

Working Policy Paper
of the
AEI – Brookings Joint Center on Regulatory Studies

**THE TRIPLE HELIX: UNIVERSITY, GOVERNMENT AND INDUSTRY
RELATIONSHIPS IN THE LIFE SCIENCES**

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May 27, 2004

This report was supported by a research grant from the Ewing Marion Kauffman Foundation.

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I. Introduction/Purpose

Over the past four decades, the life science enterprise has changed dramatically. At one time, the domains of academe, industry and government existed largely as parallel universes. Scientific discoveries from our universities were applied and developed independently by industry to create marketable products and thereby build shareholder equity under the watchful eye of government regulators. This separation no longer exists.

Today we find the roles and interests of universities, corporations and government intimately intertwined in a complex combination of financial, intellectual, personal and legal relationships. On the one hand, these relationships seem to have fostered collaboration, productivity, innovation and wealth. On the other, many observers find them troubling because the competing commitments and interests that result may threaten the integrity of the scientific endeavor itself, particularly in the biomedical and health-related sciences.

The purpose of this paper is to present data regarding the nature, extent and consequences of the 'triple helix' of relationships between academe, the government and industry in the life and health related sciences. First, we present what is currently known regarding the nature and extent of relationships that exist between government and academic scientists and industry. Next we provide evidence supporting the benefits of these relationships for individual scientists, their institutions and the advancement of science. Then we discuss the potential risks of these relationships. In the next section we provide a set of guiding principles and management and policy suggestions regarding the disclosure and management of relationships among the various sectors. In the final section of the paper we discuss the potential implications of academic industry relationships for governmental industry relationships.

II. Highly Integrated Structure of Modern Life Science Enterprise

A. Structure of Relationships

Before trying to describe the extent and consequences of relationships that make up the triple helix, it is useful to define more precisely the structure of some of the potential relationships that exist between scientists and organizations in these sectors. For the purpose of this paper, relationships with industry are defined as arrangements in which academic or government scientists or administrators carry out research or provide intellectual property in return for considerations of various types (research support, honoraria, consulting fees, royalties, equity, etc.). The following types of relationships are among the most common but do not exhaust the alternatives:

1. Research relationships: the support by industry, usually through a grant or contract, of university-based research (Blumenthal, et al., 1996b).
2. Consulting relationships: the compensated provision of advice or information, usually by an individual academic or government scientist or administrator, to commercial organizations. Examples of consulting relationships include, but are not limited to service on boards of directors, service on scientific advisory boards, etc. (Jones, 2000).
3. Licensing relationships: the licensing of government or university owned technologies to industry. These relationships are often negotiated and managed by an office of technology transfer located within the government, universities, medical schools and often within independent hospitals and research facilities (Kauffman Foundation Scientific Advisory Committee, 2003).
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. It is important to note that equity relationships can stem from consulting

and licensing relationships described above. For example, relationships of this type often occur when cash-poor start-up companies use equity to compensate faculty for consulting or other services in lieu of actual cash payments. However, scientists may also participate in the founding of new commercial entities, sometimes taking much larger amounts of equity in return for contributions of intellectual property (Bowie, 1994).

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 (Blumenthal et al, 1996a). On rare occasion, industry may provide training opportunities for scientists in governmental agencies, but provision of financial support for such training is not the norm

6. Gift relationships: gift relationships are based on the transfer of scientific and non-scientific resources, independent of an institutionally negotiated research grant or contract, from industry to academic or governmental scientists. Examples of gifts include, but are not limited to discretionary funding, equipment, food, trips to meetings, biomaterials , etc. (Campbell et al, 1998).

These and other forms of relationships may occur singly or in combination. The mixed forms (such as those involving research support, gifts and consulting or equity holding) often raise the most troubling concerns about conflict of interest because multiple relationships often involve more money (both real and potential) than single forms of relationships with industry.

B. Prevalence and Magnitude of Relationships

In this section we review what is known regarding the prevalence and magnitude of Academic Industry Relationships (AIRs) and Government Industry Relationships (GIRs).

1. Academic Industry Relationships

The most recent nationally-representative data on the prevalence and magnitude of AIRs in the life sciences stem from surveys of company executives and faculty members conducted in the mid 1990's (Blumenthal, et al, 1996a, Blumenthal et al, 1996b). A 1994 survey of senior executives of science companies revealed that over 90 percent of the firms responding to the survey participated in some form of academic industry relationship. The most prevalent form was retention of university faculty as consultants (88 percent). Fifty nine percent supported university based research either in the form of a grant or a contract and 38 percent supported the training of students and post-doctoral fellows. Seven percent of companies reported that faculty members were significant equity holders in their companies (Blumenthal et al, 1996a).

A 1995 survey of 2052 faculty members at the fifty most research-intensive US universities revealed that 28 percent of respondents reported receiving some research support from industrial sources (Blumenthal et al, 1996b). The prevalence of support was greater for researchers in clinical departments (36 percent) than those in non-clinical (21 percent) departments. This finding is likely explained by the fact that clinical trials and other forms of clinical research are conducted in clinical departments rather than in basic science departments.

Another common form of relationship was based on consulting. Among basic scientists at the 50 most research-intensive universities in the U.S., 60% had consulted in the three preceding years (35.2% had consulted with a private company and 24.5% for a public

company). Among the 60% of who consulted, 26% reported these activities as a major source of supplementary income (Jones et al, 2000).

The most commonly reported relationship was a gift relationship between academic scientists and industry (Campbell et al, 1998). Among life science faculty in the 50 most research intensive universities, we found that almost half (43%) received research-gifts, independent of a grant or a contract from industry in the three years preceding the study. The most widely reported gifts received from industry were biomaterials (24%), discretionary funds (15%), research equipment (11%), trips to professional meetings (11%) and support for students (9%).

Another source of data regarding scientists' relationships with industry comes from a review of the University of California at San Francisco (UCSF) annual faculty disclosure forms from 1990-1999 (Boyd & Bero, 2000). This study found that 7.6% of principal investigators at UCSF had some form of personal financial ties to industry. A third of these reported temporary speaking engagements for companies, a third involved the investigator holding a paid position on a scientific advisory board or board of directors and 14% related to the ownership of equity in a firm. Finally, 12% of the 7.6% of PI's with industry relationships at UCSF reporting financial ties to industry involved investigators with multiple relationships including, but not limited to equity ownership, consulting income and management interests.

A final source of data on academic-industry relationships is from a series of case studies examining the extent to which senior leaders of four of the largest, most research intensive academic health centers had relationships with industry (Campbell et al, 2004). Examples of study participants included: university presidents, provosts or chancellors, medical school deans, the vice deans for research, chairs of life science and medical school departments, investment officials, directors of development, directors of technology transfer, directors of public affairs, the chief financial officers, development officers, general counsel, and members of the IRB. Based on 49 confidential interviews across the four institutions, the vast majority of the university officials interviewed had at

least one relationship with industry. Examples of officials' relationships included having founded companies, owning equity in companies they participated in founding, being paid speakers, and serving as trustees and consultants. Many respondents reported engaging in several of these relationships. Institutional leaders with these relationships included university presidents and vice presidents, deans, and department chairs.

2. Government Industry Relationships

There are no comprehensive, systematically collected, publicly available data that could be used to explore the nature and extent of relationships between government scientists and administrators and industry. However, the recent series of newspaper articles regarding financial relationships between senior scientists at the National Institutes of Health and industry resulted in a Congressional concern about the nature and extent of these relationships (Willman, 2004, Grady, 2004). In response, the Director of the NIH convened a special advisory group to explore the background and propriety of such relationships (Marshall, 2003) and to issue a report containing appropriate policy recommendations for dealing with them. The report of the advisory committee was released on May 6, 2004. Following the release of the advisory committee's report, Congressional hearings have been held to further investigate the issue.

The full extent of relationships between scientists at other government agencies and corporations is unknown. This does not mean that these relationships do not exist. Opportunities for such relationships, involving consulting arrangements and equity positions are certainly not unique to the biomedical and health-related sciences. Without much difficulty, one can imagine a government physicist or engineer entering into such a relationship with a defense or aerospace contractor. Unless disclosed, either through mandatory public financial disclosures or investigative reporting, the public is not likely to know whether or not such relationships do, in fact, occur.

III. Benefits of Academic Industry Relationships

This section presents the empirical evidence supporting the benefits of academic industry relationships which have been systematically studied. Most of the existing literature focuses on the institutional benefits that accrue as a result of research relationships. However, a small body of evidence has emerged regarding the personal financial benefits resulting from consulting relationships.

A. Funding for University Research

The most obvious benefit of research relationships with industry is that these arrangements provide funds to support the research conducted in academic institutions. In a 1994 survey of senior research executives at 306 life science companies in the US reported that their companies supported more than 1,500 academic-based research projects at a cost of over \$340 million (Blumenthal et al., 1996a). Based on these reports, it was estimated that the life science industry as a whole supported more than 6,000 life science projects and expended \$1.5 billion for academic-based research in the life sciences.

B. Academic Productivity

Contrary to what many believe, the receipt of industry research funding is not associated with detectable adverse effects on academic productivity. Indeed, if anything, research funding from industry is associated with significantly greater academic productivity on the part of involved university investigators. In our 1994-95 survey of over 2000 life science faculty, those with funding from industry published significantly more articles in peer-reviewed journals in the previous 3 years than faculty without industry funding (14.6 vs. 10.1 respectively, $p < .05$) (Blumenthal et al., 1996b). Because of the cross sectional nature of the data, it is impossible to establish causality between industry

funding and increased productivity. It may be that industry funding provides resources to investigators that increase their publication productivity. Alternatively, it may also be that industry seeks out the most productive researchers. While we cannot know for sure, it is likely that some combination of these two explanations is at work.

Academic researchers benefit from increased publications, since reports of original research in peer reviewed journals represent one of the main criteria by which faculty are awarded promotions, tenure, prizes, future research grants, positions in professional organizations, and ultimately a place in the history of the scientific endeavor (Fox, 1985). At an institutional level, more publications by faculty translate into greater prestige, and, perhaps, an increased ability to attract top students, faculty and future research funding.

C. Commercial Productivity

In addition to publications, research relationships are associated with an increased likelihood of commercial activities. Compared to faculty without research relationships, those with industry funding were significantly more likely to report that they had applied for a patent (24% v. 42%), had a patent granted (12.6% v. 25%), had a patent licensed (8.7% v. 18.5%), a product under review (5.5% v. 26.7%) a product on the market (10.8% v. 26.1%) or a start-up company (6.0 v. 14.3%) (Blumenthal et al, 1996b). A number of additional benefits may accrue to faculty as a result of these commercial opportunities including financial returns, the opportunity to see the results of their research developed into useful products and services, and, perhaps, enhanced career opportunities in the industrial sector.

Universities benefit from faculty commercialization since their policies often provide the institution with the option to participate in commercial ventures such as supporting the costs of filing a patent in exchange for a portion of the licensing revenues or by providing venture capital funding for a start-up in exchange for a share of the future profits of that firm. On rare occasions, universities have also reaped sizable rewards from royalties on

licensed patents and from the sale of equity in start-up companies based on faculty research.

D. Early Access to Cutting Edge Information, Data and Materials

Perhaps one of the most important benefits of AIRs may be that these relationships allow for the bi-directional flow of the most recent research results of faculty and students; often months or years ahead of competitors (either academic or commercial). It is common for most research relationships with industry to allow a commercial sponsor 30-90 days to review the results of the research they sponsored prior to submission for publication. An executive of a company said that in his field the published literature is "...miles behind the front line of what is happening in universities" (Bowie, 1994). For faculty, relationships with industry provide access to industry biomaterials (such as cell lines, reagents, and tissues), equipment, and other research-related resources that may not be available outside of a relationship.

E. Personal Compensation

There are no comprehensive publicly available data regarding the personal financial benefits that accrue to individual scientists or administrators as a result of their relationships with industry. To our knowledge the only published data stem from the analyses of faculty annual disclosure forms at UCSF described above (Boyd & Bero, 2000). Of the 488 faculty disclosures examined, 34% were honorarium for an occasional speaking fee that produce on average \$2,500 per year. Of the individuals who received industry money for public speaking, 90% received less than \$10,000 annually.

Consulting arrangements also produced income for UCSF faculty. One third of all faculty disclosures involved paid consulting arrangements providing up to maximum of \$120,000/year for involved faculty. Of the individuals who received industry money consulting, more than half (61%) received less than \$10,000 annually.

IV. Risks Associated with Industry Relationships

In recent years, much has been written about the potential risks associated with industry relationships (Krimsky, 2003; Bowie, 1994; Bodenheimer T, 2000; Angell M, 2000). Derek Bok, the former president of Harvard University, articulated the risks of industry relationships when he wrote; "...relationships may divert the faculty. Graduate students may be drawn into projects in ways that sacrifice their education for commercial gain. Research performed with an eye towards profit may lure investigators into conflicts of interest or cause them to practice forms of secrecy that hamper scientific progress. Ultimately, corporate ties may undermine the university's reputation for objectivity." (Bok, 2003). In this section we provide evidence supporting the existence of risks associated with secrecy in science, bias in the reporting of research, negative impacts on education and conflicts of interest.

A. Secrecy in Science

Openness in academic science is, or perhaps was, a fundamental norm underlying the social structure of academic science. However, there is strong evidence supporting the belief that relationships with industry compromise this norm (Blumenthal et al, 1997; Campbell et al, 2002). Data from a national survey of genetics researchers and other life scientists found that those with research funding from industry were significantly more likely to delay publication of their research results by more than 6 months to allow for the commercialization of their research. Such delays may be problematic in rapidly advancing fields, fields characterized by intense competition among labs for a common scientific achievement (such as genetic sequencing), and for individual scientists who may continue to work on problems that have already been solved, resulting in a wasting of scientific resources—including time and tax dollars.

B. Bias in the Reporting of Research Results

In recent years, a significant body of research has emerged suggesting that relationships between academic scientists and industry have an impact on the content of scientific reports emerging from industry-supported research. In 2004 a meta-analysis of 23 studies of the impact of academic industry relationships in the outcomes of science found, “..a statistically significant relationship between industry sponsorship and pro industry conclusions.” (Bekelman 2003). Examples of scientific areas in which industry funded studies led to pro-industry conclusions include, randomized clinical trials in multiple myeloma, economic analyses of oncology drugs; nicotine and cognitive performance, non-steroidal anti-inflammatory drugs and calcium channel blockers. This is not to say that industry-funded research is intentionally biased towards pro-industry findings. It may be that industry selectively funds research likely to yield favorable conclusions or that industry-funded studies address different questions than non-industry funded studies. Regardless of the reason, the association between industry relationships and pro-industry results exceeds what would be expected based on chance alone.

C. Negative Impact on Education and Training

Another risk mentioned by Derek Bok was that research relationships with industry might have a negative impact on scientists-in-training. A 1985 survey of 693 advanced trainees in the life sciences at 6 universities found that 34 percent of respondents whose faculty advisor(s) were supported by industry felt constrained in discussing their research results with other scientists (Gluck, et al, 1986). Further, this study found that graduate students and post-doctoral fellows whose projects were supported by industry reported significantly fewer publications on average (2.62) than those with no industry support (3.67). To date there has been no subsequent national study of the effects, both positive and negative, of academic industry relationships on the educational activities of universities.

D. Financial Conflicts of Interest

In this paper a financial conflict of interest (FCOI) is defined as a state in which one's primary professional interests conflict with a secondary interest of a financial nature (Thompson, 1993). Applying this definition to scientists and administrators requires that we explicate their primary and secondary interests. The primary interest of academic life scientists is the search for understanding of biological processes and communication of that understanding to the research community and in many instances, the education of the next generation of scientists. An additional primary interest for physicians in academic health centers--defined as medical schools and their owned or affiliated teaching hospitals and faculty--is providing patient care. The primary interest of administrators of government and academic scientific organizations is leadership of the organization to facilitate the work of scientists. All other interests are secondary, including institutional or personal financial gain, enhancing one's professional status, power, or recognition.

These secondary interests are not improper in and of themselves. As stated by the editor of the Journal of the American Medical Association, "Conflicts of interest are considered ubiquitous and inevitable in academic life, indeed, in all professional life." (DeAngelis, Fontanerosa and Flanagin, 2001). In fact, secondary interests are often approved, and in some cases encouraged by institutions (such as consulting and the faculty ownership of equity in a company stemming from one's research). They often exist as a byproduct of a researcher's primary interest and, as shown above, can provide resources to enhance the pursuance of the researcher's primary mission (such as receiving research funding from industry or gifts).

Numerous examples of FCOIs exist in the modern scientific enterprise:

1. Scientists who own equity in firms that could directly benefit financially from the results of their research.

2. Scientific administrators who have relationships with companies that could directly benefit financially from research being conducted by individuals whom they supervise.
3. Scientists who are paid to promote company products and services at professional meetings.
4. Clinical scientists who receive bonus payments for meeting enrollment goals in clinical trials.

It is important to note that this list is not exhaustive of all FCOIs but illustrative of the types of FCOIs that can exist. For many individuals and organizations the mere perception of an FCOI is seen as problematic. Individuals and organizations holding such views may fail to understand that some FCOIs are inevitable, and result from the structure of science rather than a breaking of the rules or some form of misconduct.

E. Misconduct

Financial conflicts of interest become misconduct (including bias) when the pursuit of an individual's primary interests is superseded by a financial secondary interest. Examples of FCOIs that become misconduct include, but are not limited to:

1. A scientist who engages in research misconduct (such as falsification of data, giving an inappropriate poor review to a paper under consideration to a national journal, etc.) because doing so will financially benefit the individual or a company with which the individual has an interest.
2. A physician who enrolls ineligible patients in a clinical trial in order to boost the amount of money he/she receives from patient recruitment.

3. An individual who thwarts a study sponsored by a competitor of a company with which he/she has an interest.

4. A scientist who consciously presents information in a biased manner in order to influence the listeners towards a product or service being offered by a company in which he/she has an interest.

5. A university administrator who gives preferential contracts to a firm with which he/she has an interest.

Instances of misconduct are believed to be relatively rare in the current scientific environment. There are several possible explanations for this. First, it is likely that institutional and government policies regarding FCOIs like those provided by the Association of American Medical Colleges and other groups limit the extent to which misconduct occurs. Second, it is also possible that the culture of science and the prevailing normative practices successfully discourage such behavior. However, it is also possible that mechanisms to detect the frequency and severity of misconduct in academic science are ineffective. Unfortunately, comprehensive, empirical data do not exist to address this question.

V. Current Policies and Practices Regarding Disclosure and Management of Industry Relationships

Efforts to disclose and manage AIRs take a number of forms ranging from reliance on unwritten academic norms and customs to explicit university policies to federal regulation to state and federal law.

Academic norms tend to support principles such as academic freedom, freedom of publication, and university control of the research direction and outcomes (Merton, 1968). A compelling case however can be made that norms alone have not proven effective in managing the risks of AIRs and GIRs, as both academic and government scientists have actively resisted strengthening prohibitions against establishing financial relationships with industry, even when they clearly pose clear conflicts of interest.

The public sector has long complemented institutional culture and norms with explicit regulation of AIRs. Governmental agencies such as the Public Health Service (PHS) and the National Science Foundation (NSF) have had established regulations regarding individual financial conflicts of interest since 1995, including conflicts of interest on the part of university officials in research sponsored by one of those two federal agencies. These regulations require institutions to have in place policies and procedures that require disclosure of some, but not all relationships, and take appropriate action to manage or eliminate the conflict prior to the expenditure of federal research funds.

Specifically, PHS policy requires that all relationships which may affect PHS funded research and which result in the receipt of more than \$10,000 annually or 5% of the total equity in a company must be disclosed to university officials. The nature of such relationships need not be reported to the federal agencies. The agencies need only be informed that a conflict of interest was identified and managed or eliminated. The details of how conflicts are identified and managed and whether such management is appropriate

or effective are not currently under the purview of the federal government.

Operationally, this casts the burden of management solely on the institution rather than the government, and accordingly, the institutions bear any costs and risks associated with this oversight.

In 1998 The Food and Drug Administration (FDA) adopted its own set of rules for disclosing and managing financial conflicts of interest on the part of external parties. These rules require that investigators that receive compensation in excess of \$25,000 from a corporate sponsor of a trial in which the investigator is engaged, disclose those relationships to FDA, but not until the time of filing for the new drug application (NDA), after the study has already been completed. If the FDA determines that the relationship may have undermined the objectivity of the data, the agency may decline to accept those data in support of the market approval or labeling indication. This is probably sufficient to dissuade most investigators and companies from manipulating studies, but one can imagine that disclosure or elimination of conflicting relationships before launching a trial might be more effective.

The failure of the government to develop uniform policies for all federal agencies is frustrating to many and likely contributes to confusion and non-compliance. The existing rules also do little to specifically protect human subjects in research. In fact, this is not at all surprising, because they were never intended to do so. Rather, they were intended to protect scientific integrity and objectivity. For nearly four years, the Department of Health and Human Services has been working on guidance for institutions, IRBs and investigators regarding financial relationships that may threaten the interests and well being of human subjects.

Some states also have laws regulating conflicts of interest on the part of state officials and state employees. These laws generally apply to officials and certain employees of public institutions of higher education. For example, California law requires that principal investigators who receive more than \$250 from a non-governmental source must disclose their financial interests in the sponsor of the research.

In addition, professional organizations, notably, the Association of American Medical Colleges (AAMC), have also taken a leadership position on this issue by developing explicit policy positions on AIRs in clinical research—representing a significant advance in debate on this issue. The AAMC Task Force on Individual Financial Interests in Human Subjects Research made the following recommendations (among others):

1. Institutions should have a standing institutional conflict of interest committee or process,
2. Institutions should adopt mechanisms to ensure that disclosures are readily accessible in the institution,
3. Institutions should have clearly defined written policies on financial interests in clinical research. (Association of American Medical Colleges, 2001),
4. Most importantly, in all research involving human subjects, institutions should begin with a presumption that for both investigators and institutions, no financial relationships that could compromise the interests or well being of the participants will be tolerated, and that this presumption may be rebutted, but only under compelling circumstances.

Presently, the impact of the AAMC's and other policies and practices on the disclosure and management of AIRs is not known. However, while virtually all major research universities have a process for disclosure, there is great variation in institutional policies and practices in this area.

Further, a content analysis of the conflict of interest policies at the 100 universities that received the most funding from the NIH in 1998 found the disclosure policies varied widely across institutions. For example, 55% of the policies required disclosures from all faculty members while 45% only required faculty who were principal investigators to disclose. Also, less than 20% of institutional policies specified limits on faculty financial relationships with industry and 12% provided specific limits on the amount of time publications may be delayed (Cho, et al, 2000).

However, the fact that universities have policies and practices about the disclosure and management of relationships does not mean these policies are enforced or that they are effective in preventing misconduct. A survey of the conflict of interest policies, at U.S. institutions receiving more than \$5 million in funding from the NIH or the NSF, found that the management of conflicts and penalties for non-disclosure were almost universally discretionary (Bekelman, 2003).

VI. Empirical Observations

Based on the data presented above we provide the following set of observations:

1. The modern scientific enterprise is composed of a set of complex, deeply integrated financial relationships between government, industry and university based scientists and their organizations.
2. These relationships have benefits for individual scientists, their institutions and the overall progress of science.
3. These relationships have risks including, but not limited to misconduct, increased secrecy, and bias in the reporting of research results which cannot and should not be ignored.
4. These risks, like the benefits, exist for all faculty members who conduct academic activities including research, teaching and, perhaps patient care—not just those who conduct clinical research.
5. The existence of both risks and benefits suggest that an optimal strategy for both government and academia is to manage GIRs and AIRs in such a way as to minimize the risks while preserving these relationships.
6. A general approach to managing GIRs and AIRs should involve disclosure of all such relationships relevant to private and public authorities, identification and elimination of relationships that pose, a priori, unacceptable risks, and careful monitoring of relationships where the benefits are seen to outweigh the risks.

VII. Suggestions for Policy and Management

Based on the observations presented above, we provide a set of suggestions for policy and management of AIRs.

A. Standardize Disclosure Policies of Academic Industry Relationships

At present, there is wide variation in the disclosure policies and practices at universities. In order to avoid the potential for institutions to benefit from having low standards related to disclosure of academic industry relationships we suggest the following:

Harmonized, uniform policies related to the disclosure of AIRs should be developed and adopted by the academic community.

Virtually all universities have a mechanism for the disclosure of academic industry relationships. However, there is great variation from institution to institution in who must disclose. Thus, we suggest that:

All faculty who conduct research or teach and all institutional administrators at the level of department chair and above disclose their relationships, including relationships of immediate family, with industry to a committee designated to receive and review such disclosures.

There is also wide variation in what relationships universities require to be disclosed. Since various types of relationships with industry have been shown to have an increased potential to negatively affect both research and teaching, we suggest that:

Universities require annual disclosure of all licensing, consulting, honoraria and gift relationships that have an annual value of \$10,000 or more and are related to an individual's area of professional expertise. ,

Universities require annual disclosure of all equity relationships (excluding equity held as part of a mutual fund, 401k, etc.) among individual faculty and senior administrators, or their immediate family members, valued at \$10,000 or more or when an individual's holdings represent more than 5% of all of a firm's stock in companies related to the individual's area of professional expertise.

As mentioned above, a content review of the disclosure policies at all medical schools in the United States and the 170 institutions that received more than \$5 million in funding from the National Science Foundation found that in almost every instance, penalties for nondisclosure were totally discretionary and uniformly non-specific (McCrary et al, 2000). Therefore, we suggest:

All institutions should establish specific, mandatory penalties for failing to disclose relationships with industry as specified by institutional policies.

B. Independent Review/Consideration of Disclosures

It is the responsibility of academic institutions to carefully review the disclosures of faculty and administrators. The public health service (PHS) requires that institutions designate a single individual to review disclosures related to PHS-funded research. However, since most major universities have a large number of faculty who would be required to disclose under the suggestions above, and because of the complex nature of certain relationships, we believe disclosures should be reviewed by a formal committee that is adequately staffed. Further, in order to provide a measure of transparency similar to the review of clinical research protocols by IRBs we suggest that:

All disclosures be reviewed and approved by a quasi-independent review committee made up of members from the institution and the local communities

C. Institutional Oversight of AIRs

Since there is wide variation between universities in the frequency of certain types of AIRs, the organizational structure of universities, and academic decision making structure/processes it is important to vest significant institutional discretion regarding the review and oversight of AIRs at the local level. In providing oversight we suggest that:

Institutions have significant flexibility to decide which relationships require oversight and how to design, implement and evaluate institutional oversight plans and activities.

Currently, the federal government has done little to assist institutions in this regard. According to a review article (Henderson & Smith, 2002), government controls on financial conflict of interests form an overlapping, incomplete and occasionally conflicting message to investigators and institutions involved in partnerships with industry, making compliance difficult, and creating the potential for considerable variation in actual policy at the local level. In order to assist universities, we suggest that:

Universities should receive clear, unambiguous guidance from the federal government concerning their responsibilities and accountabilities with regard to assuring the integrity of research and the protection of human subjects in the context of AIRs.

Presently, there is no comprehensive source of data regarding the oversight activities of universities, beyond the case study at the University of California at San Francisco. Without data it is difficult for institutions to learn from themselves or each other in this area. Thus, we suggest:

Aggregate, de-identified data on annual disclosures by faculty members and senior administrators (including a summary of the decisions of the institutional oversight committees regarding these relationships) should be made public on a regular basis.

D. Data-withholding and Bias in Science

As mentioned above, the most recent data available suggest that 12% of universities provide specific limits on the amount of time publications may be delayed in the context of faculty members' relationships with industry (Cho, et al, 2000). In order to ensure that scientific findings are published in a timely manner and to allow sufficient time to protect intellectual property in science, we suggest that:

Institutions should adopt a uniform policy that prohibits suppression of data. Corporate sponsors of clinical trials and the FDA should adopt and adhere to a policy that the results of clinical trials, regardless of outcome, be made available to the public in an appropriate format.

Given the amount of research in most universities and the highly technical nature of the research, we believe the responsibility for protecting the integrity of scientific publications and presentations rests primarily with the investigators leading the research efforts. As a result we suggest that:

All authors should fully disclose all academic industry relationships, in addition to the source of the research funding, related to a publication in a journal according to the guidelines outlined above.

All presenters should fully disclose all academic industry relationships, in addition to the source of research funding, related to a presentation at a conference or professional meeting according to the guidelines outlined above.

Ghostwriting of manuscripts by industrial sponsors of research or their agents should be prohibited.

E. Review of Selected National Policies

As demonstrated above, AIRs have been shown to be associated with significant benefits as well as risks including increased likelihood of commercialization of university-based research (Blumenthal et al, 1996b). Two of the major stimuli for AIRs and GIRs were the passage of the Bayh-Dole Act and the Stephenson-Wydler Act in 1980. These policies have been in place for almost a quarter of a century with no comprehensive review to see whether changes could increase the productivity of AIRs and GIRs for the nations economy and public health. Therefore, we suggest:

The impact of the Federal legislation that underlies the nation's efforts to commercialize life sciences research, such as the Bayh-Dole Act and the Stephenson-Wydler Act, should be reviewed by appropriate organizations in order to determine if modifications might improve the effectiveness of technology transfer from the academic and government sectors to the industry sector.

VIII. Potential Implications for Government Industry Relationships

As demonstrated above, there is a substantial corpus of empirical data, collected primarily through large national surveys and case studies showing that AIRs in the life sciences are a fundamental part of the modern life science enterprise. These data—which are now relatively old—have supported the development and implementation of policies and practices of individual universities, scientific journals and professional associations to address the risks associated with these relationships. However, while we know that government scientists and administrators comprise an important part of the life science enterprise and we know that they have relationships with industry (Willman, 2004) there are no comprehensive, publicly available data to illuminate the risks and benefits of these relationships.

Such studies are desirable and possible. Two sources of such data are apparent. The first source could be through case studies and anonymous surveys of government scientists and administrators in federal agencies such as the National Institutes of Health, the National Science Foundation, the Food and Drug Administration and others. A second potential source of data about GIRs is the annual disclosure forms filed by federal employees. These forms, de-identified if necessary, should be made available for analysis.

In 1995, the NIH revised its policies for requiring public disclosure of financial statements by highly compensated employees, including senior scientists (Grady, 2004). The threshold for triggering public disclosure was raised to a level that resulted in a 64% decrease in the number of open public disclosure of financial statements. Between 1995 and 2004, consulting relationships between NIH scientists and industry increased, in some cases amounting to many tens of thousands to over a hundred thousand dollars cumulatively for some very senior individuals (Grady, 2004). In some cases these relationships existed with companies that stood to benefit financially from the actions of

the NIH officials. It is well recognized that such relationships have the potential to color objectivity in the grant-making process, or to undermine the credibility of the NIH, as responsible stewards in the investment of public funds for research. This risk is significant.

The benefits of GIRs are likely similar to those associated with AIRs. Relationships that foster more interaction among scientists with shared goals are likely to enhance creativity and productivity, and there can be little doubt that financial incentives are effective motivators of individual and organizational behaviors, both good and bad, and this is probably true both inside and outside government. To the extent that these relationships can speed the development of new discoveries and technological advances, society may benefit. As stated earlier however, to believe that these goals are likely to be achieved without the potential for abuse by some in the system is probably naïve.

Because the government does not receive compensation for intellectual property or commercialization of products, it is likely that the financial benefits of such relationships flow primarily to the companies and the government scientists involved in these relationships. Indeed, the primary financial benefit of GIRs is likely to be personal compensation. For consulting relationships the Los Angeles Times identified hundreds of consulting relationships between senior NIH officials and industry totaling millions of dollars (Willman, 2004). The public may also benefit by allowing some forms of GIRs to the extent that these relationships enhance the ability of the government to retain the very finest scientists for government stewardship of the public investment in science.

The risks of GIRs are likely to be similar to those of AIRs. But, GIRs may be perceived by the public and elected officials as more problematic than AIRs.

Because the NIH and other federal research funding agencies have the primary responsibility for managing the public investment in science, openness and disclosure of GIRs are essential. One can make a case that these reporting requirements must be at least as stringent as those for academic institutions. It is harder to make a strong case for

having a less stringent policy for non-government institutions. In the end, a consistent policy would probably be the most reasonable and effective approach.

Increased oversight of GIRs will likely emerge in the future. Given the increased concern about GIRs on the part of elected officials, it may be that oversight cannot be left to the scientists and funding agencies alone. In the case of the GIRs at NIH, the office or organization with oversight responsibility should have some measure of independence of the scientific establishment itself. Failure to adequately manage GIRs could result in a loss of the public confidence—a precious resource that should be protected at all costs.

The prevalence and complexity of relationships among academia, government and industry are likely to continue to grow and evolve in years ahead, and the prospects for good to come from them is very real--so is the possibility of harm. We must continually look for new approaches to ensure the integrity and objectivity of science, and protect the well being of research participants.

The views expressed are those of the authors alone and do not necessary represent the views of Harvard Medical School, Partners HealthCare, the Institute for Health Policy or the Ewing Marion Kauffman Foundation.

Research Funding:

This research was supported by a research grant from the Ewing Marion Kauffman Foundation. The Ewing Marion Kauffman Foundation of Kansas City works with partners to advance entrepreneurship in America and improve the educational achievement of youth. The Kauffman Foundation's interest in helping to propagate new ideas and advance entrepreneurship has resulted in a focused view of the specific processes of innovation creation and commercialization. The late entrepreneur Ewing Marion Kauffman established the Kauffman Foundation in the mid-1960's. Information about the Kauffman Foundation is available at www.Kauffman.org.

Author Disclosure:

In 2003-2004, Dr. Campbell received more than \$10,000 in consulting income for research services provided to the Panel of Life Science Advisors of the Kauffman Foundation under subcontract to the George Washington University.

References:

Angell M. Is academic medicine for sale? *New England Journal of Medicine* 2000; 342: 1516-1518.

Association of American Medical Colleges. Protecting Subjects, Preserving Trust, Promoting Progress—Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research. Washington, DC: December 2001.

Bekelman JE, Li Y, Gross CP. Scope and Impact of Financial Conflicts of Interest in Biomedical Research. *Journal of the American Medical Association* 2003; 289: 4: 454-465.

Blumenthal D, Causino N, Campbell EG, Louis KS. Relationships between academic institutions and industry in the life sciences--An industry survey. *New England Journal of Medicine*. 1996a;334:368-373.

Blumenthal D, Campbell EG, Causino N, Louis KS. Participation of life-science faculty in research relationships with industry. *New England Journal of Medicine*. 1996b; 335:1734-1739.

Blumenthal D, Campbell EG, Anderson MS, Causino N, Louis KS. Withholding of research results in academic life science: Evidence from a national survey of faculty. *Journal of the American Medical Association* 1997;277(15):1224-28.

Bodenheimer T. Uneasy alliance: Clinical investigators and the pharmaceutical industry. *New England Journal of Medicine* 2000; 342: 1539-1544.

Bok D. *Universities in the Marketplace: The Commercialization of Higher Education*. Princeton NJ: Princeton Press: 2003.

Bowie N. (1994). *University-Business Partnerships: An Assessment*. Rowan & Littlefield Publishers, Inc., Lanham.

Boyd E, Bero L. Assessing faculty financial relationships with industry: A case study. *Journal of the American Medical Association* 2000; 284(17): 2209-2214.

Campbell EG, et. al. Institutional Academic Industry Relationship: Results of Case Studies. *Accountability in Research*. 2004 (paper under review).

Campbell EG, Blumenthal D, Louis KS. Looking a gift horse in the mouth: Corporate gifts that support life sciences research. *Journal of the American Medical Association* 1998;279(13):995-99.

Campbell EG, Clarridge BR, Gokhale M, Birenbaum L, Hilgartner S, Holtzman NA, Blumenthal D. Data-withholding in academic genetics: Evidence from a national survey. *Journal of the American Medical Association* 2002; 287(4): 473-481.

Cho M, et al. Policies on Faculty conflicts of interest in biomedical research. *Journal of the American Medical Association* 2000; 284(17):2203-2208.

DeAngelis CD, Fontanerosa PB, Flanagan A. Reporting financial conflicts of interests and relationships between investigators and research sponsors. *Journal of the American Medical Association* 2001, 288 (1): 89-91.

Fox MF. Publication, Performance and Reward in Science and Scholarship. In John C. Smart (Ed.) *Higher Education: Handbook of Theory and Research*. Vol. I. 1985, 255-382.

Gluck M, Blumenthal D, Stoto M. A. (1987). University-relationships in the life sciences: Implications for students and post-doctoral fellows. *Research Policy*. 16, 327-366.

Grady D. Medical research dealings explored by senate panel. New York Times, January 23, 2004.

Henderson JA, Smith, JJ. Financial conflict of interest in medical research: Overview and Analysis of Federal and State Controls. Paper submitted to the Food and Drug Lay Journal. May 2002.

Jones LM. The Commercialization of Academic Science; Conflict of Interest for the Faculty Consultant. University of Minnesota Doctoral Dissertation, 2000.

Kauffman Foundation Scientific Advisory Committee. Technology Transfer and Commercialization in the Life and Health Sciences. A report prepared for the Panel of Advisors on the Life Sciences Ewing Marion Kauffman Foundation, 2003.

Krimsky S. Science in the Private Interest: Has the Lure of Profits Corrupted Biomedical Research? Rowman & Littlefield Publishers, Inc. 2003.

Marshall E. Zerhouni pledges review of NIH consulting in wake of allegations. Science 2003; 302:2046.

McCrary SV, et al. A national survey of policies on disclosure of conflicts of interest in biomedical research. New England Journal of Medicine 2000; 343(22): 1621-1626.

Merton RF. Social Theory and Social Structure. New York: The Free Press. 1968.

Thompson DF. Understanding financial conflicts of interest. New England Journal of Medicine 1993; 329:573-76.

Willman D. Probe sought into NIH officials outside work. Los Angeles Times, January 17, 2004.

Appendix: Listing of Policy Suggestions

- 1. Harmonized, uniform policies related to the disclosure of AIRs should be developed and adopted by the academic community.*
- 2. All faculty who conduct research or teach and all institutional administrators at the level of department chair and above disclose their relationships, including relationships of immediate family, with industry to a committee designated to receive and review such disclosures.*
- 3. Universities require annual disclosure of all licensing, consulting, honoraria and gift relationships that have an annual value of \$10,000 or more and are related to an individual's area of professional expertise.*
- 4. Universities require annual disclosure of all equity relationships (excluding equity held as part of a mutual fund, 401k, etc.) among individual faculty and senior administrators, or their immediate family members, valued at \$10,000 or more or when an individual's holdings represent more than 5% of all of a firm's stock in companies related to the individual's area of professional expertise.*
- 5. All institutions should establish specific, mandatory penalties for failing to disclose relationships with industry as specified by institutional policies.*
- 6. All disclosures be reviewed and approved by a quasi-independent review committee made up of members from the institution and the local communities*
- 7. Institutions have significant flexibility to decide which relationships require oversight and how to design, implement and evaluate institutional oversight plans and activities.*
- 8. Universities should receive clear, unambiguous guidance from the federal government concerning their responsibilities and accountabilities with regard to assuring the integrity of research and the protection of human subjects in the context of AIRs.*
- 9. Aggregate, de-identified data on annual disclosures by faculty members and senior administrators (including a summary of the decisions of the institutional oversight committees regarding these relationships) should be made public on a regular basis.*

10. *Institutions should adopt a uniform policy that prohibits suppression of data. Corporate sponsors of clinical trials and the FDA should adopt and adhere to a policy that the results of clinical trials, regardless of outcome, be made available to the public in an appropriate format.*
11. *All authors should fully disclose all academic industry relationships, in addition to the source of the research funding, related to a publication in a journal according to the guidelines outlined above.*
12. *All presenters should fully disclose all academic industry relationships, in addition to the source of research funding, related to a presentation at a conference or professional meeting according to the guidelines outlined above.*
13. *Ghostwriting of manuscripts by industrial sponsors of research or their agents should be prohibited.*
14. *The impact of the Federal legislation that underlies the nation's efforts to commercialize life sciences research, such as the Bayh-Dole Act and the Stephenson-Wydler Act, should be reviewed by appropriate organizations in order to determine if modifications might improve the effectiveness of technology transfer from the academic and government sectors to the industry sector.*