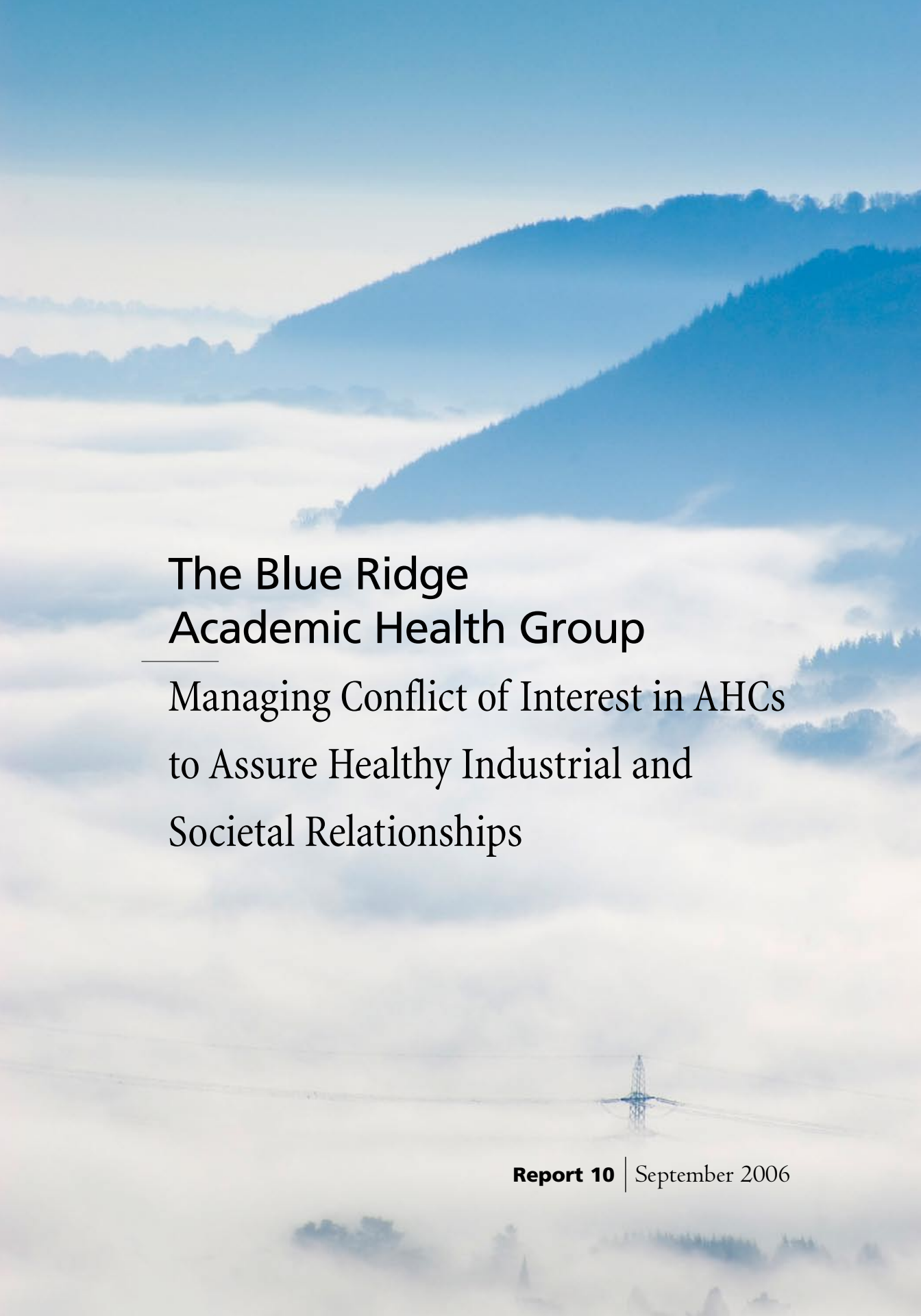

The Blue Ridge Academic Health Group

Managing Conflict of Interest in AHCs to Assure Healthy Industrial and Societal Relationships

Report 10 | September 2006

Mission: The Blue Ridge Academic Health Group seeks to take a societal view of health and health care needs and to identify recommendations for academic health centers (AHCs) to help create greater value for society. The Blue Ridge Group also recommends public policies to enable AHCs to accomplish these ends.

The Blue Ridge Academic Health Group

Managing Conflict of Interest in AHCs to Assure Healthy Industrial and Societal Relationships

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Report 10: Managing Conflict of Interest (COI) in AHCs to Assure Healthy Industrial and Societal Relationships

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The Blue Ridge Academic Health Group (Blue Ridge Group) studies and reports on issues of fundamental importance to improving our health care system and enhancing the ability of the academic health center (AHC) to sustain optimal progress in health and health care through sound research—both basic and applied—and health professional education. In nine previous reports, the Blue Ridge Group has sought to provide guidance to AHCs that can enhance leadership and knowledge management capabilities; aid in the adoption and development of Internet-based capabilities; contribute to the development of a more rational, comprehensive, and affordable health care system; improve management, including financial performance; address the cultural and organizational barriers to professional, staff, and institutional success in a value-driven health system; improve the education of physicians and other health professionals, lead comprehensive health care reform; and revive medical professionalism (Blue Ridge Academic Health Group 1998a, 1998b, 2000a, 2000b, 2001a, 2001b, 2003, 2004, 2005).

The Blue Ridge Group has been advocating for a "value-driven" health care system for nearly a decade. A healthy population is a paramount social good. A value-driven health system would manage both individual and population health and promote safety, quality, and efficiency. Through competition and rewards, providers, payers, states, communities and individuals alike would have incentives to achieve improvements in health. Universal and equitable access to evidence-based, effective care would help ensure that population health, information, and data management strategies can be implemented. A value-driven health system also would maintain the highest standards of professionalism and integrity in the pursuit of health and healing.

For more information, visit our web site at www.blueridgegroup.org.

The Blue Ridge Group has been advocating
for a "value-driven" health care system
for nearly a decade. A healthy population
is a paramount social good.

Executive Summary

In this, our 10th report, the Blue Ridge Group reviews the issue of conflict of interest (COI), particularly in the relationship between academic/nonprofit/government (ANG) health professionals and institutions and their partners and sponsors in the private sector. COI can compromise the integrity of research, education, care, and service. Even the appearance of COI can undermine the public's trust in and support for this vital work. Yet, the development and enforcement of COI policies at universities and AHCs is still very much underdeveloped—a work in progress. To further this work, we describe the emerging best approaches for managing COI and recommend action steps to improve COI policy and management. Additionally, to address gaps and problem areas in COI law and regulation, we recommend that the Institute of Medicine (IOM) become engaged to conduct a thorough review of this issue and to recommend updated approaches, which will further define COI issues in public/private sector collaboration to meet national and global health goals.

PART I.

Introduction

Conflict of interest is an increasingly significant problem in the complex relationships between ANG sector health professionals and institutions and their private sector partners and sponsors. COI can compromise the integrity of research, education, health care, and service. Even the appearance of COI can undermine the public's trust in and support for this vital work. For the sake of achieving optimal progress in advancing health and healing, ANG health professionals and institutions must better understand and manage COI.

In 1980, Congress passed the Bayh Dole Act (Bayh Dole), marking a watershed in public policy designed to facilitate scientific collaboration between the public and private sectors (Bayh Dole 1980). A brief history explains why this even was significant. In 1945, having overseen coordination of scientific efforts in the United States (which had played critical roles in the Allied victory in World War II), Vannever Bush catalyzed the creation of the National Science Foundation (NSF) and the National Institutes of Health (NIH). These government agencies would invest heavily in research at universities and help sustain the strong ties between academic science, industry, and the military that had been so successful in aiding the war effort. Yet, despite the ensuing large increase in discovery and the knowledge base, the process for translating discoveries and innovations into useful products and services often was slow and inefficient. Opportunities were lost. America's intellectual property patent and laws were major impediments. Among other problems, the laws held that the federal government retained title to any discovery made with government funds. This discouraged the private sector from developing ideas and technologies created in federally funded labs.

Bayh Dole marked the culmination of numerous efforts to reform U.S. patent law, enabling individuals and institutions to claim title to any invention or innovation made while supported in whole or in part by government funds. And it explicitly encouraged academic institutions and other public sector owners of such intellectual property to employ private sector partners to translate discoveries and innovations into new products and services. In an economy increasingly based on the development and exploitation of knowledge, Bayh Dole asks universities to be important engines of economic development.

Bayh Dole opened many new pathways for technology transfer, but it did not provide a comprehensive road map. In the intervening years, there has been tremendous expansion, innovation, and collaboration between the nonprofit and for-profit sectors. Evidence shows real gains for technology transfer. However, both the non-profit and for-profit sectors have experienced significant challenges in defining these relationships and in managing the resulting conflicts of interest. The challenge is to ensure the integrity of patient care, education, and basic and clinical research, especially in the drug and device development process. At stake is the public trust in AHCs and others in the ANG sector that rely upon that trust in carrying-out their missions.

The Blue Ridge Group believes that university AHCs and their administrators, researchers, and health professionals have special obligations to

protect the public interest by both maximizing opportunities for technology transfer and by being vigilant in ensuring the integrity of public/private sector relationships and their work products.

Conflict of Interest: What is it? Why should we care?

COI is best defined as "situations in which primary and secondary interests coexist" (Thompson DF 1993). Such situations can exist for both individuals and institutions. Primary interests within the academic environment include facilitating higher learning and the search for new knowledge and "truth" in the classical sense (AAUP 1954). Within the AHC and the health professions, these are supplemented by the primary interest of the patient, while seeking to help him or her, articulated in the Hippocratic Oath: "First, do no Harm".

Conflicts of interest matter for the AHC for two major reasons. **First**, they implicate the integrity of research and other activities associated with the environment and conditions for "free inquiry," within which scientists and others search for knowledge and truth. The search for truth and the infrastructures that support it rely largely on the public's trust and popular willingness to support such free inquiry with public funds. **Second**, COI is of special concern in the clinical research, health care, and education environments. Human vulnerability in light of disease and injury creates a moral imperative for the integrity of caregivers while the reliance of students and trainees on their teachers and mentors creates a moral imperative for the commitment of educators to the best interests of their students.

COI is not new in the academic or clinical environments. Long-standing secondary interests and sources of conflicts requiring management within academia and the nonprofit sector include hubris, the desire for academic promotion, competition for sponsored research support and "interesting cases," competition to be the first to publish discoveries, an aspiration for a good reputation and for higher pay and revenues, and competing commitments or outside interests. The public policy shift to enable greater collaboration with private industry is only the latest wrinkle in the challenge of earning and maintaining public trust in the integrity of research, training, and clinical care in the academic and nonprofit sectors. But it is a big wrinkle.

Bayh Dole opened a new and growing array of methods, influences, and situations through which secondary interests (including the primary interests of for-profit enterprises) can impinge —or give the appearance of impinging—on the integrity of academic, professional, nonprofit, and governmental activities. While individuals and businesses in the for-profit sector may share many of the goals, values, and missions of non-profits or professionals, the rules and imperatives of survival in the market place ultimately impose profit-making as the primary interest. Officers and directors owe a fiduciary duty to the company and to the shareholders to produce a return on investment. ANG individuals and institutions often fail to fully comprehend the implications of their participation with the private sector, especially secondary interests that may conflict with primary ANG interests and responsibilities.

The public policy shift to enable greater collaboration with private industry is only the latest wrinkle in the challenge of earning and maintaining public trust.

Research by Bekelman and colleagues underscores just how extensive are industry ties between the public and private sectors in research. Approximately one quarter of all U.S. investigators now have private industry ties, and roughly two thirds of academic institutions hold equity in start-ups that sponsor research performed at the institutions (Bekelman, et al. 2003). The financial rewards of industry collaboration can be significant. In university research alone, total private industry financial contributions now dwarf total public and private foundation support (Moses and Martin 2001). There is evidence of increasing private sector support for both basic and clinical research and of increasing returns to universities for their efforts in patenting and licensing of discoveries and innovations (E&Y 2000).

Exhibit 1: Categories of Faculty Relationships with Industry that give rise to COI

1. **Research relationships:** Support by industry, usually through a grant or contract.
2. **Consulting relationships:** The compensated provision of advice or information, usually from an individual academic or government scientist or administrator, to a commercial organization.
3. **Licensing relationships:** The licensing of government- or university-owned technologies to industry, often negotiated and managed by an office of technology transfer located within the government, universities, medical schools, or independent hospitals.
4. **Equity relationships**: The participation by academic or government scientists in the founding and/or ownership of new companies commercializing university- or government-based research.
5. **Training relationships:** In these cases, industries provide support for the research or educational expenses of graduate students or postdoctoral fellows, or contract with academic institutions to provide various educational experiences (such as seminars or fellowships) to industrial employees.
6. **Gift relationships:** Gift relationships are based on the transfer of scientific and nonscientific resources, independent of an institutionally negotiated research grant or contract, from industry to academic or governmental scientists.

(Campbell, et al 2005)

Understanding the COI Challenge

The challenges of identifying and managing COI in the academic environment are many. The entire ANG sector in the Bayh Dole era has become increasingly entrepreneurial. Faculty in AHCs now are expected not just to pursue discovery and innovation but also upon approaching or achieving such milestones to work immediately with the institution's "technology transfer" office to file patents and to seek licensees. Many faculty become entrepreneurs themselves and start companies to exploit their own discoveries, sometimes employing colleagues and/or students. Many serve in a variety of roles for private sector companies, including as board members, consultants, and advisers. These roles can range from participation in basic research to product development, from sales and marketing to professional education. Many types of remuneration are employed in these relationships, from direct payments to grants of stock and stock options, from consulting or lecture fees to direct or indirect support of an individual's research or laboratory and/or other university interests.

All of these relationships can "make sense" in the context of a particular situation or transaction. Yet each carries varying degrees of "secondary interest" implications that need to be known—and in many cases managed. Some must be prohibited outright.

Much has been written about COI in academia and the nonprofit sector. The sholarly literature on the subject spans the fields of health policy, ethics, law, politics, business, and the professions. And a popular, journalistic literature—often based on examples, reports and exposes of poorly managed COI—covers these issues often in all the major public and private journalistic and news media. Yet development and enforcement of COI policies at universities and AHCs is still very much underdeveloped—a work in progress.

PART II.

Findings

For our purposes, several findings stand out in this literature.

FINDING #1. ***COI matters a great deal to our public***

COI is a recurrent issue with a clear capacity for creating headlines of the type that most individuals and institutions would like to avoid. The capacity for headline creation indicates a strong public interest in the integrity of bioscience policy and practice. A single tainted study or a lone injured patient is sufficient to elicit public notice and outrage.

In recent years, a number of such scandals as well as tragic incidents involving research subjects have surfaced, raising important questions about whether investigators and/or their institutions have sufficiently identified and mitigated potential or actual secondary interests in the outcomes of the studies (Altman LK 2006). Many of these incidents have occurred at some of our nation's most prestigious medical centers and universities, including Harvard (Leary WE 1989), Johns Hopkins (Levine J 1990), the University of Pennsylvania (Vogel G 2000), and the Cleveland Clinic (Armstrong D 2005). Scandal concerning COI also penetrated recently to the heart of the conduct and sponsorship of federal research at the NIH (Willman D 2003). And many of the most prestigious medical and biomedical research journals also have felt the effect of COI questions, including the *New England Journal of Medicine* (NEJM) (Goozner 2004) and the *Journal of the American Medical Association* (JAMA) (Armstrong D 2006).

These examples are just a few of the better-known COI cases. COI revelations and scandals continue to strain and damage the public's trust in academic and nonprofit research and clinical care. We can and need to do better.

FINDING #2. ***COI mostly occurs not as a "headliner" issue, but in ways that are cumulative, less immediate, more subtle, and perhaps in the longer term even more damaging.***

More and more is becoming known about the mechanisms and effects of "secondary interests" for academic and other nonprofit-based individuals and institutions.

- Surveys of representative published biomedical research in a number of fields show significant statistical relationships between industry sponsorship and positive research results (Bekelman, et al. 2003).
- There are examples of clinical research studies where researchers have failed to divulge relevant industry sponsorship or ties and where reported results have been more positive than would be expected from a random sample (Bekelman, et al. 2003).
- Growing evidence indicates that even relatively small or "token" gifts, such as some of those provided by pharmaceutical companies to doctors and trainees, act to influence the gift recipients and to stimulate attention to secondary interests. (Wazana 2000; Dana & Lowenstein 2003).
- Studies and reports of COI reveal causes by the secondary interests of researchers and professionals acting as consultants for biotechnology, pharmaceutical, and financial sector companies (Topol & Blumenthal 2005).
- New light is being shed on the increasing problem of institutional COI, where the institution has put itself in the position of having to manage multiple and significant "secondary interests" that can otherwise damage its integrity (Johns et al. 2003).
- Concern is growing about researchers and clinicians who serve as researchers and consultants to financial and investment organizations where their advice or scientific judgment can result in significant, if unintended and unforeseen, COI issues (Bekelman, et al. 2003).

In addition to this growing body of evidence concerning ties to the private sector, widespread concern is spreading within academia about how private sector relationships are exacerbating related faculty and staff conflicts, including conflicts with respect to:

- commitment and service to home institutions —e.g., where time involved in private sector relationships conflicts with the commitments required to the institution;
- mentoring and training of students—e.g., where students are directed to work for, or on projects of interest to, a faculty member's new start-up company.

- academic freedom—e.g., where faculty might agree with a private sector sponsor to delay publication or refuse to share research results with colleagues and the larger research community (Blumenthal 2003; Boyd and Bero 2000).

While the financial ties and conflicts with external partners may create the most potential for headlines in the popular press that undermine the public's trust, other forms of secondary interest and conflict also can have a significant effect on the integrity of the academy and the missions of the ANGs.

FINDING #3. ***Academic, professional, and nonprofit sectors have been slow to address COI policy and implementation.***

Universities that receive federal funds are required to establish policies that prevent faculty, staff, trainees, and board members from using their positions for private financial gain for themselves and their families. The policies also prohibit financial interests in vendors, gifts, gratuities and favors, nepotism, research, training, and other areas such as political participation and bribery. These requirements cover more than research conflicts. (McCrary et al. 2000)

However, surveys of academic institutions show that a wide variation in the development, content, and enforcement of COI policies. Whereas some institutions have developed extensive policies and attendant processes for implementing them, others have hardly addressed these issues at all. Cho et al. and McCrary et al. surveyed university COI policies and found significant variation and gaps in COI policy and implementation. The typical institution requires disclosure of faculty financial interests only annually and fewer than one-fifth specified limits or prohibitions on faculty activities (Cho et al. 2000:2207). In another study, only 1% of 250 institutions surveyed had policies requiring the disclosure of potential COI information to the relevant institutional review boards (IRBs) or to research subjects (McCrary et al. 2000:1621). The same variation and gaps exist in policies promulgated by professional societies (Ibid).

In the government sector, the NIH recently conducted a careful review of COI policies for employed researchers but only after the Los Angeles Times ran a series of articles alleging improper financial ties between NIH researchers and industry partners (Willman 2003).

Equally important, research also shows that almost no information is available on how or how well COI policies are implemented or enforced within universities, professional societies, or the rest of the nonprofit sector (Boyd et al. 2004).

Others are equally convinced that there is a clear obligation on the part of the research community to be proactive in ensuring that results from studies involving human subjects are reported so that anyone can learn the results (Sim and Detmer 2005).

FINDING #4. ***There is a lack of coordination or standardization of COI policies, procedures, implementation, and enforcement across the ANG sector.***

Most AHCs, professional associations, and organizations have developed COI policies (e.g., AAMC 2001, 2002; AMA 2001; ASGT 2002). The Uniform Requirements for Manuscripts adopted by the International Committee of Medical Journal Editors (ICMJE) requires disclosure to all subjects and to journals of all COIs (ICMJE 2003). The pharmaceutical industry has developed a comprehensive policy concerning COI (PhRMA 2004). The Federation of American Societies of Experimental Biology (FASEB) has adopted a "consensus statement on overarching principles and voluntary standards for the conduct and management of academia/industry interactions from the scientists' perspective" (FASEB 2005, vi). The Association of American Medical Colleges (AAMC) has adopted "Principles for Protecting Integrity In the Conduct and Reporting Of Clinical Trials" (Ehringhaus and Korn 2006; see Appendix 5).

Yet while some in the AHC community have called for the adoption of uniform standards (Korn 2000; Cho et al. 2000; Campbell, et al. 2005; Brennan et al. 2006), "each boat on its own bottom" seems to be the overriding philosophy of leadership in the AHC community. As a result, little sharing of common standards, policies, or enforcement mechanisms has taken place either

within or between universities until recently. And few organizational and technological resources are available to support the promulgation of standards, data reporting, or monitoring (Boyd et al. 2004). Experience shared within the Blue Ridge Group suggests that variation in the culture and management of particular AHCs precludes standardization of policy and practice in COI management. At the same time, these myriad separate guidelines, principles, strictures, and policies —and also their uncertain enforcement—are acknowledged to be sources of risk to institutions and individuals.

Schools of medicine at both Harvard and the University of Pennsylvania have developed and amended model COI policies over time (see appendices 1 and 2). Both of these institutions' policies are comprehensive. They cover similar ground and espouse similar principles. Yet, an expectation remains that each institution will evolve its own implementation, enforcement, and practices—its own COI culture. As stated in the Harvard policy, "it is expected that a common institutional experience in the application of these guidelines will gradually evolve" (appendix 1). Nevertheless, these two institutions' policies are very good models for others to use in developing institutional COI policies, and we recommend them.

FINDING #5. ***The ANG sector has failed to be proactive in educating its public about its many relationships with the private sector and about the measures being taken to protect the integrity of bioscience and health care.***

Much of the public and the press only encounter COI issues when something goes wrong. The pubic policy imperative to explore this new ground, take some risks, and develop these relationships is not understood. Instead, the public repeatedly finds reason to be skeptical of the capability and commitment of many in the ANG sector to their primary interests in the face of apparent secondary interests, especially the potential pecuniary rewards of relationships with the private sector.

One important implication of these findings is that the public trust necessary for sustaining support of ANG research and care activities is at risk. While there has been sustained support of the NIH budget over many years along with a recent doubling of this investment, this support was won only after significant efforts. It cannot be taken for granted. Most importantly, in the post 9/11 environment, strong competition for public resources to address national security. Regardless, support for basic and clinical research funding can erode further.

The COI issue has had one additional significant effect. The lack of proactive attention to COI issues has led to a broad spectrum of regulatory

For our Public and our Patients

Martin and Kasper have suggested that, because medicine addresses a basic human need, institutions, professionals, and others involved in the public, nonprofit sector of health care and research owe their public the following:

- to know that the biomedical research they support will be a search for truth, uncontaminated by even a perception of bias.
- to see that discoveries with the potential to improve health are rapidly translated into practice through clinical trials.
- to be confident that participation in the development of new therapies will be safe, with fully informed consent obtained at the outset and access to outcome data provided during follow-up.
- to know about any potential adverse effects that might influence their consent to participate in the research.
- to be assured that neither the decision to ask patients to participate in a clinical trial nor the assessment of the risks patients may incur will be prejudiced by an investigator's personal profit motives.

(Martin and Kasper 2000)

guidelines and legal enforcement that has steadily "annexed terrain previously controlled by professional ethics" (Studdert et al, 2004). This effect is deeply troubling. The continuing erosion of the sphere of professional self-regulation and autonomy undermines medical professionalism itself. It threatens the social legitimacy and authority that is critical to the future of the profession and its capacity to guide public policy. The importance of understanding and addressing the erosion of professionalism was the focus of the last Blue Ridge Group Report (BRG 2005).

Appendix 3 provides hypothetical examples of COIs that are becoming more and more prevalent within academic health centers and their medical schools. Such complex COIs tax the capabilities of even those institutions with relatively comprehensive COI management commitments (Ehringhaus & Korn (AAMC) 2004).

PART III.

A Growing Pallet of Solutions

A pallet of approaches to managing COI is growing within the ANG sector, approaches that should be adopted and further developed. In summary, they are:

Transparency and Full Disclosure

Almost universally, academic and professional journals, societies, and granting agencies are advocating the principles of transparency and full disclosure of industry ties (AAMC 2004, 2006, AMA, NEJM, ASGT 2000). Transparency involves full and timely disclosure of all actual or apparent secondary interests resulting from private sector or other relevant relationships. This element is fundamental to COI policy. The best COI policy will fail if disclosures are not made, are inaccurate, or are insufficiently complete. However, many analysts understand that full disclosure by itself often is insufficient, especially to a lay public or to patients, who may be ill-equipped to evaluate the nature or potential impact of such secondary interests. Further action is indicated, ensuring that disclosure is meaningful to a broad array of the public to whom we are responsible (Weinfurt et al. 2006).

New Strictures on Gifts and Remuneration

Brennan et al. have suggested a series of simple but strong measures to limit the effects of some common health industry practices currently practiced at some academic health centers. Ample evidence exists that all of these practices can and do implicate secondary interests, which affect both physician and trainee behavior and expectations. Among the recommendations are:

- a prohibition on "all gifts ($0 limit), free meals, payment for time for travel to or time at meetings, and payment for participation in online CME from drug and medical device companies to physicians . . .,"
- a prohibition of all pharmaceutical samples to physicians to be replaced by a system of vouchers or similar arrangements for low-income patients,
- the exclusion from hospital and medical group formulary and formulary oversight committees of anyone with a financial relationship with a drug manufacturer; a prohibition of direct (and much indirect) industry support for CME programs and for physician travel, to be replaced by contributions to university-controlled central funding repositories with open reporting on the uses of such funds,
- a prohibition of faculty serving on industry speakers' bureaus or in other capacities where the primary function is purely the marketing of products,
- a prohibition on faculty publishing articles or editorials that are "ghost written" by industry employees, and
- a new transparency for consulting and research contracts, including public posting of the terms, along with the requirement that such contracts provide for specific deliverables. Also recommended is that AHCs create an institutional mechanism to manage industrially-based funding and fees rather than leaving this process directly in faculty hands (Brennan et al, 2006).

The best COI policy will fail if disclosures are not made, are inaccurate, or are insufficiently complete.

Many of these recommendations would alter or prohibit policies and practices that are routine in most AHCs and are unlikely to stop without institutional action. Where once these practices might be dismissed as insignificant, in the Bayh Dole era, arguably they have become more relevant as COI challenges have expanded dramatically. Industry believes that these practices do effectively influence faculty, staff, students, trainees, and even the institutions overall. The adoption, with some local adjustments, of the Brennan et al. recommendations deserves open and active discussion and consideration.

Independent and External Oversight or Separation Methods

In some areas of COI, conflicts and secondary interests are unable to be adequately or appropriately managed by employees or other individuals with close ties to the parties or interests that constitute the COI. This scenario is especially true where the institutions themselves have conflicts. For instance, a university may hold licensing agreements with or own an equity stake in one or more start-up biotechnology, pharmaceutical, or medical supply company, and the university has need of a vendor in one of these areas. In cases like this, where the institution itself may have a conflict, strong arguments exist for establishing independent review panels (IRPs) consisting of nonaffiliated people, who have the expertise and experience to evaluate and manage real and potential conflicts (Barnes et al., 2003; Johns et al. 2003). Additionally, institutions can manage institutional conflicts through "separation methods," separating the decision-making in regard to investments from the flow of information from clinical, research purchasing, or other relevant operations—therefore, one is unable to influence the other (Johns et al. 2003).

Members of institutional review boards (IRBs) who review and oversee studies involving human subjects are never allowed to profit from their connection with the review. Both law and policy now prohibit IRB members from having any financial interest in the research they review.

Special Purpose Entities

Related to the separation method, another important method for COI management is establishment of "special purpose" institutional entities dedicated to the management of COI. These groups can include research institutes that a university might create with private or industrial partners. Prominent examples include the Howard Hughes Medical Institutes' laboratories at various sites and the Whitehead Institute at the Massachusetts Institute of Technology (Moses and Martin 2001; see www.hhmi.org/ Accessed August 10, 2006). Ohio State University Medical Center (OSUMC) offers another example. OSUMC has developed a nonprofit public benefit corporation called UMC Partners through which venture investments, start-up companies, and partnerships with the private sector are structured and managed (see www.umcpartners.org/ Accessed August 10, 2006).

Another approach is establishment of entities that can hold equity and receive royalties on behalf of faculty, other university employees, or the institution itself (Moses and Martin 2001). All decisions about management and disposal of investments and assets are made by this entity's independent financial advisers or board. The entity operates in a manner similar to a mutual fund, and it may be structured similarly to those used in clinical practice foundations, common in AHCs (Ibid).

In all of these cases, relationships with the private sector are cloistered into dedicated, separate entities where COI can be more systematically managed.

Zero Financial Interest Tolerance

Certain positions and situations require a zero-tolerance financial interest policy for individuals. For example, members of IRBs who review and oversee studies involving human subjects are never allowed to profit from their connection with the review. Both law and policy now prohibit IRB members from having any financial interest in the research that they review. Johns et al. have called for a policy that applies to all institutional decisions-makers and prohibits financial interests in research being conducted at the institution (Johns et al. 2003).

AHCs are urged to discuss and subsequently adopt these procedures if transparent discussion at the institutional level shows a need for such action.

The Blue Ridge Group believes that AHCs must devote new and significantly more resources to getting control of and managing COI. Each AHC and AHCs collectively should consider this entire portfolio of COI management options and strategies and develop a coherent strategy for addressing this challenge. The results of these deliberations should be shared with the public.

A positive recent development is the establishment of a significant group dedicated to sharing and developing COI policy among AHCs. The Forum on Conflict of Interest in Academe (FOCI Academe) is a fast-growing organization of leaders within medical schools and AHCs involved in COI review, management, and policy development. FOCI Academe is dedicated to providing a forum for leaders in biosciences and health care to understand, develop, and promote the highest levels of ethical and professional standards and is now affiliated with the AAMC (see www.forummeeting.com/ Accessed August 2, 2006).

Exhibit 1:

The Forum on Conflict of Interest in Academe (FOCI Academe)

Purpose

The purpose of the organization is to provide a forum for leadership in the biomedical arena for those who oversee and manage conflicts of interest to promote the highest ethical and professional standards in the conduct of their institutions as they carry out their missions of patient care, research, education, business, and service. The organization will address the following at the institutional and national level:

A. The development and review of policies on COI;

B. Consistent best practices in the implementation of these policies;

C. Productive academic/industry relationships that benefit the institutions and thereby the public without undue influence of the relationships upon the integrity of decisions made by the institutions;

D. Education of the institutional faculty and employees, trainees, and officials and the enhancement of institutional cultures that promote ethical and professional behavior in institutional and personal relationships with industry; and

E. Education of the media and the public on COI issues.

Through its discussion of and engagement in these focus areas and others, the organization will enhance public confidence and trust in the institutional oversight of conflict of interest matters.

--From the Bylaws of FOCI Academe

FOCI Academe not only addresses particular conflict of interest issues as they arise but also it proactively creates a better policy and regulatory environment and a road map for ANG collaboration with the private sector.

PART IV.

At Stake: Global Health Security

Extensive and increasing ANG collaboration with the private sector is now integral to almost the entire spectrum of biomedical and clinical research and health care, and therefore, to medical progress. Conflicts of interest in relationships between ANG and private industry are inevitable and will continue. ANG individuals and institutions must take aggressive steps to understand, anticipate, and manage these conflicts. However, since the passage of Bayh Dole, legal, professional, regulatory, and administrative activity and policy have taken primarily defensive and reactive stances. As ANG and industry sectors explore and forge relationships, "rear-guard" actions that defend and enforce traditional academic, professional, and organizational values and ethics are unfolding. While this "defensive" focus is absolutely vital to the integrity of the professions and to public trust in nonprofits, the ANG sector must develop a far more proactive approach. Collaboration with the private sector is likely to become even more extensive and more important to the future of health and health care (Emanuel, et al. 1999).

The multiple and burgeoning relationships between the ANG and private sectors are producing unprecedented technologic progress and promise vastly many more. Scientists and clinical investigators now talk with increasing confidence and certainty about the likelihood of new breakthroughs based on recent rapid advances in genomics, proteomics, nanotechnologies, computational and systems biology, and a host of other fields of discovery that industry collaboration has accelerated. Similarly, new drugs and devices, ranging from cancer therapeutics to drug-infused stents, from remote telemedicine capabilities to robotics and extraordinary new developments in imaging and nuclear medicine, all reflect the rapid uptake in the marketplace of discoveries and innovations.

Importantly, both the health care marketplace and the discovery and development process are global in scope. Certainly the pharmaceutical industry is multinational as are clinical trials. But globalization means more than just new opportunities. It also introduces new and unprecedented global health threats. As Thomas Freedman has noted, the world is essentially flat again (Friedman 2005). Because of the mobility of people worldwide, localized disease outbreaks can quickly become global outbreaks. HIV/AIDS, SARS, drug-resistant TB, pandemic "bird flu," and many other threats, both natural and man-made, show evidence that health security is a paramount issue. Even population health threats that develop more slowly, such as the current epidemic of obesity and diabetes, require unprecedented resources and new approaches.

Experience to date suggests that we are only minimally prepared locally, nationally, and internationally to confront, prevent, or manage health in the age of globalization. Public health organizations and agencies worldwide are increasingly identifying risks and promoting proactive policies and interventions. Yet public policy in general, and AHCs and the medical professions in particular, appears to be insufficiently engaged in understanding and planning for the levels of resources, capabilities, technological sophistication, and public/private cooperation that may be required to meet foreseeable health challenges.

Health security as well as first-rate biomedical research in its own right—local, national, and international—requires world-class and worldwide knowledge generation, discovery, innovation, and entrepreneurialism. Additionally, our global health challenges also requires the capital, manufacturing, and marketing capabilities of industry as well as the authority and logistical and budgetary support of governments worldwide.

Above all, achieving the appropriate levels of resources and capabilities for our global health challenges requires an extraordinary commitment and effort on the part of the health professions, especially the medical profession. Strong and organized leadership in medicine and the other health professions is indispensable in defining and marshalling necessary public and private resources. This process includes explaining the realities of our "flat" world to both policymakers and the public and advocating for the resources necessary to health security, including preparedness and intervention.

In this context, leadership is critical. The arena

of public policy has many competing claims for allocation of resources. To be treated not simply as another "special interest," ANG medical and health professional leadership must bring an unimpeachable integrity, commitment, and track record to marshal necessary resources, capabilities, and commitments. Important to this challenge is the robust engagement of such leaders in defining and championing appropriate public/private sector relations.

From a Mine Field to a Field of Dreams

The Bayh Dole Act enabled a broad advance of the forces of public and private sector collaboration. Yet, for more than 20 years, these forces have had to advance through a difficult minefield, painstakingly and not without significant casualties. It is time to move public policy towards a more friendly terrain. By drawing on the lessons learned to date, the realities of our current environment, and our projected health care challenges, we should aspire to create more of a "field of dreams:" a regulatory and standards-based playing field to which ANG and industry will more naturally be drawn for appropriate and necessary collaboration.

Current laws have developed in specific areas of interest and provide a foundation for broad-based COI regulation and guidance.

1. Internal Revenue Service (IRS) and state not-for-profit law provides regulations concerning private inurement, while intermediate sanctions rules prevent self-dealing by non-profit board members and executives (see, e.g., www.irs.gov/charities/charitable/article/0,,id=123298,00.html).
2. Federal and state anti-kickback law "curtails corrupting influences of money on health care decisions" (42 U.S.C. § 1320-7a (2004)).
3. The so-called "Stark" laws regulate physician referrals (See: Omnibus Budget Reconciliation Act of 1989 (P.L. 101-239); Omnibus Budget Reconciliation Act of 1993 (P.L. 103-66); Social Security Act Amendments of 1994 (P.L. 103-432)).
4. Food and Drug Administration (FDA) regulations address objectivity in research and the soundness of data submitted to support FDA applications, providing for disclosure of conflicts by investigators—but not explicitly for the management or elimination of conflicts (see www.hhs.gov/ohrp/humansubjects/finreltn/finalguid.pdf. Accessed August 8, 2006).
   a. The Public Health Service (PHS) regulations require every investigator to report on any significant financial interests that may reasonably appear to be effected by the research before application for funds is submitted to PHS, including NIH and CDC (DHHS 2005).
5. The False Claims Act, which imposes liability for knowingly submitting a false claim for payment to the federal government, is being employed increasingly to prosecute Medicare and Medicaid fraud (31 U.S.C. §§ 3729-3733 (2004); see Krause JH 2002).
6. The NSF has regulations similar to the PHS, which require entities with more than 50 employees and that receive NSF funds to report to NSF only COIs that CANNOT be managed (NSF 2005).
7. IRB members and process: FDA and PHS regulations provide that no review by an IRB member is allowed of a study in which the member has a conflicting interest. However, "conflicting interest" is not defined but has been interpreted as being broader than financial interests (Barnes M 2005).
8. No Institutional Animal Care and Use Committee (IACUC) member can participate in review in which member has conflicting interest (see www.iacuc.org/ and http://grants.nih.gov/grants/olaw/olaw.htm Accessed August 10, 2006).
9. Common law cases on COI. There is a growing body of case law on COI. For example, Moore v Regents of U California held that "a physician who is seeking a patient's consent for a medical procedure must, in order to satisfy his fiduciary duty and to obtain the patient's informed consent, disclose personal interests unrelated to the patient's health, whether research or economic, that may affect his medical judgment." (793 P.2d 479 (Cal. 1990)) see www.richmond.edu/~wolf/moore.htm. Accessed August 9, 2006).

10. The pharmaceutical industry has adopted a "code on interactions with health care professionals." Although voluntary, the code represents an industry-wide standard that reflects current standards in law and regulation to which the vast majority of the pharmaceutical industry subscribe (PhRMA 2004).

However, substantial gaps exist in the current regulatory environment for COI in public/private relationships. They include:

1. COI policies of AHCs often fail to directly address Stark and anti-kickback law issues. These laws and regulations apply far beyond the research context.
2. Non-financial COIs most often fail to be addressed.
3. Rather than direct regulation of institutional COIs, only indirect applications of IRS and state not-for-profit laws are applied to prevent dealing in the assets of a nonprofit for the benefit of either insiders or for nonprofit purposes.
4. If research is neither used for an application to the FDA nor funded by PHS or NSF, no federal rules apply at all on COIs of investigators.
5. IRB and IACUC rules are limited. They forbid all conflicts including those beyond financial conflicts, but the extent of forbidden conflicts fails to be defined.
6. Remedies, limits, and management strategies are undefined and uncharted in most COIs (Barnes 2005).

COI law and regulation are a complex patchwork of standards and initiatives that remain ill-defined and unfinished and that suffer from significant gaps. As a result, many unsuspecting or unprepared individuals and institutions continue to face legal and ethical exposure as they seek to understand and manage primary and secondary conflicts of interest. Also at risk are the people they serve, including patients, students, and the public at large. Most troubling, perhaps, is that no entity or authority is empowered to either chart or implement an overall strategy to create more comprehensive and universal standards.

Despite the reluctance of some to countenance more global standardization of COI policies, the Blue Ridge Group believes that such an effort is at least worth thorough investigation. In our global era, an overarching public interest in national and global health security is present. To contribute appropriately to this interest, we should come together on these issues. Our collective solutions will be much better than if an individual ANG entity or each private company pursues only its own policies and interests concerning COI. National and global challenges require more systematic and coordinated establishment and implementation of needed policies.

Most troubling, perhaps, is that no entity or authority is empowered to either chart or implement an overall strategy to create more comprehensive and universal standards.

Recommendations:

1. **The Blue Ridge Group believes that AHCs must devote new and significantly more resources to getting control of and managing COI within their institutions and their extended family of faculty, staff, and other interested parties. The effective management of COI requires the establishmnet of an institutional culture that starts at the top and works its way through the entire fabric of the institution. Each AHC should consider the entire pallet of COI management options and strategies and develop a coherent strategy for addressing this challenge. Sufficient resources must be allocated for management and enforcement of COI, including designated managers and accountability systems.**

2. **The Blue Ridge Group recommends that AHCs and other relevant ANG organizations should support the goal of creating, where possible, a common set of standards and practices for managing COI in ANG/industry relationships. Participation in FOCI Academe) is highly recommended as a forum and vehicle for leaders in biosciences and health care to understand, develop, and promote the highest levels of ethical and professional standards. The affiliation of FOCI Academe with the AAMC should greatly enhance this effort's visibility, reach, and influence (see www.forummeeting.com/ Accessed August 2, 2006).**

3. **The Blue Ridge Group recommends that the Institute of Medicine (IOM) take charge of a review of the current laws, regulations, and relationships between the public and private sectors in technology transfer. The IOM should make recommendations concerning appropriate policies or directions for further policy development, filling current gaps in regulation. This policy could produce more sophisticated and appropriate legal and regulatory frameworks, within which public/private collaborations and relations can be ideally developed.**

4. **Such public policy guidance must have the input of all stakeholders in the nonprofit, government, and private sectors. To begin to create the groundwork for more consistent international approaches, laws such as those applying to the European Union and other parts of the world should be examined. The IOM should work with other academies around the world to evaluate, create, and pursue common ground.**

5. **Leading health and professional organization in the United States, including the AAMC, AAHC, AMA, and equivalent organizations in the other health professions, should review their own approaches to this topic at the local, national, and global level and prepare to offer leadership in developing and implementing revised and enhanced COI policies.**

Conclusion

The challenges of managing COI are significant and require all stakeholders to understand not only the risks to individuals and institutions of failure to adequately address COI but also the risk to the progress of health care. Furthermore, failure to address COI and engage these issue proactively sets us on a collision course with the overarching public interest in national and global health.

AVAILABLE AT: www.hms.harvard.edu/integrity/conf.html. ACCESSED AUGUST 9, 2006.
HARVARD MEDICAL SCHOOL POLICY ON CONFLICTS OF INTEREST AND COMMITMENT

Introduction

An important goal of the Harvard Faculty of Medicine is to make scientific discoveries that will benefit the sick and suffering. For many years the Faculty has worked hard to achieve this goal. In 1980, the United States Congress explicitly sanctioned and facilitated this process with the passage of legislation designed to stimulate the commercialization of faculty inventions by permitting academic institutions and scientists to benefit financially if their federally-sponsored research led to commercial products. Moreover, during the past decade the rate of growth of biomedical research has outpaced federal funding, compelling universities and hospitals to develop alternative sources of revenue to support the expenses associated with their educational, research and clinical missions.

In response to these influences, biomedical research institutions have cultivated a growing variety of relationships with industry which promise to benefit the public as well as the institutions themselves, their faculty and staff, and their industrial partners. Over the last several years, these relationships have grown substantially, bringing new resources to the support of science and facilitating the translation of knowledge from the laboratory to the bedside. The Harvard Faculty of Medicine remains strongly committed to continued growth in these innovative and mutually beneficial relationships.

Together with these benefits, the growing partnership between for-profit enterprises and the University has created new possibilities for conflicts of interest. These conflicts arise from a faculty member's opportunities to benefit financially either from the outcome of his/her research or from the legitimate activities conducted in the course of his/her responsibilities as a faculty member. In light of these possibilities, there is emerging public concern regarding the appropriateness of some relationships between academic medicine and industry.

Public trust in the enterprise of academic medicine and the legitimacy of its powerful role in society require a constant amenability to public scrutiny. Consequently, it is necessary at this time to ensure the continued confidence of the public in the judgment of researchers and clinicians and in the dedication of academic research institutions to the integrity of the scientific enterprise. The strength of this assurance is based on two assumptions underlying the explicit rules and implicit norms governing faculty behavior at the Harvard Medical School:

1. that the vast majority of scientists are honest and conduct their research with the highest standards and integrity, and,
2. that, for the vast majority of cases, self-regulating structures and processes in science are effective.

Based on these assumptions, the Faculty of Medicine believes that with clear guidelines and principles, in conjunction with appropriate mechanisms for supervision and monitoring, cooperation between industry and academic medicine is consistent with the highest traditions of the medical profession and can energize scientific creativity.

This policy is intended to serve as a guide for faculty members in structuring their relationships with industry and other outside ventures in view of their academic responsibilities for teaching, research and patient care. Faculty members are expected to make reasonable inquiry as to whether their relationships and activities fall within the provisions of the policy. It is not the intent of this policy to regulate or eliminate all situations of conflict of interest, but rather to enable faculty members to recognize situations that may be subject to question and ensure that such situations are properly reviewed and, if necessary, resolved as applicable. Thus, an integral part of the policy is a disclosure mechanism whereby faculty members regularly review their activities. The guidelines are intended to maintain the professional autonomy of scientists and physicians inherent in the self-regulation of science. These guidelines should be viewed as complementing and elaborating upon the Faculty of Medicine's Statement on Research Sponsored by Industry.(1)

The policy fulfills two other purposes as well. First, it provides faculty members with meaningful guidance for the continued development and future structuring of productive relationships with industry. Second, by virtue of its explicit nature and provision for full disclosure, the policy will provide assurance to the faculty, the University, and most importantly the public, that such relationships have been examined and will be conducted in a manner consistent with institutional and public values. It is expected that these relationships will allow the University and its affiliated Hospitals to pursue energetically new knowledge in the biomedical sciences and to insure that the transfer of such knowledge to the care of patients is rapid and cost-effective.

Types of conflict

Conflicts of Commitment

With the acceptance of a full-time appointment in the Faculty of Medicine, an individual makes a commitment to the University (and Hospital, if part of a hospital-based department or other health-care institution) (2) that is understood to be full-time in the most inclusive sense. Full-time members of the Faculty of Medicine are expected to devote their primary professional loyalty, time, and energy to their teaching, research, administrative responsibilities and, where applicable, patient care at the School and its affiliated Hospitals. Accordingly, they should arrange outside activities and financial interests so as not to interfere with the primacy of these commitments. The Faculty of Medicine recognizes that its members may engage in outside professional work, and to the extent these activities serve the Faculty's interests, as well as those of the participant, the Faculty of Medicine approves of such involvement. However, no more than twenty percent (20%) of a full-time faculty member's total professional effort may be directed to outside work, not to exceed the equivalent of one working day per week. Potential conflicts of commitment must be disclosed and resolved as described in the section on implementation in Appendix B.

Members of the Faculty whose appointments are less than full-time are expected to devote professional loyalty, time, and energy to their teaching, research, patient care, and administrative activities, in accordance with their agreed-upon time commitments.

Conflicts of Interest

A Faculty Member (3) is considered to have a conflict of interest when he/she, any of his/her Family, or any Associated Entity possesses a Financial Interest in an activity which involves his/her responsibilities as a member of the Faculty of Medicine. Included in these responsibilities are all activities in which the Faculty Member is engaged in the areas of teaching, research, patient care and administration.

Guidelines for conflict of interest

The following is a representative and non-inclusive list of extramural relationships subject to this policy. These examples have been divided into three groupings.

Categories I(a), I(b), I(c), and I(d) consist of relationships that are generally not allowable, with certain de minimis exceptions. Categories II(a) - (g) consist of relations that are generally allowable only after disclosure, review, and approval with oversight by the University or affiliated Hospital with advice from a standing committee of the Harvard Faculty of Medicine when requested. Another classification (Category III) consists of instances that will ordinarily be permissible following disclosure and, where necessary, the implementation of oversight procedures designed to ensure academic standards, intellectual values, and institutional integrity. Lastly, there is a category of relationships (Category IV) that are thought to be allowable because they are (a) accepted practices and (b) generally minimal in their personal financial impact.

These classifications are not intended to serve as a rigid or comprehensive code of conduct or to define "black letter" rules with respect to conflict of interest. It is expected that the guidelines will be applied in accordance with the spirit of the mission of Harvard Medical School in education, research and patient care. By this process, it is expected that a common institutional experience in the application of these guidelines will gradually evolve. The complexity of the subject matter is such that the current guidelines and their ensuing interpretations should be formally reviewed on a periodic basis.

The impact of a Faculty Member's conflict of interest on student training (including that of post-doctoral fellows and other trainees) is of special concern to the Faculty of Medicine. Many of the specific issues related to student training have already been addressed in the Faculty of Medicine's Statement on Research Sponsored by Industry. As noted in that policy, students and trainees "should not ordinarily participate in research that involves confidential information or otherwise constrains their right to publish or communicate freely." Additionally, as set forth in more detail below, the Faculty is particularly concerned about the content and quality of the training experience for students whose research is sponsored by a for-profit business and whose preceptors have a personal interest in that business.

It is essential that Faculty Members demonstrate at all times their commitment to the highest intellectual and ethical standards in all aspects of research, particularly research in which opportunities for conflict may exist. As a corollary, the training experiences of students are expected to incorporate the values of objectivity in research and the importance of public trust.

Lastly, the rigorous application of the guidelines will be particularly important in the case of persons exercising significant authority. There are those in the Faculty of Medicine who have substantial influence over others by virtue of their major role in professional appointments, promotions, tenure decisions, allocation of space and determination of salary. Typically these individuals hold positions such as Chief Executive Officer (CEO or equivalent title) of an affiliated Hospital, Dean or Executive Dean of the Faculty of Medicine, or Heads of

Departments. While the guidelines are applicable to all Faculty, these individuals must take particular care not to become involved in research relationships that would lead to their personal financial gain or that would adversely affect the professional or academic advancement of junior faculty members.

CATEGORY I **(a), (b), (c),** and **(d)** Activities are Generally Not Allowable. The only exceptions are conflicts that arise in extraordinary circumstances such as the recruitment of a new Faculty Member, where a conflict may be allowed to continue for a finite time period with disclosure and the approval of the Standing Committee, the Dean and the CEO.

Research Activities

I(a) A Faculty Member Participating in Clinical Research on a Technology owned by or contractually obligated(4) to a Business(5) 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-supervised Sponsored Research support or post-market royalties under institutional royalty-sharing policies.(6)

I(b) A Faculty Member receiving University- or Hospital-supervised 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. Sponsored Research (and the prohibition of equity ownership) is considered to have ended when the term of the Sponsored Research agreement has ended and publications reporting on the research are completed (or the decision made not to publish). It is the Faculty Member's responsibility to determine when that time has been reached.

De Minimus Exception to Category I (a) and I (b) Conflicts

(a) A Faculty Member may continue to hold stock or similar ownership interest in a Business in a situation which would otherwise create an impermissible Category I (a) or I (b) conflict only if all of the following conditions are met:

1. The stock or similar ownership interest must be in a publicly held, widely traded Business.
2. The current value of the stock or similar ownership interest may not exceed $30,000 at any time.
3. There must be no relationship between acquisition of the stock or similar ownership interest and research to be conducted. Situations that satisfy this requirement include stock or similar ownership interest acquired in arms-length transactions or by family gift sufficiently prior to the beginning of the research to assure the lack of a relationship and stock or similar ownership interest acquired by inheritance. In any such situation there must be complete independence between a purchase decision or other acquisition and the research.
4. While meeting the above criteria excepts a Faculty Member from what would otherwise be an impermissible Category I (a) or I (b) conflict, it does not except a Faculty Member from other conflict categories such as Category II(e) which imposes an obligation to disclose a Financial Interest in the research in any publication or presentation.

(b) A Faculty Member may consult for a Business in a situation which would otherwise create an impermissible Category I (a) conflict only if all of the following conditions are met:

1. The amount of money received by the Faculty Member for consulting relationships, fees or honoraria from a given Business should not exceed $20,000 a year. Consulting relationships include contractual relationships with a Business (or from an agent or other representative of such Business), service on advisory boards and any other relationship whereby the Faculty Member receives, or has the right or expectation to receive, income from a Business in exchange for services. Honoraria include commissioned papers and occasional lectures (no more than four lectures a year) for which money is received, either directly or indirectly, from a given Business (or from an agent or other representative of such Business)

2. While meeting the de minimis criteria above excepts a Faculty Member from what would otherwise be a Category I(a) conflict, it does not exempt the Faculty Member from other possible conflict categories such as Category II(e) which imposes an obligation to disclose a Financial Interest in the research in any publication or presentation.

External Activities

I(c) A full-time Faculty Member is not permitted to take an Executive Position (responsible for a material part of the operations of a Business such as Chief Executive Officer, Chief Operations Officer, Scientific Director or Medical Director) in a for-profit Business

engaged in commercial or research activities of a biomedical nature.

I(d) A Faculty Member who serves on the Board of Directors of a Business is not permitted to Participate in Clinical Research on a Technology owned by or obligated to the Business regardless of whether he/she has a Financial Interest in the Business and is not permitted to receive Sponsored Research from that Business regardless of whether he/she has an equity interest in the Business. This provision does not apply to a Faculty Member who is a member of a Scientific Advisory Board and who does not either hold an Executive Position or serve on the Board of Directors.

CATEGORY II **(a) - (g)** Activities that May be Allowable Only after Disclosure, Review, and Approval by University or Affiliated Hospital with Advice from the Standing Committee When Requested:

Research Activities

II(a) A Faculty Member conducting research externally that would ordinarily be conducted within the University or Hospitals.

Committee Participation

II(b) A Faculty Member participating in the consideration by a committee of the FDA, other governmental agency, or private insurer of Clinical Research on a Technology which is owned by or contractually obligated to a Business in which that Faculty Member, a member of his/her Family, or an Associated Entity has a Financial Interest.

External Activities

II(c) A Faculty Member making clinical referrals to a Business in which such Faculty Member, a member of his/her Family, or an Associated Entity has a Financial Interest.

II(d) A Faculty Member possessing a Financial Interest in a Business which competes with the services provided by the University or any Hospital with which the Faculty Member is affiliated.

Public Disclosure

II(e) A Faculty Member publishing or formally presenting research results, or providing expert commentary on a subject, without simultaneously disclosing any Financial Interest in a Business which owns or has a contractual relationship to the Technology being reported or discussed or which sponsors the research being reported or discussed.

Administrative Responsibilities

II(f) A Faculty Member taking administrative action within the University or any affiliated Hospital which is beneficial to a Business in which he/she has a Financial Interest.

Applicants for Public Health Service and/or National Science Foundation Research Funding

II(g) Under federal regulations(7) a Faculty Member who is an applicant for Public Health Service and/or National Science Foundation funding has a potential conflict under the federal regulations, if the Faculty member, spouse and/or dependent children have a "significant financial interest," which could directly and significantly affect the design, conduct or reporting of the federally funded research.

***"Significant Financial Interest"* for Category II(g) Conflict**

For the purposes of a Category II(g) conflict, as defined above, a "significant financial interest" consists of "anything of monetary value" from the Business, including salary, consulting fees, honoraria, equity interests and intellectual property rights, with the exception of salaries, royalties and remuneration from University or an affiliated Hospital, honoraria for presentations sponsored by public or non-profit entities or income from service on advisory or review panels for public or non-profit entities. Also excepted for the purposes of a Category II(g) conflict are salary, royalties or other payments that, when aggregated for the Faculty Member, spouse and/or dependent children, are not expected to exceed $10,000 over the subsequent twelve months and equity interests, that, when similarly aggregated, do not exceed $10,000 in value or, if the monetary value cannot be ascertained, 5% ownership interest in the business.

Resolution of Category II(g) Conflict

A Category II(g) conflict as defined above must be resolved by management, reduction or elimination, prior to the expenditure of funds from the Public Health Service and/or National Science Foundation. Possible resolution of Category II(g) conflicts may include, but is not limited to, public disclosure of the significant financial interest, monitoring of research by independent reviewers, modification of research plans, disqualification from participation in Public Health Service and/or National Science Foundation funded research, divestiture of the significant financial interest, and severance of relationships that create the Category II(g) conflict.

CATEGORY III Activities that are Ordinarily Allowable Following Disclosure and, Where Necessary, the Implementation of Oversight Procedures:

Research Activities

III(a) A Faculty Member Participating in Clinical Research on a Technology developed by that Faculty Member or a member of his/her Family, unless the activity falls under the guidelines of Category I.

III(b) A Faculty Member assigning students, post-doctoral fellows or other trainees to projects sponsored by a for-profit Business in which the Faculty Member, a member of his/her Family, or an Associated Entity has a Financial Interest, unless the activity falls under the guidelines of Category I. (See section on Mentor's Obligation to Students and Trainees below)

Board Memberships

III(c) A Faculty Member serving on the Scientific Advisory Board of a Business from which that Faculty Member or a member of his/her Family receives University- or Hospital-supervised Sponsored Research support or with which the University has a substantial contractual relationship known to the Faculty Member, unless the activity falls under the guidelines of Category I. See Category I(d) above.

External Activities

III(d) A Faculty Member assuming an Executive Position in a not-for-profit Business engaged in commercial or research activities of a biomedical nature.

CATEGORY IV Activities that are Routinely Allowable:
IV(a) A Faculty Member receiving royalties for published scholarly work and other writings.
IV(b) A Faculty Member receiving post market royalties under institutional royalty-sharing policies.

MENTORS' OBLIGATIONS TO STUDENTS AND TRAINEES

(a) Trainees (medical students, graduate students and post doctoral fellows) must always be encouraged to conduct research in areas that optimize their training. Special care must be taken to assure that a trainee's research is not designed to (and does not appear to) enhance their mentor's Financial Interest, and is not adversely affected by that interest or by contractual aspects of the Sponsored Research agreement that inhibit scientific communication or that commit intellectual property rights to the industrial sponsor.

(b) Before embarking on a research project, a trainee must be provided by the mentor with a clear description of 1) the source of funding of the research project, including any corporate support of the research to be undertaken, 2) any personal Financial Interest the mentor has in a Business, that sponsors the research, or has or is seeking licensing rights in the research or in the Technology being studied, and 3) any restrictions that might be imposed on the scientific communication of the data.

(c) Written approval must be obtained before a trainee can be assigned to conduct research which is sponsored by a Business or which involves a Technology to which the Business has licensing rights, and in which the mentor has any Financial Interest.

1. In the case of graduate students (Ph.D., M.D./Ph.D., M.P.H., and D.M.Sc. candidates), permission must be given by the chairperson (or desiginated Faculty member or committee) for the graduate program and by the mentor's department chairperson
2. In the case of medical and dental students (M.D., and D.M.D. degree candidates), permission must be given by the mentor's Medical School department chairperson. Additionally, for research in the Quadrangle departments, permission must be give by the Dean for Academic and Clinical Programs. For research in the Hospital, permission must be given by the appropriate Faculty Dean.
3. In the case of postdoctoral fellows, permission must be given by the mentor's Medical School department chairperson.

(d) A trainee may appeal his/her involvement in any industrially Sponsored Research or research which involves Technology to which a Business has license rights when the trainee believes that he or she is being adversely affected by any conflict of interest (real or apparent) resulting from the mentor's relations with the sponsoring Business or with any Business that may benefit from the trainee's research or from the Sponsored Research agreement. The appeal should be made as appropriate to the Dean for Academic and Clinical Programs, the Hospital's Faculty Dean, and or the School's or Hospital's Ombudsperson.

(e) A Faculty Member must also disclose his or her Financial Interests in a Business that sponsors the research or which has or is seeking licensing rights in the research or in the Technology being studied, to members of the research laboratory and/or research team. This includes disclosure to prospective students, trainees, and

new faculty before those individuals make a decision to join the laboratory or research team.

APPENDIX A- OPERATING DEFINITIONS

(a) An **"Associated Entity"** of a Faculty Member means any trust, organization or enterprise other than the University or any affiliated Hospital over which the Faculty Member, alone or together with his/her Family, exercises a controlling interest.

(b) "Business" means any corporation, partnership, sole proprietorship, firm, franchise, association, organization, holding company, joint stock company, receivership, business or real estate trust, or any other legal entity organized for profit or charitable purposes, but excluding the University, any affiliated Hospital, any Private Medical Practice, or any other entity controlled by, controlling, or under common control with the University or an affiliated Hospital.

(c) "Clinical Research" means any research or procedure involving human subjects in vivo or the use of human samples for the development and evaluation of patient therapies such as diagnostic tests, drug therapies, or medical devices. It includes early clinical studies, evaluative research, epidemiological studies and clinical trials. It excludes research using commercially obtained de-identified human cell lines as well as commercially obtained de-identified human tissue. It also excludes research that uses human tissue obtained from institutional tissue banks where the individual identifiers are unknown to the researcher. In general, the term includes all research required to be reviewed by an institution's Institutional Review Board.(8)

(d) "Executive Position" refers to any position which includes fiduciary and other responsibilities for a material segment of the operation or management of a Business. It specifically includes the titles of "Scientific Director" and "Medical Director".

(e) "Faculty Member" means any person possessing either a full- or part-time academic or fellowship appointment in the Faculty of Medicine. Full-time Faculty Members on sabbatical or other paid leave are considered full-time for the purposes of the Policy. Full-time Faculty Members on approved unpaid leave are not considered full-time for these purposes.

(f) The **"Family"** of a Faculty Member includes his/her spouse, minor/dependent children, and other persons living in the same household.

(g) A **"Financial Interest"** is an interest in a Business consisting of: (1) any stock, stock option or similar ownership interest in such Business, but excluding any interest arising solely by reason of investment in such Business by a mutual, pension, or other institutional investment fund over which the Faculty Member does not exercise control; or (2) receipt of, or the right or expectation to receive, any income from such Business (or from an agent or other representative of such Business), whether in the form of a fee (e.g., consulting), salary, allowance, forbearance, forgiveness, interest in real or personal property, dividend, royalty derived from the licensing of Technology, rent, capital gain, real or personal property, or any other form of compensation, or any combination thereof.

(h) "Hospital" means a Harvard Medical School affiliated institution, including hospitals and health and research institutions.

(i) "To Participate" means to be part of the described activity in any capacity, including but not limited to serving as the principal investigator, co-investigator, study designer, research collaborator, provider of direct patient care, or author on a publication of the research study. The term is not intended to apply to individuals who provide primarily technical support or who are purely advisory, with no direct access to the data (e.g., control over its collection or analysis), unless they are in a position to influence the study's results or have privileged information as to the outcome. This definition applies to a Faculty Member receiving sponsored research or participating in non-clinical research in the same way that it applies to a Faculty Member participating in clinical research, including such activities as collaboration, study design, and authorship.

(j) "Private Medical Practice" means the professional services rendered by a physician, including departmental practice plans, and the procedures integral to those services.

(k) "Sponsored Research" (9) means research, training and instructional projects involving funds, materials, or other compensation from outside sources under agreements which contain any of the following.

1. The agreement binds the University or Hospital to a line of scholarly or scientific inquiry specified to a substantial level of detail. Such specificity may be indicated by a plan, by the stipulation of requirements for orderly testing or validation of particular approaches, or by the designation of performance targets.

2. A line-item budget is involved. A line-item budget details expenses by activity, function or project period. The designation of overhead (or indirect costs) qualifies a budget as "line item."
3. Financial reports are required.
4. The award is subject to external audit.
5. Unexpended funds must be returned to the sponsor at the conclusion of the project.
6. The agreement provides for the disposition of either tangible or intangible properties which may result from the activity. Tangible properties include equipment, records, technical reports, theses or dissertations. Intangible properties include rights in data, copyrights or inventions.

(l) "Technology" means any compound, drug, device, diagnostic, medical or surgical procedure intended for use in health care or health care delivery.

STANDING COMMITTEE ON CONFLICTS OF INTEREST AND COMMITMENT

The Dean of the Faculty of Medicine will appoint a standing committee. This Standing Committee on Conflicts of Interest and Commitment will be comprised of representatives from both the clinical and preclinical faculty and will be responsible for reviewing cases which are brought to its attention by the Office of the Dean. It will review such cases and will make recommendations for conflict resolution to the Dean. The Committee will develop procedures for implementing the disclosure and approval process, the establishment of oversight protocols, and the handling of cases involving non-compliance and breach, and the designing of appropriate subsequent disciplinary actions.

The Standing Committee is responsible for reviewing the implementation of the policy on a regular basis and providing oversight to assure that the policy is applied consistently to the Faculty including both those based in the Quadrangle and those based in the affiliated Hospitals. The Standing Committee is responsible for reviewing cases which may be referred to it where the application of the policy to an individual is unclear. Finally, the Standing Committee will continue to review both the policies of other institutions and any government requirements in this area and to recommend changes to the policy when appropriate.

The Office of the Dean is responsible for overseeing the implementation of the policy by all affiliated institutions, including the process and mechanism for disclosure and resolution. This Office will review all breaches of the disclosure process, including (a) failures to comply with such process, whether by virtue of a Faculty Member's refusal to respond or by his/her responding with incomplete or knowingly inaccurate information, (b) failures to remedy conflicts, and (c) failures to comply with a prescribed oversight plan. Such cases will be forwarded to the Standing Committee for review. Based on its review, the Committee will make recommendations to the Dean for further action. In all cases, Faculty Members will be provided the explicit opportunity to respond in person and in writing to the issues raised in the course of such review. Any such written response will be appended to the Committee's report for review by the Dean and, in the case of Hospital-based Faculty Members, the Hospital CEO. The Committee will also be available to advise affiliated Hospitals on the application of the guidelines to specific cases as disclosed by their Faculty.

DISCLOSURE PROCESS AND IMPLEMENTATION

The Office of the Dean has the ultimate responsibility for confirming compliance by all Faculty Members with the policies of the Faculty of Medicine. Such responsibility extends not only to Quadrangle-based Faculty but also to Faculty based in the affiliated Hospitals.

Submission of Disclosure Forms

1. The Office of the Dean is responsible for the dissemination, collection and review of the disclosure forms for members of the Faculty of Medicine. Each Hospital will designate a responsible office or individual to serve as a liaison representative to the Office of the Dean.
2. All members of the Faculty of Medicine, both full- and part-time, are required to complete and submit a disclosure form on a regular basis. Updated forms must be submitted throughout the year if changes arise which the Faculty Member believes may either: (a) give rise to a conflict of interest or (b) eliminate a conflict previously disclosed.
3. Individuals holding fellowship positions are not required to complete and submit a disclosure form unless they believe that they are involved in or may be involved in a situation which gives rise to a conflict of interest. The Office of the Dean is responsible for sending individuals who hold fellowship positions appropriate notification of their obligations under the policy.
4. Disclosure forms should be returned to the Office of the Dean for initial review. The Office of the Dean will be responsible for providing the forms to the designated Hospital liaison representative for Hospital review. In consultation with the Office of the Dean, each

Hospital will establish its own mechanism for review of the forms to ensure compliance with the disclosure process. This mechanism will include written reminders for Faculty Members to return disclosure forms, as well as statements encouraging Faculty Members to seek assistance in the event of questions or special circumstances. Offices providing such assistance will be designated in each of the Hospitals as well as in the Quadrangle. Regardless of the mechanism selected, disclosure forms which implicate any conflict category should be reviewed regularly by the department head. The disclosure forms will be considered strictly confidential, and it will be the responsibility of the designated offices in the Quadrangle and Hospitals to ensure that the information disclosed in the forms is available only to the individuals duly charged with the responsibility for review. Similarly, offices of department heads, the Dean and the President will be required to establish means for the preservation of confidentiality.

5. In the case of Faculty Members who hold the positions of CEO (or equivalent title) of an affiliated hospital, Dean or Executive Dean of the Faculty of Medicine, or heads of departments, the regular, as well as interim, disclosure and review processes will proceed as follows:
   - chairs of the preclinical departments will report directly to the Dean of the Faculty of Medicine;
   - chairs of the clinical departments will report directly to the Hospital CEO, with copies to the Dean;
   - the Dean and Executive Deans of the Faculty of Medicine will report to the University President;
   - hospital CEOs (or individuals with equivalent title) will report to the Executive Committee of the Board of Trustees of the hospital, with copies to the Dean.

Review of Disclosure Forms

Following disclosure and upon receipt of disclosure forms from the Office of the Dean, each institution will review the forms for its Faculty and the Office of the Dean will review forms for Quadrangle-based faculty. Each institution will notify the Office for Research Issues in the Office of the Dean of the resolution of identified Category 1(a), 1(b), I(c), and I(d) conflicts as well as those instances that may require review and approval by the Standing Committee.

The CEOs and the department heads are expected to notify the Office of the Dean immediately of any cases that require review by the Standing Committee, no matter when the cases occur.

Establishment of Oversight Protocols

The hospital CEO (in the case of hospital-based Faculty) and the Standing Committee (in the case of Quadrangle-based Faculty) are responsible for designing and proposing appropriate oversight mechanisms. They are expected to seek advice from individuals outside as well as within their institutions in preparing such mechanisms. The associated rationale and details must be presented to the Office of the Dean for review and approval.

Implementation Process under Public Health Service and National Science Foundation Regulations

1. Disclosure required by the Public Health Service and National Science Foundation regulations should be made on appropriate forms at the time of grant application submission to the appropriate offices in the Quadrangle and affiliated institutions.
2. Resolution of impermissible Category I(a) and I(b) conflicts identified in the federal application disclosure process should be made by the appropriate Quadrangle or affiliated Hospital officials. Notice of such resolution should be forwarded to the Office for Research Issues in the Office of the Dean. The Standing Committee will review these and other resolutions as appropriate.
3. Decisions as to the appropriate resolutions of Category II(g) conflicts identified in the federal application process should be made by the appropriate Quadrangle or affiliated Hospital officials. Notice of such resolutions should be forwarded to the Office for Research Issues of the Office of the Dean. The Standing Committee will not as a matter of course review such resolution decisions, but reserves the right to do so.
4. In the case of Public Health Service funding applicants, appropriate Quadrangle and affiliated Hospital officials are responsible for notifying the Public Health Service, prior to the institution's expenditure of any funds under the award, of the existence, but not the nature, of a conflict and that the conflict will be managed, reduced or eliminated, at least on an interim basis, within 60 days after it is identified. Such officials are also responsible for informing the Public Health Service that corrective action has been or will be taken when an applicant Faculty Member does not comply with the policy.
5. In the case of National Science Foundation funding applicants, appropriate Quadrangle and affiliated Hospital officials are responsible for certifying to the National Science Foundation that all identified conflicts have been satisfactorily managed, reduced or

eliminated prior to the institution's expenditure of any funds under the award.

COMPLIANCE RESPONSIBILITY

The Faculty of Medicine expects its members to comply fully and promptly with the policy, including the requirements of disclosure. However, it is anticipated that instances of technical non-compliance will occur. It will be the responsibility of the Standing Committee to make recommendations to the Office of the Dean for resolution of such cases.

Instances of deliberate breach of policy, including failure to file or knowingly filing an incomplete, erroneous, or misleading disclosure form, violations of the guidelines or failure to comply with prescribed monitoring procedures, will be adjudicated in accordance with applicable disciplinary policies and procedures of the Faculty of Medicine and of the affiliated hospitals. Possible sanctions will include the following:

1. Formal admonition;
2. The inclusion in the Faculty Member's file of a letter from the Office of the Dean indicating that the individual's good standing as a member of the Faculty has been called into question;
3. Ineligibility of the Faculty Member for grant applications, Institutional Review Board (IRB) approval, or supervision of graduate students;
4. Non-renewal of appointment;
5. Dismissal from the Faculty of Medicine.

Adopted by the Faculty Council, March 22, 1990
Amendments Adopted September 22, 1993
Amendments Adopted September 20, 1995
Adopted by the Harvard Medical Center, May 16, 1990
Amendments Adopted December 13, 1993
Amendments Adopted December 18, 1995
Amended May 25, 2000
Amended May 26, 2004

Footnotes:

[1] See Statement on Research Sponsored by Industry. (go back to source)

[2A] similar parenthetical insert may be inferred throughout this document. (go back to source)

[3A] series of operating definitions of terms appearing with initial capital letters is found in Appendix A of this policy. (go back to source)

[4] By license or exercise of an option to license. (go back to source)

[5] The definition of 'Business' excludes the University, any affiliated hospital, any Private Medical Practice or any entity controlled by, controlling, or under common control with the University or affiliated hospital. (go back to source)

[6] The exemption for royalties under institutional royalty-sharing policies applies to post-market royalties through institutional royalty agreements and not to a Faculty Member's share in equity, licensing fees, milestones payments and other payments received by the institution as part of licensing or other agreements with a Business in which the investigator has a right to share, that are sometimes characterized as "royalties". A Faculty Member's share in such non post-market royalties should be considered to be personal Financial Interests and subject as such to the provisions of the Policy. (go back to source)

[7] Public Health Service Final Rule 42 CFR Part 50 and 45 CFR Part 94; National Science Foundation Rule 59 FR 3308 and 60 FR 35820. (go back to source)

[8] In a time of increasing translational research, it is difficult to arrive at a definition of "clinical research" that precisely delineates research having a direct and immediate impact on human health. There may be pre-clinical studies, for example some kinds of research in animal models or certain translational research, that can have as direct an influence on human health as do clinical studies involving human subjects. While the recommended definition of "clinical research" does not include such pre-clinical research. Faculty Members and institutions should recognize the potential for conflict of interest where the Faculty Member has a related financial interest allowed under Category 1(b). (go back to source)

[9] Adopted from the Harvard University Principal Investigator's Handbook, 1988. (go back to source)

UNIVERSITY OF PENNSYLVANIA SCHOOL OF MEDICINE

II.E.10. Conflict of Interest Policy for Faculty Members *AVAILABLE AT: www.upenn.edu/assoc-provost/handbook/ii_e_10.html. Accessed on August 9, 2006. [See also, Human Resources Policy Manual, Policy No. 003 on Use of University Property] (Source: Office of the Provost, Almanac, March 8, 1983 revised 1991)*

Introduction

This policy applies in full to all Standing Faculty, Standing Faculty-Clinician-Educators, and all full-time members of both the Associated Faculty and Academic Support Staff, hereinafter simply designated faculty members. Parts of it also apply to those with part-time faculty appointments; these cases are noted in the appropriate sections. The details of this policy derive from the following general obligations:

a. All employees are required to conform to the mores and ethical standards of the University and the rules promulgated to enforce them.
b. Employment as a faculty member presumes a primary commitment of time and intellectual resources to the academic mission of the University and its functioning as a community.

The following sections cite specific types of activity that have commonly been found to conflict with these obligations, and the procedures and regulations that have been devised to identify and resolve such conflicts. They are intended to serve as examples and not as a comprehensive compilation. Situations not covered by them will be judged in the light of the above general obligations.

Examples of actions that run counter to the first general obligation include nepotism, discrimination on the basis of irrelevant characteristics, inappropriate use of the University's name, and exploitation of any aspect of association with the University for unacceptable purposes or private gain. They are proscribed at all times for all faculty members, extending to those in part-time employment as noted in the relevant sections of this document. Excessive commitment of time or mental effort to extramural engagements or other non-University activities during the academic year constitutes a violation of the second general obligation. As used in this policy, the academic year is defined for each faculty member as that portion of the year during which he or she receives a salary from the University for services.

Conflict of Interest in the Allocation of Time and Effort to Extramural Activities

The University recognizes that its faculty members are not employees in the usual sense, and that a precise allocation of academic time and effort is inappropriate. Their pursuit of knowledge in their areas of competence is presumed to be a lifelong commitment. A limited association of faculty members with government, professional agencies, and public or private organizations is appropriate, especially when it may enhance their competence as scholars.

Policy on Extent of Extramural Activities. Forms of extramural activity include part-time engagement for a fee as a technical or professional consultant or practitioner and formation or association with business enterprises or non-profit organizations.* In principle, both such associations are approved under the following conditions:

a. Faculty members should not engage in such extramural associations to an extent that detracts significantly from their availability for normal academic duties. These commitments in aggregate should not exceed one day per seven day week during the academic year. Exceptions to this will be permitted only in unusual circumstances and require the specific approval of the president or provost, the academic dean and the department chair.
b. Faculty members shall make known to their department chairs and academic deans the prospect of each continuing engagement, including, at least, all engagements expected to extend for a substantial portion of an academic term. Faculty members should decide to enter a relationship only if, after discussion with their department chairs and academic deans, there is concurrence that the proposed engagement will not conflict with the faculty members' professional obligations to the University, or with the University's outstanding or prospective commitments for teaching and research.
c. In addition to the prospective disclosure cited above, all faculty members must report on the extent of their extramural activities of all types as detailed below.

Conflict of Financial Interest between the University and Extramural Organizations

Members of the faculty or of their immediate families (including parents, children, siblings, spouse) may have significant investments or interests or hold official positions in extramural business organizations, whether or

not they have undertaken to perform continuing work or services for them. Such economic or official relationships are of concern if:

a. The organizations are engaged in activities that parallel activities in which the University is currently or prospectively engaged, and in which faculty members play (or might appropriately play) a role in their academic capacity; or
b. The organizations have a present or prospective relationship with the University, e.g., as suppliers of goods or services or as parties to research contracts, and the conduct of those relationships may involve faculty members in their academic capacities; or
c. The engagements undertaken by faculty members under the aegis of extramural business organizations might be suitable and appropriate activities for execution within the University.

Policy on Disclosure of Relationships with Organizations that are Suppliers or Potential Competitors of the University

In any of these situations, faculty members shall be required to report the facts and circumstances to their department chairs and academic deans so that appropriate steps may be taken to avoid conflicts of interest, especially ones in which faculty members may benefit from a knowledge of confidential information.

In the foregoing it assumed that those with part-time faculty appointments will not normally participate in University decisions that could engender such conflicts of interest for them. Whenever this condition does not obtain, the policy stated above extends to them. Furthermore, in any circumstances in which part-time faculty members are engaged in externally sponsored research projects contracted with the University, or in which they stand to benefit from a knowledge of confidential information, full disclosure of their relationships with relevant extramural organizations and of the facts pertaining to any potential conflict is required.

Policy on Acceptance of Engagements through Extramural Organizations

Faculty members with positions or connections in extramural organizations who wish to undertake engagements through those organizations rather than the University are obliged to offer first to the University each such engagement (grant, contract, client, etc.) in which they would assume one or both of the following relationships to the engagement:

a. Owner, executive or other principal decision-making position responsible for the conduct of that business enterprise; and/or
b. Principal investigator or other substantial responsibilities for the satisfaction of the engagement.

By requiring that each engagement be offered to the University, the following ends are served:

1. The disclosure of the type, scope and extent of extramural activities is achieved, in accord with University policy;
2. The decision as to whether an engagement is appropriately undertaken as a University or extramural activity is shared with the University administration, thereby avoiding possible conflicts of interest, and the appearance of such conflicts.

Faculty members intending to conduct engagements in business enterprises with which they are associated shall disclose in writing to their department chairs and deans:

a. The nature and terms of the proposed enterprise, and
b. The reasons why it should be conducted as an extramural activity.

If the chairs and deans agree that the engagements are not appropriate as a University activity, and if they conclude that the other conditions of the extramural consulting policies of the University will be met, then they will advise the faculty members to proceed. Otherwise, they may require that the engagements be conducted within the University.

Disclosure of University Affiliation in Publications of Extramural Organizations

Faculty members who form or associate with extramural business enterprises or non-profit organizations should exercise particular care that their University affiliation is appropriately cited in publications of such organizations. Problems that can arise from failure to observe this injunction include:

a. Such an organization, by reason of the participation of faculty members, might be considered to have some formal or informal relationship to the University.
b. Faculty members by reason of their positions in such organizations might be expected to discharge duties and responsibilities for those organizations that would be inconsistent with their primary duty to the University.

Disclaiming University Relationships. A business enterprise or non-profit organization, with which a fac-

ulty member has a connection, may release to the public from time to time publications concerning itself and its activities. In all such publications it may be desirable and, in many cases, required by law that a faculty member's affiliation with the University be disclosed.

The impact of such disclosure will depend on the circumstances. At one extreme a faculty member might serve as a member of the board of directors of an established business or non-profit organization, where there is not even a remote implication that such organization is in any way connected with the University of Pennsylvania. At the other extreme all or a large number of the principals of an organization (officers, directors, promoters and substantial shareholders) may be faculty members. In such cases, there is a strong implication that the organization may be connected with the University of Pennsylvania, even that the University bears some responsibility for its activities and success. In these cases, an express statement of the form,

The _____ has no connection, directly or indirectly, with the University of Pennsylvania.

in prominent type, should be included in all publications released by such organization. The provost shall have the power to require such a statement to be included in all organizational publications that refer to faculty members, when it is in his or her judgment necessary.

The foregoing rules extend to part-time faculty members, when their association with the University is mentioned in an organizational publication.

Affirmation of Obligations to the University. A faculty member may have a position of responsibility (continuing or temporary) with an extramural business organization. In such cases it should be made clear in any publications of the organization that the obligations, in terms of both time and responsibility, of the faculty member to the extramural organization are limited by and subject to the policy of the University of Pennsylvania. This alerts both the public and the faculty member's business associates that duties to the extramural organization are thus limited. This is especially necessary in the case of corporate officers who are normally regarded as owing a comprehensive fiduciary duty to the corporation and its shareholders. The suggested format for such a disclosure is:

> J. Smith, a vice president of this corporation, is a member of the faculty of the University of Pennsylvania and as such is subject to limitations by the University on the time that may be devoted to the affairs of this corporation. In any instance where the interest of this corporation may conflict with the interest of the University of Pennsylvania, J. Smith will resolve such conflict in favor of the University of Pennsylvania.

The Provost shall have the power to require such a disclosure in any instance where he or she adjudges it necessary.

Conflict of Interest in Externally Sponsored Research
Regulations concerning sponsored research may be found in the "Guidelines for the Conduct of Sponsored Research". Further details and regulations may be found in the current Research Investigators' Handbook, available from the Office of Research Administration, and Guidelines for Extramural Activities of Faculty of the University of Pennsylvania Medical Center and Health System.

The University encourages its faculty members, including those in part-time employment, to participate in externally sponsored research projects whether supported by government agencies, foundations, associations, or other non-profit organizations; or by corporations, partnerships or other for-profit entities. In any sponsored project, faculty members are expected to avoid use of the project for their private financial gain other than in the form of salary support or of royalties resulting from commercialization of intellectual property rights in accordance with University policies. However, there may be unusual circumstances where the interests of the University would be served if a faculty participant in a sponsored project were to assume an entrepreneurial role, as, for example, by direct participation in a private enterprise providing funds in support of the project. Assumption of such a role would not be a violation of these guidelines if approved in advance and reviewed periodically by the relevant Dean and the Vice Provost for Research. Examples of situations from which conflicts of interest may arise include, but are not limited to, the following:

a. Undertaking or orientation of sponsored research to serve the needs of a private agency or enterprise in which a responsible staff member has an interest.
b. Purchase of major equipment, instruments, materials or other items for externally sponsored research from any agency or enterprise in which a responsible staff member has an interest.
c. Acceptance of any limitations on the free publication of and access to the results of any sponsored research. Exception may be granted by the provost for privileged information, but only in the form of a delay in the release of such information. The delay will only on rare occasions exceed three

months. Those wishing to engage in research of a kind whose results cannot be so disseminated may only do so as an extramural consulting activity under the conditions previously described.

d. Transmission to any private agency or enterprise, use for personal gain, or other unauthorized use of the work product, results, materials, records, or information gathered from sponsored research that is not made generally available through publication or other free access.
e. Acceptance of gratuities or special favors from a private agency or enterprise with which the University conducts business in connection with a sponsored research project.

Disclosure to Responsible University Officials. Before participating in any sponsored research project, all faculty members must give written notice of their extramural consulting relationships or other sponsored research projects that may relate in any way to the project to the appropriate department chairs and through them to the deans and vice provost for research. Any significant financial or managerial interests that may relate in any way to the project must be disclosed in writing to the vice provost. Any faculty members engaged in sponsored research projects must disclose in the same manner any change in their outside activities or interests. In the light of such disclosures, the University will take appropriate steps to neutralize or eliminate potential conflicts of interest.

Distribution of Effort. The sponsoring agency supporting research must not be misled as to the amount of intellectual effort that faculty members are actually devoting to these research projects. A system of precise time accounting is incompatible with the inherent character of the work of faculty members, because the various functions that they perform are closely interrelated and do not conform to any meaningful division of a standard work week. However, if externally sponsored research agreements provide that faculty members will devote a definite fraction of effort to the projects, or if it is agreed that they will assume specified responsibilities in relation to such research, demonstrable relationships between the stated efforts or responsibilities and the actual extent of their involvement are to be expected. Each faculty member, in such circumstances, shall confirm the fraction of effort devoted to the projects in the effort reports required of all faculty members who are so engaged.

Advice and Guidance. Any questions concerning potential conflicts of interest, appropriate distribution of effort, or other problems associated with externally sponsored research, should be addressed to the office of the Vice Provost for Research.

Requirements for Reporting Extramural Activities and Obligations

At the end of each academic year, each faculty member shall submit to his or her department chair and dean a report of his or her extramural activities during that year, containing the following information:

a. Number of days (or hours, if preferred) of extramural activities for fee (include consulting, professional practice, outside teaching commitments, lectures for honoraria, etc.);
b. Names of organizations (government agencies, private firms, partnerships, etc.) for which the extramural activities conducted represented a continuing engagement;
c. Number of days (or hours, if preferred) of extramural activities on behalf of businb ess enterprises in which they have financial interests or official positions.
d. Names of business organizations in which the faculty member is a significant owner, partner, officer, director, or staff member, etc.

The last item shall also be reported by all part-time faculty members for whom any of the following conditions obtain:

- The organization is a supplier of the University and the part-time faculty member participates in the decision to engage its services.

- The organization supplies goods or services to the University to be used in the performance of externally sponsored research projects in which the part-time faculty member participates.

- The part-time faculty member is privy to confidential University information that could be used to the business advantage of the organization.

- The affiliation of the part-time faculty member with the University may be mentioned in any publication of the organization.

Forms for the reporting of extramural activity are available from the Office of the Provost.

All faculty members must also report on a continuing and timely basis to the appropriate administrators the relevant circumstances, as noted in the sections cited, whenever any of the following conditions are met:

a. They have or wish to initiate a relationship with an extramural business organization that is or may become a supplier or competitor of the University (see section II.E.10 on Policy on

Disclosure of Relationships with Organizations that are Suppliers or Potential Competitors of the University).

b. They wish to undertake an engagement (grant, contract, client, etc.) through an extramural organization (see section II.E.10 on Policy on Acceptance of Engagements through Extramural Organizations).
c. They intend to participate in a sponsored research project that may be related to their other sponsored research projects, to any of their extramural consulting relationships, or to any organization in which they have significant managerial or financial interests (see section II.E.10 on Policy on Acceptance of Engagements through Extramural Organizations).

Employment of More than One Family Member (Source: Office of the Provost; Almanac, December 16, 1997)

University policy permits the employment of more than one member of a family (defined as being related by blood, marriage and former marriage, or adoption, or defined as partners recognized under University benefits policy), whether or not the persons concerned are in the same academic or administrative department. The University's primary concern in such cases of appointment, as in all others, is that faculty or staff members are the best candidates with respect to the requisite qualifications for employment. The University has a parallel concern, however, in the avoidance of a conflict of interest or the appearance of such conflict, where an employee's professional decisions or actions pertaining to the performance of his or her job would be colored by considerations arising from a family relationship with another employee. The University also recognizes that the appointment of two or more family members, especially within the same department, could generate pressures and prejudice among colleagues. To guard against such conflicts and abuses, the following rules must be observed:

A. Family Members Appointed to the Faculty

No faculty member shall participate in any way whatsoever in the decision to employ, promote, reappoint, or terminate the appointment of a member of his or her family on the Standing Faculty or the Associated Faculty. Any proposal to employ as a faculty member a person who is related to a member of the faculty or administration must be brought to the attention of the dean before an offer of appointment is made. In cases where there is a potential conflict of interest in the professional relationships of family members or with respect to other employees of the University arising from the family relationship, the department chair must outline in writing the steps being taken to avoid or manage conflicts of interest or the appearance of such conflicts, subject to approval by the dean. Deans will report such arrangements to the provost in the course of normal administrative oversight.

No faculty member shall participate in any other decision, including determining the salary, teaching and/or administrative assignments, and space assignments, directly and individually affecting a member of his or her family on the Standing Faculty or Associated Faculty.

B. Family Members Appointed to Non-faculty Positions

Faculty members should take care to avoid conflicts of interest or the appearance of such conflicts in the employment of, and in any ongoing University-related professional relationship with, a family member in a non-faculty position. All decisions regarding such employment should be conducted in strict conformance with the Human Resources Policy.

C. Reporting

In the course of normal administrative oversight, department chairs or other heads of department will report periodically to deans, and deans will report to the provost, on steps that have been taken to avoid or manage conflicts of interest or the appearance of such conflicts among faculty members and/or academic administrators who are related as family. In each case, the faculty members and/or academic administrators who are subject to such reports shall receive copies of such reports on a timely basis.

These requirements extend to part-time faculty appointments whenever such a person may exercise decision-making power over the employment and/or administration of a family member employed by the University.

* Including part-time employment by another academic institution. Such employment may be inappropriate for a faculty member whose primary commitment of time and intellectual resources is to the academic mission of the University of Pennsylvania and its functioning as a community. A full-time faculty member who considers employment for research or teaching at another academic institution during the period of his or her employment by the University should treat this prospective employment as a continuing engagement and follow the procedures outlined below.

SELECTED HYPOTHETICAL EXAMPLES OF DIFFICULT CONFLICTS OF INTEREST

(1) The Chair of the XXX Department has a startup company that proposes to sponsor the research of Dr. Doe, assistant professor of XXX.

The chair supervises the young faculty member (salary, space, resources, promotion).

Problem 1: Chair's official status raises this scenario to an institutional conflict of interest (ICOI).

Problem 2: Raises issues of perception by other faculty of potential favoritism.

(2) Department Chair has an extensive consulting relationship with a company that proposes to sponsor the Chair's research—an example of a personal COI.

The Chair assigns the project to Assistant Professor Doe as the PI to avoid the COI but will remain involved.

Problem: Arguably an ICOI because the authority of Chair could influence the outcome.

(3) EVP/Dean/COO invests $50K to take institutional equity in Dr. Smith's startup company to develop vaccines (in good, but short-sighted, faith).

Problem 1: Company wants to fund research in the institution (clinical research—usually a non-starter!)

Problem 2: Dr. Smith wants to pipeline all of his future technology to his company.

(4) Dr. Smith asks the university to license the vaccine technology that he generated in his university laboratory to his company.

Problem: ICOI because institution has equity in company and would receive royalties. Institution has duty to ensure that the technology is transferred in the way that is most likely to benefit the public.

(5) Dr. Zee, the Service Chief, routinely recommends the surgical sutures, stents, and other devices purchased by the hospital. Dr. Zee is compensated >$10K each as a consultant and speaker for the suture company and holds >$20K stock in the device company.

Problem: ICOI with the institutional vendor policy.

(6) Dr. Lee holds a position as officer (or member of the board of directors) of a company that proposes to sponsor research or do business with institution.

Problems: ICOI because Dr. Lee has fiduciary duties to both entities. These duties include:

- Duty of reasonable care to the company—to maximize shareholder profit.
- Duty of loyalty to both—to the best interests of the company/institution.
- Duty to follow Doctrine of Corporate Opportunity—to preserve any business opportunities for the corporation.
- Duty to avoid conflicts of interest.

Recusal is a safe harbor but only if it is "real;" difficult for major shareholders.

Several corporate sanctions are available for corporate officers who breach their duties.

(7) CASH Co. wants to sell major equipment to the clinical system. To sweeten the deal, it offers to fund fellowships, hospital space, and/or research tied to an agreement that all supplies for the equipment will be purchased from CASH.

Problem: Potential ICOI because funding is a write-off for CASH but has the appearance of being a bribe (always think of defending against headline news.) Plus, the IRS sees this practice as "excess benefits, unless extensive fair market value studies are documented

(8) Dr. Bart receives $50,000/yr in consulting or other personal fees and/or has equity interests (stock, options) in FLOW Co.

FLOW proposes to pay Dr. Bart personally (not through the institution) if Dr. Bart will conduct a training course for FLOW (using FLOW'S devices). FLOW wants Dr. Bart to use the institution's resources (space, personnel, resources, hospital facilities, patients) to teach the course. "Students" could include other physicians and fellows or the personnel of BART.

Problem 1: This is a personal COI for Dr. Bart. It becomes increasingly serious, depending on the resources that are used. It gets most serious if she were to involve patients.

Problem 2: Institutional COI if FLOW also provides a "gift" to the Department (e.g. funding for fellows; funds to name a surgery suite).

SHARED RESPONSIBILITY, INDIVIDUAL INTEGRITY: SCIENTISTS ADDRESSING CONFLICTS OF INTEREST IN BIOMEDICAL RESEARCH March 13, 2006

Federation of American Societies of Experimental Biology (FASEB) *The FASEB Board of Directors approved this report on December 9, 2005.*

The guiding principles to aid investigators in addressing these challenges are:

Guiding principle 1: Investigators have a responsibility and commitment to conduct scientific activities objectively and with the highest professional standards.

Guiding principle 2: The primary responsibility of full-time investigators is to the institution. Outside activities shall complement, not compromise, institutional responsibilities.

Guiding principle 3: It is appropriate and beneficial for academic institutions to develop and enforce their own mechanisms of review and oversight of investigator relationships with industry.

Guiding principle 4: The academic community can and shall monitor itself through peer review of industry relationships. Institutional committees that include peer members from the same institution are appropriate and effective in reviewing disclosures of investigators' industry relationships.

Guiding principle 5: Investigators want and need clear guidance, efficient processes, and adequate support mechanisms from their institution throughout their participation in industry relationships.

Guiding principle 6: Investigators shall have access to, and be involved in the analysis and/or interpretation of all data generated in the research.

Guiding principle 7: Mutual understanding of constraints, principles, and policies regarding access, analysis, and dissemination of research information, data, and materials among investigators and their students and trainees, institutions, and sponsors is beneficial.

Guiding principle 8: Investigators shall not enter into agreements with companies that prevent publication of research results. Pre-publication review by an industry sponsor shall occur in a timely manner (no more than thirty to sixty days) so as not tounnecessarily delay study publication.

Guiding principle 9: Investigators shall be aware of and adhere to individual journal policies on disclosure of industry relationships.

Guiding principle 10: Consulting and advisory board relationships shall be carried out in a transparent and accountable manner and be disclosed as they are initiated.

Guiding Principle 11: When investigators have consulting relationships with an investment firm related to their area of expertise, all parties shall be aware of the specific circumstances involved.

Guiding principle 12: Investigators shall not use federal funds to the benefit of a company, unless this is the explicit purpose of the mechanism used to fund the research (e.g., Small Business Innovation Research and similar grants).

Guiding principle 13: When investigators own significant equity in a company with which research is conducted, all parties shall be aware of the special circumstances involved.

Guiding principle 14: When holding a significant role in a start-up company, investigators shall be guided by agreed-upon limits to the scope of the relationship.

Guiding principle 15: Investigators shall be aware of and adhere to requirements of federal funding related to disclosure of inventions. Investigators shall adhere to patent law and institutional requirements.

Guiding principle 16: Investigators shall not seek to influence their institution's technology transfer decisions for personal gain.

Guiding principle 17: A mentor's outside commercial interests shall avoid impeding a trainee's timely progress toward his/her degree, restricting a trainee's right to publish his/her dissertation research in a timely manner, compromising a trainee's career progress, or restricting a trainee's freedom of inquiry.

Guiding principle 18: Mentors and institutions should make trainees aware of their rights and responsibilities in industry relationships.

Guiding principle 19: Investigators shall regard all significant financial interests in research involving human subjects as potentially problematic and thus requiring close scrutiny.

Approved by AAMC Executive Committee, January 6, 2006 (Excerpt) (Full text available at www.aamc.org/research/clinicaltrialsreporting/clinicaltrialsreporting.pdf Accessed August 10, 2006).

Appendix 5

PRINCIPLES FOR PROTECTING INTEGRITY IN THE CONDUCT AND REPORTING OF CLINICAL TRIALS

ISSUE Public concern is high regarding the timely and complete reporting of clinical trial results, primarily when the trials are sponsored by the drug, biologicals, or device industries. Because academic researchers and their institutions often play a prominent role in such trials, these concerns challenge the integrity of the academic medical research community as well as the sponsors of the trials.

BACKGROUND Despite a number of external initiatives that have heightened standards for reporting clinical trial results, the AAMC has been troubled by evidence that significant variation continues to exist within the academic community over the application of appropriate standards for analyzing and reporting the results of sponsored clinical research, especially clinical trials sponsored by industry. Accordingly, the AAMC, in collaboration with the Centers for Education and Research in Therapeutics and the BlueCrossBlueShield Association, has developed a set of principles, recommendations, and guidelines, rooted in sound science and sound ethics, to guide the medical schools, teaching hospitals, and professional societies that comprise the AAMC's membership and be broadly disseminated in the professional community. Assuming that broad consensus is reached within academic medicine, the sponsors will work to win acceptance of the principles by industry, the FDA and NIH, non profit sponsors of clinical trials, patient advocacy groups, and ultimately, the entire medical community.

CONSENSUS PRINCIPLES The following principles should apply to all clinical trials conducted in academic medical institutions regardless of the source of funding. They encompass single site as well as multisite studies, although operationalization of the principles may differ across study types and sizes. For purposes of these principles, "clinical trials" should be defined by reference to the ICMJE definition: "Any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome." "Medical intervention" means "any intervention used to modify a health outcome", including "drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like."1 This definition explicitly excludes phase 1 and early phase 2 studies (but not all late phase 2 studies), and it includes all phase 3 and 4 clinical trials, including studies of new indications for approved products.

Publications and Public Availability of Research Results

1. Researchers and their institutions have an ethical obligation when conducting human research to seek to make the results available publicly.

2. Contracts between sponsors and institutions for conducting clinical trials should require a good faith effort to publish the results of such trials in a peer reviewed journals in a timely fashion.

3. Contracts for clinical trials should contain a commitment of adequate funding to cover the full costs of the analysis defined in the protocol and the costs associated with publishing the results. This principle applies even when the study is terminated for any reason prior to meeting its pre-specified objectives.

4. All trials meeting the ICMJE requirements2 for registration should make their results publicly available, by means of a link to any peer reviewed publications and by posting the results in an online accessible repository, within 18 months of submission of a manuscript for publication.

5. After publication of the results, the sponsor, the investigators, and their institutions should adopt a model for public sharing of the data underlying publications similar to that of NIH, which permits exceptions for confidential or proprietary information.

Registration of Clinical Trials

6. Within 21 days of initiating enrollment of participants, any clinical trial covered by these principles should be fully registered pursuant to the ICMJE requirements4 for registration. Registration must include the assignment of a unique identifying number to each clinical trial.

7. Registration should be accomplished either in clinicaltrials.gov or in another public, non-profit, international registry and should include all the elements required by that registry.

8. Insofar as is feasible, trial registration data should be regularly updated to include a link to all published reports associated with the study.

Lead Investigator and Steering Committee

9. A multisite clinical trial, at the outset, should identify a lead or principal investigator and a steering committee to represent the full body of investigators.

Publication and Analysis Committee

10. A multisite clinical trial, at the outset, should establish a publication and analysis committee [hereinafter P&A committee]. It is essential that the P&A committee be independent of the sponsor's control, have access to the full data set, understand and implement the prespecified analysis plan, and have the resources and skills both to interpret that analysis and perform additional analysis if required. In order to prevent any appearance of undue influence by the sponsor, the P&A committee should contain a majority of participating, non-sponsor-employed investigators, with appropriate skills in analysis and interpretation of clinical trials. The P&A committee and the steering committee may have the same membership.

11. The P&A committee in multisite clinical trials (or the principal investigator of single site studies), through a qualified expert of its choosing, preferably a member of that committee, should have the right to access any data generated during the study that the committee deems necessary to ensure the integrity and validity of the study and its full reporting.

12. The P&A committee in multisite clinical trials (or the principal investigator in single site studies) should require that the sponsor of the study perform its analysis of trial data in a defined period of time. The committee (or PI) should be able to conduct its own analysis through an expert selected by it, to the extent it deems this necessary. Whenever feasible, the expert should be agreed upon by the P&A committee and the sponsor.

13. The sponsor should share with the P&A committee all analyses called for by the study that the sponsor conducts of any biological materials it receives during the course of the study.

14. The P&A committee or PI should make a good faith effort to disseminate the results of the study through peer reviewed mechanisms.

Individual Publication

15. Site-specific publications in multisite trials have an unavoidable potential for bias. Because they are almost never part of the original analytic plan, they are often misleading, and should be strongly discouraged. However, to respect an academic institution's commitment to academic freedom, site-specific analyses should nonetheless be permitted with conditions. Accordingly, an individual site investigator in a multisite trial should be free to analyze and publish data from the individual site, consistent with sound principles of science and analysis, but only after review and comment by the P&A committee and only after publication of the study as a whole, or, in the absence of acceptance of the full publication, within 2 years from the specified end points or earlier termination of the study.

Authorship

16. Ghost or guest authorship is unacceptable. Authorship implies independent, substantial, and fully disclosed participation in the study and in the preparation of the manuscript. It is acceptable for employees of the sponsor to participate in drafting and publication activity, but only if their roles are fully disclosed.

17. Institutions conducting clinical trials should adopt as policy the standards of authorship defined by the ICMJE.

18. Where applicable, investigators should use the CONSORT principles5 as guidance for publication of trial results.

19. Investigators should fully disclose, and journals should publish, the existence of all relevant financial interests, including consultancies of any investigator, in all communications of trial results.

20. Any manuscript submitted for publication should accurately disclose the role of each author in conducting the study and preparing the manuscript. Such information should also be disclosed in any public presentation of study results, to the extent practicable.

21. Manuscripts submitted for publication should disclose all previous publications involving the same protocol or database.

22. Manuscripts submitted for publication should be accompanied by the protocol and pre-specified analysis plan and all dated amendments to them, and any deviations to the pre-specified plan should be identified and discussed.

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