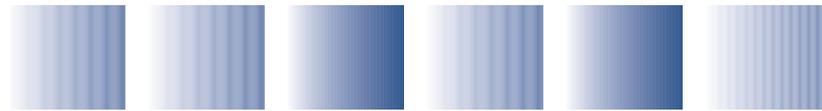


U.S. Medical School Policies on Individual Financial Conflicts of Interest

Results of an AAMC Survey

Susan Ehringhaus, J.D., and David Korn, M.D.



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Abstract: We report the results of a survey undertaken by the Association of American Medical Colleges of U.S. medical school policies on individual financial conflicts of interest. The results present encouraging evidence that the academic medical community is grappling with the difficult issues engendered by its complex relationships with industry, and has substantially improved its ability to meet its paramount obligations to protect human subjects and scientific integrity in the face of widespread individual financial interests in research. However, gaps and inconsistencies in policy protection remain, and the survey results highlight substantial opportunities for continuing improvement.

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Introduction

In October of 2000, in a climate of rising public skepticism about the diligence of academic medical institutions in protecting human research subjects, the Association of American Medical Colleges (AAMC) announced the formation of a new task force on Financial Conflicts of Interest in Clinical Research.² The task force was charged with responding to deepening public concern about the extensive financial self-interests of clinical researchers and their institutions³ by forging consensus principles, recommendations, and guidelines for the oversight of financial interests in research involving human subjects. The task force published two reports, the first dealing with individual, and the second with institutional financial conflicts of interest in human subjects research.⁴

The AAMC Task Force Report on Individual Financial Interests in Human Subjects Research

The first report, *Protecting Subjects, Preserving Trust, Promoting Progress — Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research (Guidelines)* (December 2001), provides a model for baseline standards and practices in the oversight of individual financial interests in human subjects research. During the period surrounding the development of the AAMC task force's

recommendations, other policy recommendations emerged from the government and the academic community, ranging from broad findings and policy statements to discipline-specific standards, as for gene therapy and clinical cancer trials.⁵ Some of the commentary suggested or concluded that institutional policies were deficient in protecting human research subjects in the presence of individual financial interests.⁶

Slightly more than one year after the publication of the task force's *Guidelines*, the HHS Office of Public Health and Science solicited public comment on a draft guidance statement⁷ (now issued in final form⁸) that reflected many of the AAMC recommendations. The PHS guidance statement challenged academic institutions to demonstrate to the public and policymakers that they have accepted their responsibility to strengthen, through their own policies, the protection and oversight of human subjects research when financial self-interests are present. Accordingly, in May 2003 AAMC undertook a study to ascertain the characteristics of policies of academic medical centers and especially, to compare the policies with the recommendations of the task force.

Study Design

The survey instrument asked respondents to describe key features of their institutional policies on individual conflicts of interest.⁹ Responses were collected over a period of nine months, ending in February 2004.

² Cohen, J.J. "Trust us to make a difference: Ensuring public confidence in the integrity of clinical research." *Acad. Med.* 2001; 76:209-214.

³ Angell, M. 342 *NEJM* 1516 (2000).

⁴ 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," (December 2001), www.aamc.org/members/coitf/firstreport.pdf [hereinafter *Guidelines*]; Association of American Medical Colleges, "Protecting Subjects, Preserving Trust, Promoting Progress II: Principles and Recommendations for Oversight of an Institution's Financial Interests in Human Subjects Research," (October 2002), www.aamc.org/members/coitf/2002coireport.pdf [hereinafter *Principles*]; Ehringhaus and Korn, "Conflicts of Interest in Human Subjects Research," 2002-03; v. XIX n.2: 75-81.

⁵ See, e.g., Association of American Universities, task force on Research Accountability, Report on Individual and Institutional Financial Conflict of Interest (Oct. 2001); American Medical Association, E-8.0315 Managing Conflicts of Interest in the Conduct of Clinical Trials, www.ama-assn.org/ama/pub/category/8471.html; American Society of Gene Therapy, www.asgt.org.

⁶ See, e.g., U.S. General Accounting Office, Biomedical Research: HHS Direction Needed to Address Financial Conflicts of Interest (GAO-02-89)(November 2001); OIG Report OEI-01-97-00195, "Recruiting Human Subjects: Pressures in Industry-Sponsored Clinical Research" (June 2000); OIG Report OEI-01-97-00196, Recruiting Human Subjects: Sample Guidelines for Practice (June 2000); OIG Report OEI-05-99-00350, FDA Oversight of Clinical Investigators (June 2000); OIG Report OEI-01-97-00197, "Protecting Human Research Subjects: Status of Recommendations" (August 2000).

⁷ Draft "Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection", 61 Federal Register 15,456 (March 31, 2003).

⁸ "Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection", 69 Federal Register 26,393 (May 12, 2004).

⁹ www.aamc.org/members/coitf/coiquestionnaire2003.pdf.

Study Results

The study results reflect for all accredited U.S. allopathic medical schools a response rate of 82% (n = 126). They present a remarkably full picture of the current state of policies at academic medical centers as well as the first systematic evidence of the response of the academic medical community to deficiencies identified in the published commentary and to the recommendations in the AAMC *Guidelines*.

Primary results are percentages of the total number of institutional respondents (n = 103) to alternative answers to the survey questions. Summaries of responses to open-ended questions are also provided. Secondary results are presented for differences in responses between (1) public and private schools, (2) schools ranked among the top 40 and those ranked 41 or higher in NIH awards to medical schools for 2003 (the latest year for which results are available), and (3) public and private schools in the top 40. It is not appropriate to try to evaluate the statistical significance of differences in responses because we are dealing with essentially the total population of schools. However, we have chosen to report differences of >15% as noteworthy.

Results Related to AAMC Task Force Recommendations

The survey results describe the extent to which policies of academic medical centers are consistent with the core AAMC recommendations. These recommendations include an acknowledgment of the special obligations attendant on human subject research in the presence of significant financial interests (SFI); a rebuttable presumption or similarly high standard against a researcher with a SFI in human subjects research from conducting that research except under compelling circumstances; rigorous review and monitoring standards; close coordination with institutional IRBs; and full disclosure to research subjects as well as in publications and other communications. The task force did not attempt to spell out what “compelling circumstances” might be, recognizing that assessment of these circumstances tends to be highly case-specific

and situational, but they were unequivocal that the bar be set high. The expectation may be captured by concluding that the research could not be conducted as safely or effectively anywhere else.

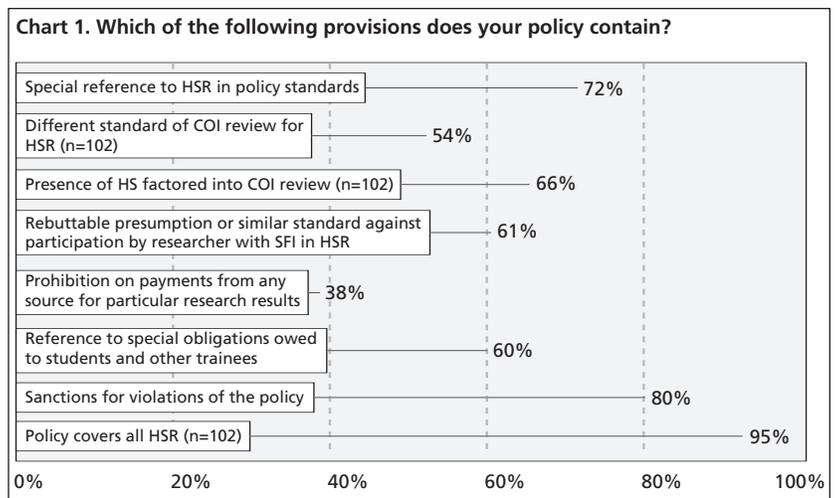
It should be noted that the subject matter of some AAMC recommendations might be addressed not in an institution’s conflict of interest policies but in other institutional policies. Though respondents were encouraged to answer questions based on all of their applicable policies, the survey may not have captured all the ways in which institutions regulate the many aspects of individual conflicts of interest.

i. Recent Policy Changes

63% of respondents report that since December 2001, changes have been made in their university’s or academic medical center’s (as applicable) policies on individual financial conflicts of interest in human subjects research. 52% of these respondents state that changes were made to increase the protection of human subjects in research in which there were individual financial interests.

ii. Policy Characteristics

Respondents were asked to select those provisions shown in Chart 1 that appear in their policies on individual financial interests in human subjects research.¹⁰



¹⁰ Abbreviations used in charts are the following: HSR = human subjects research; SFI = significant financial interest; COI = conflict of interest; IRB = institutional review board.

iii. Policy Definitions

Policies of 98% of respondents contain a definition of significant financial interest or similar concept. 68% use the PHS standard (\$10,000), and 27% use a lower dollar standard. Only one respondent reported using the \$25,000 FDA threshold for disclosure.

Several types of financial interests are not included or fully covered within the current federal regulations¹¹ but are recommended for reporting and review by the AAMC *Guidelines*. Respondents were asked to indicate which of those non-federally mandated financial interests are included within their policy definitions of significant financial interests. 61% include equity in non-publicly traded companies, regardless of percentage share of equity; 64% include equity in non-publicly traded companies, regardless of estimations as to valuation; 38% include royalty income from the institution above a certain threshold; 33% include royalty income from the institution regardless of amount; and 64% include non-royalty payments not directly related to reasonable costs of research.

The policies of 81% of the respondents permit a researcher with a significant financial interest to conduct human subjects research when compelling circumstances are judged to exist.¹²

iv. Process for Evaluation of Disclosures of Potential Conflicts

Some of the AAMC task force's recommendations relate to the process for the evaluation of disclosures of potential financial conflicts of interest in human subjects research, including the creation of a standing committee on conflicts of interest. 76% of respondents report that they have established such a committee, but of these, only 21% indicate that the committee includes representation from outside the institution, as urged by the task force.

Agreements licensing university technology frequently create significant financial interests for the investigator/inventor. Under Bayh Dole, a portion of royalties received by the institution must be shared with the inventor¹³, and most institutional policies incorporate a royalty-sharing requirement in their patent or intellectual property policies. The task force recommended that such agreements be reviewed by the standing conflicts of interest committee because of the agreements' potential to create significant financial interests in royalty rights and/or equity shares, and thus potentially to "debar" researchers (and perhaps their institutions pursuant to institutional conflicts of interest policies) from future research on the technology involving human subjects.

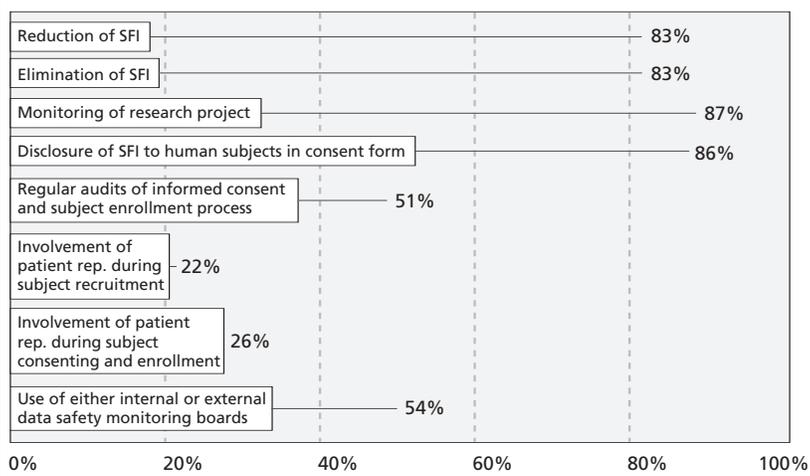
54% of respondents have adopted this recommendation. 49% of those who have not provide for some other review of such agreements that ranges in formality and degree of association with the technology transfer office.

v. Management of Conflicts of Interest

Chart 2 displays a range of the management techniques either suggested or required by the respondents' policies.

When research involving the participation of a researcher with a SFI is permitted to go forward, 85% of respondents require monitoring of that research, and of these, periodic written reports of monitoring activities are required by 74%. In these circumstances, disclosure is required to all of the officials and individuals shown in Chart 3.

Chart 2. In the management of permitted COIs in HSR, which of the following are either suggested or required by the policy?



¹¹ 42 C.F.R. 50.600 *et seq.*

¹² Only 26% (n = 101) have attempted explicitly to define compelling circumstances or a similarly high standard in the policy documents.

¹³ 35 U.S.C. 202(c)(7)(B).

b. Public Compared to Private Institutions

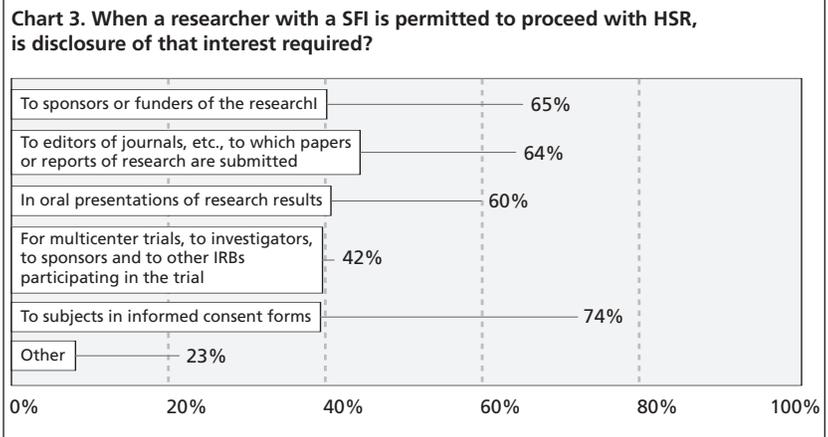
Differences (>15%) between features of conflicts of interest policies of public and private medical schools appear in only two areas.¹⁴ 47% of the publics use a different standard of conflicts of interest review when human subjects are involved, compared to 65% of the privates. 28% of public institutions’ conflicts of interest committees include outside representation, compared to only 9% of private institutions.

c. Stratification by NIH Award Rankings

Differences (>15%) between key characteristics of conflicts of interest policies of those medical schools ranking in the top 40 of NIH medical school award recipients and all others appear in several areas,¹⁵ as displayed in Chart 4.

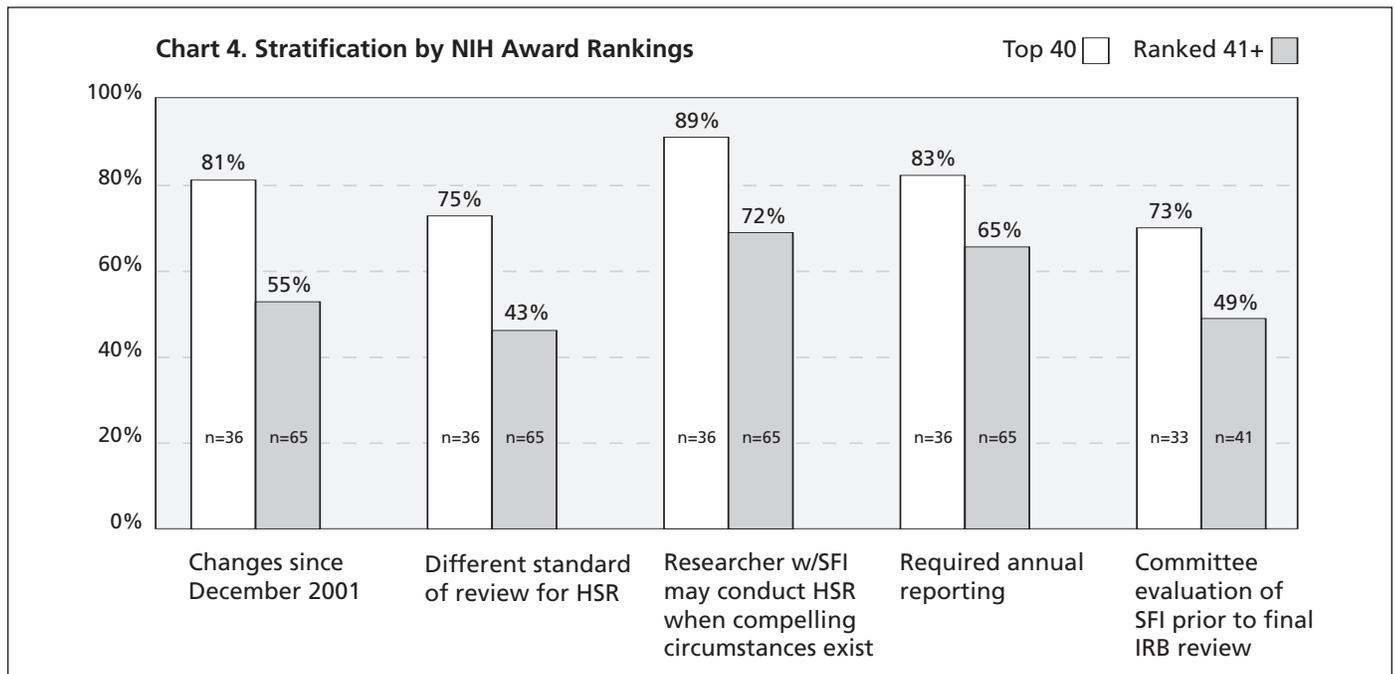
d. Public and Private Institutions in the NIH Top 40

Differences (>15%) between key characteristics of conflicts of interest policies of public and private medical schools ranking in the top 40 of NIH award recipients appear in six areas, as shown in Chart 5.



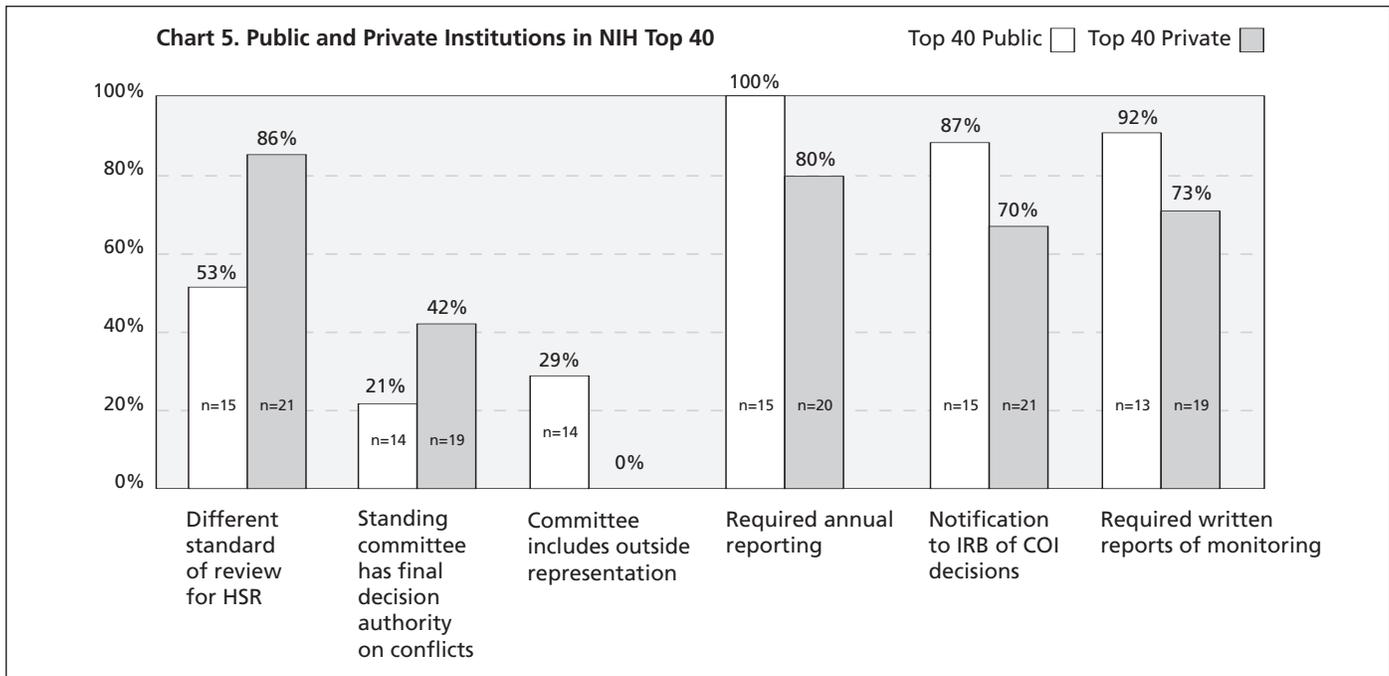
Discussion and Conclusion

The study results provide clear evidence of substantial responsiveness on the part of academic medical institutions, and for many, their parent universities, in strengthening their conflict of interest policies well beyond the minimum federal standards in recognition of the markedly changed circumstances of clinical research. Although the findings are encouraging, they nonetheless indicate that more work remains to be done.



¹⁴ Two respondents chose not to identify their institutions, and their responses are not included in this section.

¹⁵ One respondent is not ranked but is included in the “41 or higher” group. Two respondents chose not to identify their institutions, and their responses are not included in this section.



Based on the affirmative responses shown, notable areas that require greater attention include establishing a rebuttable presumption or similarly high standard for human subjects research by a researcher with a significant financial interest, explicitly prohibiting payments from any source for particular research results, and referencing in policies the special obligations owed to trainees and students. More inclusive definitions of covered financial interests are also warranted.¹⁶ We believe it is especially important for sustaining institutional credibility in the oversight and management of these complex matters that more consideration be given to including public representation on standing conflicts of interest committees. Further with respect to credibility in these circumstances, relatively few institutions appear to suggest or require the involvement of patient representatives during recruitment and consenting of subjects, regular audits of the consent and enrollment process, and the use of data safety monitoring boards.¹⁷

A disappointingly low fraction of respondents report that their standing committees evaluate significant financial interests prior to final IRB

review. Although nearly all respondents require reporting of such interests prior to undertaking human subjects research, a higher response on this measure would assure that conflicts issues are fully examined and resolved and inform IRB review, prior to IRB approvals.

Those respondents that do not require conflicts committee review of licensing agreements that create significant financial interests for researchers should consider putting in place some mechanism to assure broad awareness of potential impediments to the researcher's future research. More attention should be given to these several conflicts management techniques that can provide additional safeguards to research subjects and strengthen confidence in institutional integrity.

Only half of the respondents make special training programs on conflicts of interest policies available to the covered community. Confidence in the system by which our community regulates itself begins with full awareness and understanding of the regulatory regime by those who are covered. We believe focused training efforts are essential to this process.

¹⁶ See *infra* paragraph a.iii.

¹⁷ See Chart 2.

Interesting differences emerge between those medical schools ranking in the top 40 NIH award recipients and those ranked 41 or higher. The differences in the aggregate suggest that policies and processes in place at the top 40 institutions reflect greater consistency with core AAMC recommendations. Some of the differences found between private and public institutions may result from application of state law and policy that in certain respects, *e.g.*, the definition of reportable financial interests, may be more stringent than the existing federal regulations.

The results taken as a whole provide reassuring evidence that the academic medical community is actively engaging the challenging issues presented by its rapidly expanding relationships with industry. They also show that the institutions have substantially improved their ability to meet their paramount obligations to protect human subjects and scientific integrity in the face of widespread individual financial interests in research. The goal of the AAMC task force was to strengthen and make more consistent across the academic medical community the standards of oversight and management of financial conflicts of interest in human subjects research. The effort has begun, but much more remains to be done before we can confidently assert that “the welfare of human subjects and the integrity of research will not be compromised — or appear to be compromised — by competing [individual and] institutional interests or obligations.”¹⁸

¹⁸ *Principles* at 3.

