including options or warrants) of any amount in a *non-publicly traded* sponsor of human subjects research conducted at or under the auspices of the institution;
 2. An equity interest or entitlement to equity (including options or warrants) in excess of the *de minimis* amount (and not including exceptions for certain

¹³The AAMC should periodically reassess this threshold to determine whether the amount remains appropriate for the purpose of identifying possible ICOI. The Task Force notes also that ownership interests in subsidiary companies acting as sponsors of institutional research involving human subjects may warrant scrutiny at lower threshold amounts.

- mutual funds), as defined in the AAMC's 2001 guidelines for individual financial interests, in a publicly traded sponsor of human subjects research conducted at or under the auspices of the institution;
3. Consulting fees, honoraria, gifts or other emoluments, or "in kind" compensation from a sponsor of human subjects research conducted at or under the auspices of the institution, that in the aggregate exceeded the de minimis amount as defined in the AAMC's 2001 guidelines for individual financial interests, or are expected to exceed that amount in the next twelve months;
 4. An appointment to serve, in either a personal or representative capacity, as an officer, director, or board member of a commercial sponsor of human subjects research conducted at or under the auspices of the institution, whether or not remuneration is received for such service; or
 5. An appointment to serve on the scientific advisory board of a commercial sponsor of human subjects research conducted at or under the auspices of the institution, unless the official has no current significant financial interest in the sponsor or the investigational product and agrees not to hold such an interest for a period of no less than three years following completion of any related research conducted at or under the auspices of the institution.

IV. Other Financial Relationships That May Warrant Close Scrutiny

In addition to those circumstances identified in Section III, which must always be examined for the presence of conflict of interest, the Task Force recognizes that other financial relationships with research sponsors may warrant internal or external scrutiny, depending upon the relevant circumstances. Examples of the relationships that may fall in this category are listed below.

This list of other financial relationships that may warrant scrutiny is not intended to be exhaustive; nor does the Task Force attempt to recommend specific mechanisms for oversight of the relationships described. As a general rule, institutions should determine the nature and degree of scrutiny required for any of these relationships or interests by assessing the potential for conflict of interest and weighing the magnitude of any risk to human subjects.

The Task Force recommends that when developing policies and procedures to address potential conflicts of interest, institutions pay particular attention to the following circumstances:

- A. When an investigator, research administrator, or institutional official with research oversight authority participates materially in a procurement or purchasing decision involving major purchases from, or non-routine supply contracts with, a commercial entity that sponsors human subjects research at the institution; or
- B. When the institution has received substantial gifts (including gifts in kind) from a potential commercial sponsor of human subjects research. Evaluation of the potential sponsor's gift history might include the following:
 - (1) Whether a gift is of sufficient magnitude that even when held in the general endowment for the benefit of the entire institution, it might affect, or reasonably appear to affect, oversight of human subjects research at the institution;
 - (2) Whether a gift is held for the express benefit of the college, school, department, institute or other unit where the human subjects research is to be conducted; or
 - (3) Whether any institutional officer who has the authority, by virtue of his or her position, to affect or appear to affect the conduct, review or oversight of the proposed human subjects research has been involved in solicitation of the gift.

Although the listed circumstances are potential areas of concern, the Task Force does not intend to preclude institutions from accepting the philanthropy of corporations that sponsor human subjects research. Rather, the Task Force is recommending that institutions develop means of identifying such circumstances and managing, through disclosure and as otherwise appropriate, any actual or apparent conflicts of interest that may result. In addition, the Task Force recommends that institutions adopt clear policies governing the handling of gifts. All gifts should be accepted in conformance with those policies and reported to the development office for record-keeping purposes. Faculty should be held accountable for adhering to gift policies.

V. Structure of ICOI Reporting and Review Process

A. Institutional Conflict of Interest (ICOI) Committee

The Task Force recommends that an institution form a standing ICOI committee for the purpose of reviewing the circumstances described in Section III, (except when any conflicts of interest attendant to these circumstances have been resolved through recusal or otherwise eliminated). The Task Force recommends that the ICOI committee members be individuals who have sufficient seniority, expertise, and independence to evaluate the competing interests at stake and make credible and effective recommendations. All members of the ICOI committee should be independent of the direct line of authority for human subjects research oversight within the institution. One or more external ("public") members are strongly urged, as the inclusion of public members will increase the transparency of the committee's deliberations and enhance the credibility of its determinations. Recusal should be required whenever any member has an actual or apparent conflict of interest with regard to any matter under review.

Thus, an ICOI committee might include one or more members of the board of trustees, one or more individuals with no professional, personal, or financial ties to the institution, and one or more senior faculty. An ICOI committee should include one or more alternates to sit in place of any member who has recused himself or herself from the deliberations.

The Task Force recognizes that many institutions have created committees to review individual conflict of interest. Some institutions may prefer to rely upon those committees for ICOI review rather than forming separate ICOI committees. Each institution must determine which committee structure is most appropriate to its organizational structure and governance; however, the Task Force urges institutions to consider the advantages of separate committees, in view of the complexity and sensitivity of the issues to be considered by the ICOI committee, the need for participation by senior officials, and the strong recommendation that public members be included.

B. Reporting of Institutional Financial Interests Obtained Through Licensing Agreements.

The institution's office of technology licensing should report to the ICOI committee (or an appropriate institutional official charged with identifying circumstances for ICOI review) when, as the result of a licensing agreement, the institution takes (or intends to take) an equity interest, stock options, or any entitlement to an ownership interest in, or

royalty payments from, a potential sponsor of human subjects research conducted at or under the auspices of the institution.¹⁴

C. Reporting and Review of Personal Financial Interests of Institutional Officials

Institutional officers, board members, and administrators who oversee human subjects research -- including the president, vice president for research, deans, chairs, institute heads, and the chairs of the IRB and COI committees --should be required, under institutional policies for individual conflicts of interest, to make an annual report of any personal financial interests that might appear to be affected by human subjects research conducted at or under the auspices of the institution. (As a guide to determining *de minimis* exemptions to this policy, institutions should apply the valuation thresholds in the AAMC's 2001 guidelines for the oversight of individual financial interests in human subjects research.)

The financial reports of institutional officials with research oversight responsibilities should be received by the institution's COI or ICOI committees (or their designated representatives), as appropriate, or, in the case of senior officers and board members, by the audit or other committee or subcommittee of the board, or its designee. The reviewing committee should determine whether significant financial interests in an investigational product or in a sponsor of human subjects research may be managed effectively or should be eliminated. All such decisions should be documented and communicated to the individual and his or her superior. When the COI or ICOI committee determines that an official should be permitted to hold a significant financial interest in an investigational product or commercial research sponsor even though the official will not be formally recused from research-related responsibilities, this information should be communicated to the IRB of record.

D. Rebuttable Presumption Against Certain Institutional Financial Interests In Human Subjects Research

When reviewing any of the circumstances described in Section III, the ICOI committee should apply a rebuttable presumption against conduct of the human subjects research at or under the auspices of the institution. The presumption may be rebutted when the circumstances are compelling and the committee has approved an effective conflict management plan. Whether the ICOI committee deems the circumstances to be

¹⁴ The question of whether an institution should take an equity position in a research company is a matter for the institution to decide. Institutions should, however, develop clear policies to guide such decisions, and should consider whether equity positions might create the appearance of unacceptable conflict of interest if related human subjects research were to be conducted at the institution.

compelling should depend in each case upon the nature of the science, the nature of the interest, how closely the interest is related to the research, the degree of risk that the research poses to human subjects, and the degree to which the interest may be affected by the research. The committee should consider whether the institution is uniquely qualified, by virtue of its attributes (e.g., special facilities or equipment, unique patient population) and the experience and expertise of its investigators, to conduct the research and safeguard the welfare of the human subjects involved.

Even when the institution is deemed uniquely qualified, conflicts associated with significant risk to human subjects should be avoided whenever possible and, if permitted, should be managed closely.

E. Report of Institutional Conflicts of Interest to the Institutional Review Board

After reviewing a significant financial interest in research, the ICOI committee should communicate its conclusions, along with any management conditions to be imposed, to the institutional review board(s) having jurisdiction over the research. All relevant conflicts should be disclosed to research subjects in a form to be determined by the IRB of record.

VI. **Additional Recommendations**

- A. Multi-Center Trials. When the institution holds one of the financial interests described in Section III and any conflicts of interest will not be eliminated through recusal or otherwise, the presumption should be that the institution will not conduct related human subjects research except as the non-primary site in a multi-center trial. Even when participating as other than the primary site in a multi-center trial, the institution should not serve as the coordinating site unless the possible institutional conflicts of interest described in Section III have been eliminated.
- B. External Monitoring of Single/Primary Site Trials. Serving as the sole or primary performance site might be justified under compelling circumstances (e.g., when the research is an early-stage or feasibility trial *and* the expertise of institutional investigators is essential to the research). In such a case, however, the ICOI committee should approve the circumstances, and if advisable, the research should be subject to monitoring by an oversight body with external members (e.g., a data and safety monitoring board).

- C. External IRB Review. When the ICOI committee has determined that compelling circumstances exist as described in Section V.D (above), the institution should consider the desirability of contracting with an external IRB to provide a second level of review and oversight.
- D. Recusal. The committee that reviews financial reports of institutional officials should have the authority to recommend that formal recusal be required when an official holds a significant financial interest in an investigational product or in an entity sponsoring human subjects research. The scope of this recusal should include any involvement in matters or decisions that might reasonably appear to affect the research. Recusal is not an effective management strategy when the individual, by virtue of conflicts arising from personal financial holdings, would be precluded from fulfilling the responsibilities of his or her position. In such cases, the best interests of the institution may necessitate that the individual divest the interests or vacate the position.
- E. Interim Recusal. If an institutional official who holds a significant financial interest in an investigational product or commercial research sponsor becomes aware that he or she must take an action or participate in a decision that may affect or reasonably appear to affect the institution's human subjects research, and the official has not yet been directed by the ICOI committee (or COI committee, if applicable) to recuse himself or herself from the matter, the official should be required to disclose the circumstances to his or her superior. The superior may determine that recusal is necessary, may decline to require recusal, or may refer the matter to the ICOI committee for resolution. When the superior declines to require recusal, the reviewing committee should make the final determination as to whether recusal is in fact necessary. In any case, the superior should document his or her recusal determination and forward this documentation to the ICOI committee. The ICOI should maintain a central repository of information about all recusal determinations related to the institution's human subjects research.
- F. Hospital as a Separate Entity. At times the institution's faculty, staff, or students may conduct human subjects research at affiliated, yet legally separate, hospitals or clinical sites. The Task Force recommends that all affiliates operating under the institution's Federal-Wide Assurance (FWA) for the protection of human subjects agree to abide by ICOI policies that are the same as or no less stringent than those adopted by the institution.

- G. Accreditation. The effectiveness of an institution's ICOI policies and a formal assessment of the institution's compliance with these policies should be examined as an element of any accreditation process for the institution's human subjects protection program.

VII. IRB Members

- A. Applying the threshold valuation levels in the AAMC's 2001 guidelines for the oversight of individual financial interests, the institution should require that IRB members report annually any personal and significant financial interests that might reasonably appear to be affected by the scope of their responsibilities. These reports should include significant financial interests in sponsors of human subjects research when the IRB member is aware that the company in question is or may become a sponsor of human subjects research at the institution. The reports of IRB members should be reviewed by the institution's COI committee (i.e., the committee charged with reviewing the financial interests of faculty investigators), which should apply a presumption against significant individual financial interests in an investigational product or a commercial sponsor of the institution's human subjects research,¹⁵ and stipulate that the member should recuse himself or herself in any such circumstance, as described in VII.B.
- B. IRB members are required by federal regulation to recuse themselves from voting upon or participating in any deliberations concerning protocols in which they have conflicting interests. Institutional policies should reiterate that disclosure and recusal are required on a protocol-by-protocol basis for all IRB members. Institutions should require the IRB administrator to poll the IRB about potentially conflicting financial interests prior to the start of each meeting and to document members' responses in the meeting minutes. Institutions should consider providing the IRB administrator with a list of the research sponsors in which one or more IRB members hold a significant financial interest, to ensure that recusal occurs when necessary.

¹⁵ As described in the *2001 Guidelines*.

VIII. Disclosure

Disclosure to the IRB of record, to research subjects, and in all publications should be required whenever the institution holds a financial interest (as described in Section III) that is or could reasonably appear to be in conflict with a proposed human subjects research project under the terms of these policy recommendations, and the conflict has not been eliminated through recusal or otherwise.

The IRB of record should specify the form and content of the disclosure. When the financial interests of institutional officials are or could reasonably appear to be in conflict with the institution's human subjects research, disclosure should be required unless the official has been formally recused from participation in all matters that may affect or reasonably appear to affect the conduct, review, or oversight of the research.

Conclusion

The principles and processes articulated in this document should assist institutions in their oversight of financial interests that could have, or reasonably be perceived to have, an inappropriate effect upon human subjects research. The policy recommendations offered here are more expansive than current legal requirements or standard institutional practices. With the publication of this report, the Task Force aspires to assist the academic community in responding voluntarily and credibly to the emerging concern over institutional conflicts of interest in human subjects research. In tandem with the AAMC's *2001 Policy and Guidelines for the Oversight of Individual Financial Interest in Human Subjects Research*, these new *2002 Principles and Recommendations for the Oversight of an Institution's Financial Interests in Human Subjects Research* will contribute to maintaining public trust in the research enterprise and retaining the confidence of those who generously volunteer to participate in research.