

A NATIONAL SURVEY OF POLICIES ON DISCLOSURE OF CONFLICTS OF INTEREST IN BIOMEDICAL RESEARCH

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ABSTRACT

Background Conflicts of interest pose a threat to the integrity of scientific research. The current regulations of the U.S. Public Health Service and the National Science Foundation require that medical schools and other research institutions report the existence of conflicts of interest to the funding agency but allow the institutions to manage conflicts internally. The regulations do not specify how to do so.

Methods We surveyed all medical schools (127) and other research institutions (170) that received more than \$5 million in total grants annually from the National Institutes of Health or the National Science Foundation; 48 journals in basic science and clinical medicine; and 17 federal agencies in order to analyze their policies on conflicts of interest.

Results Of the 297 institutions, 250 (84 percent) responded by March 2000, as did 47 of the 48 journals and 16 of the 17 federal agencies. Fifteen of the 250 institutions (6 percent) — 5 medical schools and 10 other research institutions — reported that they had no policy on conflicts of interest. Among the institutions that had policies, there was marked variation in the definition and management of conflicts. Ninety-one percent had policies that adhered to the federal threshold for disclosure (\$10,000 in annual income or equity in a relevant company or 5 percent ownership), and 9 percent had policies that exceeded the federal guidelines. Only 8 percent had policies requiring disclosure to funding agencies, only 7 percent had such policies regarding journals, and only 1 percent had policies requiring the disclosure of information to the relevant institutional review boards or to research subjects. Twenty journals (43 percent) reported that they had policies requiring disclosure of conflicts of interest. Only four federal agencies had policies that explicitly addressed conflicts of interest in extramural research, and all but one of the agencies relied primarily on institutional discretion.

Conclusions There is substantial variation among policies on conflicts of interest at medical schools and other research institutions. This variation, combined with the fact that many scientific journals and funding agencies do not require disclosure of conflicts of interest, suggests that the current standards may not be adequate to maintain a high level of scientific integrity. (N Engl J Med 2000;343:1621-6.)

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SCIENTIFIC misconduct involves inherently unacceptable behavior that directly threatens the integrity of research. Conflicts of interest may inappropriately influence the design, conduct, or reporting of research, thus threatening its scientific value and the rights and interests of research subjects.

There has been growing concern about conflicts of interest in biomedical research.¹⁻⁹ The Institute of Medicine has described two opposing models for managing conflicts of interest. One model is based on the presumption that any relationships that might present a conflict must be prohibited, and the other is based on the presumption that such relationships can be handled through disclosure and peer review.^{10,11}

In 1989, the National Institutes of Health (NIH) proposed guidelines on conflicts of interest.¹² These guidelines followed the prohibition model, with provisions prohibiting researchers from holding equity interest in any company that could be affected by their research and requiring disclosure of "all financial interests" by investigators (regardless of the relevance of such arrangements to their research). The guidelines were subsequently withdrawn because they were widely viewed as too restrictive.^{13,14} In 1994, the Public Health Service (PHS) and the National Science Foundation (NSF) proposed revised guidelines based on the model of disclosure and peer review. These guidelines, which became effective on October 1, 1995, gave research institutions discretion in managing conflicts and required that the existence, but not the substantive details, of conflicts of interest be reported to the funding agency before the funds were used.¹⁵ The threshold for disclosure of conflicts of interest is \$10,000 in annual income or equity in a relevant company or 5 percent ownership of such a company. Public interest in these issues has recently surged as a result of several controversies¹⁶⁻²⁰ and the death of a participant in a phase I trial of gene therapy.²¹ We studied the policies on disclosure of conflicts of interest at medical schools and other research institutions, scientific journals, and funding agencies.

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METHODS

Sample

Between October 1999 and March 2000, we studied the policies of U.S. medical schools and other institutions that received more than \$5 million in total grants annually from the NIH or the NSF, federal agencies, and journals in basic science and in clinical medicine.

Research Institutions

We obtained the list of 127 medical schools that are members of the Association of American Medical Colleges.²² To identify other research institutions (e.g., universities) that received more than \$5 million in annual federal funding, we used lists of grants awarded by the NIH²³ and the NSF²⁴ for fiscal year 1998. A total of 304 institutions were identified; 7 did not engage in any scientific research. We designated the institution, not the policy, as our unit of analysis.

We searched for conflict-of-interest policies on institutional home pages on the World Wide Web. If this search failed, we sent the institution a letter requesting a copy of the policy, if there was one. Institutions that did not respond to this letter were sent a second letter. If there was no response to the second letter, we telephoned the institution to ask whether it had a policy and, if so, to request it. A total of 235 policies were obtained. Six additional institutions reported that they were revising their policies; these institutions were considered nonrespondents. Fifteen institutions had no policy on conflicts of interest, a finding that we confirmed by telephone with a senior official at each institution.

Federal Agencies

We studied the policies of all federal agencies that have promulgated a version of the federal "common rule" governing research involving human subjects.²⁵ The federal common rule requires a review of protocols by institutional review boards (IRBs) and provides a series of guidelines for IRB approval, including obtaining informed consent from research subjects, minimizing the risks to the subjects, ensuring an appropriate risk-benefit ratio, and protecting confidentiality. We included the Food and Drug Administration (FDA), even though it has not adopted the federal common rule, because the agency oversees pharmaceutical research. We searched for conflict-of-interest policies involving extramural, rather than intramural, researchers. If we could not locate such policies, we searched for policies involving external contractors. When our investigation suggested that an agency had no policy explicitly addressing extramural research or that the agency did not support extramural research, we confirmed this finding by telephone with a senior official of the agency.

Scientific Journals

The sample of journals was obtained from the ranking of journals performed by the Institute for Scientific Information in 1997.²⁶ We identified the 25 basic science journals and the 25 clinical journals with the highest immediacy-index rankings. Since 2 journals appeared on both lists, the total number was 48. We searched for conflict-of-interest policies in the journals and on their Web home pages. If this search failed, we called the journal's managing editor to obtain a copy of the policy, if there was one.

Analysis of Policies

We used deductive content analysis²⁷ to evaluate the policies on conflicts of interest. With this approach, the contents of documents are analyzed according to predesignated domains. We analyzed the conflict-of-interest policies by searching each document for information in the following seven content domains: the existence of a disclosure requirement, the type of conflict that must be disclosed, the persons or entities (such as trusts) with interests requiring disclosure, the parties (persons or institutions) to which information must be disclosed, when the disclosure must be made,

the use of this information by officials to whom it is disclosed, and the penalties for nondisclosure. Each domain contained several pre-designated items.

Each policy was reviewed independently by two of us. Problems encountered in analyzing the contents of the policies included vague language, redundancy, and inconsistent definitions of terms. Disagreements due to these problems were resolved by consultation with other authors. In each case, the disputed information was classified as one of the predefined items in a domain or a new item was added. A total of seven new items were added. All the policies that had already been analyzed when the new items were added were reviewed to determine whether they contained information that should be reclassified. The data were double-entered into the data base for accuracy. A randomly chosen 20 percent of items were reviewed by other authors; less than 1 percent of the items required change.

Statistical Analysis

The data were summarized with the use of descriptive statistics. Categorical differences between the medical schools and the other research institutions were analyzed with the use of nonparametric tests. Reported P values are two-tailed.

RESULTS

Research Institutions

We obtained responses from 108 of the 127 medical schools (85 percent) and 142 of the 170 other research institutions (84 percent). Fourteen of these 250 institutions (4 medical schools and 10 other institutions) reported that they had no policy on conflicts of interest, and the policy of 1 medical school addressed conflict of commitment only (i.e., the conflict that arises when an investigator accepts work outside the scope of his or her full-time responsibilities). This left 235 institutions with disclosure requirements. A total of 217 of these institutions (92 percent) had policies that had become effective after June 28, 1994, the date on which the proposed revised federal guidelines were first released.^{28,29} All data reported here are for policies that were in effect at the time of our survey.

There was considerable variation among policies in all domains (Table 1). The only nearly universal features were that the management of conflicts and the penalties for nondisclosure were totally discretionary. Nine percent of the institutions had thresholds for disclosure that were lower than the federal threshold. Ten institutions had different standards of disclosure for different types of research; typically, the standards were stricter for clinical trials than for basic science research.

Eighty-nine percent of the institutions required initial disclosure of financial interests involving the spouses or partners and minor or dependent children of investigators (persons explicitly mentioned in the PHS-NSF guidelines). A much smaller proportion of institutions (<25 percent) required that interests held by the adult children, grandchildren, or parents of investigators be reported. Only 15 policies (6 percent) required disclosure in the case of trusts. Five institutions had policies stating that the financial interests of an investigator's family, which was undefined, required disclosure.

TABLE 1. POLICIES OF 235 MEDICAL SCHOOLS AND OTHER RESEARCH INSTITUTIONS ON DISCLOSURE AND MANAGEMENT OF CONFLICTS OF INTEREST.

ITEM*	INSTITUTIONS WITH POLICIES THAT ADDRESS ITEM
	no. (%)
Type of conflict	
Income	215 (91)
Equity interest	218 (93)
Intellectual property	171 (73)
Finder's fees	2 (1)
Fiduciary interest only	134 (57)
Appearance of conflict	156 (66)
Support of the research	79 (34)
Other in-kind support	104 (44)
Policy meets federal guidelines	215 (91)
Policy exceeds federal guidelines	20 (9)†
Person (or entity) with interest requiring initial disclosure	
Investigator	235 (100)
Spouse or partner	210 (89)
Minor or dependent child	208 (89)
Another household member	75 (32)
Adult child	53 (23)
Parent	51 (22)
Grandchild	15 (6)
Another relative	36 (15)
Family (unspecified)	5 (2)
Trust	15 (6)
Party to which initial disclosure must be made	
Party within institution	235 (100)
IRB	3 (1)
Funding agency or sponsor	18 (8)
Research subjects	3 (1)
Journals	16 (7)
Collaborating researchers	1 (<1)
When disclosure is required	
Annually or semiannually	193 (82)
On material change creating new potential for conflicts	178 (76)
When conflict is anticipated	133 (57)
On application for funding	149 (63)
On award of funding	20 (9)
How disclosure should be managed	
Divestment of interest	146 (62)
Withdrawal of investigator from project	143 (61)
Disclosure to IRB	0
Disclosure to funding agency or sponsor	102 (43)
Disclosure to research subjects	0
Disclosure to journals	5 (2)
Disclosure to collaborating researchers	2 (1)
Modification of research plan	139 (59)
Monitoring of project	156 (66)
Additional peer review	16 (7)
Public disclosure	139 (59)
Mandatory management method	1 (<1)
Discretionary management method	234 (>99)
Penalty for nondisclosure	
Termination	109 (46)
Suspension	47 (20)
Salary modification	29 (12)
Nonfinancial modification (e.g., research space)	29 (12)
Reprimand	65 (28)
Disqualification from future grant applications	44 (19)
Notification of funding agency, journal, or both of nondisclosure	98 (42)
Removal of investigator from project	11 (5)
Unspecified or nonspecific penalty	108 (46)
Mandatory penalty	0
Discretionary penalty	235 (100)

*The items are not mutually exclusive. IRB denotes institutional review board.

†One institution applied criteria that were stricter than the federal guidelines to clinical research, but applied the federal criteria to basic-science research. This institution was considered to have exceeded the federal guidelines.

Less than 10 percent of the institutions required initial disclosure to research sponsors or funding agencies; an even smaller proportion required disclosure to the IRB, journals, or collaborating researchers. Only three institutions required that financial interests be disclosed to research subjects. Fifty-seven percent of the institutions required disclosure if the investigator anticipated the possibility of a conflict of interest in the future.

Only one institution had mandatory strategies for managing the initial disclosure of conflicts of interest. Only 43 percent of the institutions had policies that mentioned the possibility of disclosing details of the conflict and its management to the funding agency or research sponsor. Fifty-nine percent of the institutions had policies that mentioned public disclosure as a possibility, but very few policies defined it, and none mentioned disclosure to the IRB or research subjects as a way of managing a conflict of interest. Possible penalties for failure to disclose a conflict ranged from a reprimand to the termination of research funding or of employment. Nonspecific penalties were common, and the application of penalties was uniformly discretionary.

Among the 55 items analyzed, there were a number of significant differences between the medical schools and the other research institutions (Table 2). Although a larger percentage of medical schools than other institutions required initial disclosure to agencies or journals, most of the medical schools did not have this requirement. The policies of medical schools were also more likely to mention more ways to manage an initial disclosure of a conflict, but none of the medical schools made any of these approaches mandatory.

Federal Agencies

We obtained responses from 16 of the 17 federal agencies that met our selection criteria. Five of the 16 reported that they did not fund extramural research and therefore did not have a policy governing it. Of the remaining 11 agencies, 7 had policies that governed only external contractors, a category that could include the extramural recipients of research grants or contracts, although the policies did not explicitly say so. Only four agencies (the PHS, the NSF, the FDA, and the Department of Agriculture) had policies explicitly governing extramural researchers. The most comprehensive were the PHS-NSF policy and the FDA policy.

The PHS-NSF policy covered conflicts of interest involving individual researchers, their spouses, and their dependent children and it applied to salaries, equity interests, and intellectual-property rights. According to this policy, institutions are required to obtain disclosures from investigators about such conflicts of interest periodically, as well as when grants are submitted or when conditions change. There is no requirement that conflicts be disclosed to IRBs or

TABLE 2. SIGNIFICANT DIFFERENCES BETWEEN CONFLICT-OF-INTEREST POLICIES OF MEDICAL SCHOOLS AND OTHER RESEARCH INSTITUTIONS.

ITEM*	INSTITUTIONS WITH POLICIES THAT ADDRESS ITEM		P VALUE†
	MEDICAL SCHOOLS (N=103)	OTHER INSTITUTIONS (N=132)	
	percent		
Type of conflict			
Intellectual property	85	63	<0.001
Person with interest requiring initial disclosure			
Spouse or partner	96	84	0.003
Minor or dependent child	94	84	0.02
Another household member	24	38	0.03
Party to which initial disclosure must be made			
Funding agency or sponsor	13	4	0.01
When disclosure is required			
When conflict is anticipated	47	64	0.008
On application for funding	73	56	0.009
How disclosure should be managed			
Divestment of interest	73	54	0.003
Withdrawal of investigator from project	73	52	0.001
Disclosure to funding agency or sponsor	52	37	0.03
Modification of research plan	69	52	0.008
Monitoring of project	78	58	0.001
Penalty for nondisclosure			
Nonfinancial modification (e.g., research space)	18	8	0.03

*The items are not mutually exclusive.

†P values were determined by Fisher's exact test (two-sided).

search subjects. Institutions are required to develop strategies for managing conflicts. They must report to the agency the existence of both a conflict of interest and a strategy for managing it, but they are not required to report the details of either the conflict or its management (although the agency may request the information). The policy mentions various techniques for managing conflicts and penalties for noncompliance; none are required. Most of the institutional policies on conflicts of interest reflected the PHS–NSF policy; the items most frequently included in the institutional policies were those mentioned in that policy. Only a minority of institutions designed policies that covered more types of conflicts or that contained more requirements for managing them.

The FDA's policy requires sponsors of research to submit detailed information about conflicts of interest on the part of investigators and about strategies to minimize resulting biases. This information is submitted as part of an application for approval of a new drug based on the research conducted by the investigators. If the disclosure raises questions about the integrity of the data, the FDA may audit the data, require further analyses or studies, or refuse to use the data.

Scientific Journals

We obtained responses from 47 of 48 journals. Twenty (43 percent) reported that they had policies for the disclosure of conflicts of interest. Of these, 10 required disclosure of income and equity interests, but only 7 considered intellectual-property rights reportable, and only 1 required that appearances of conflicts be reported. Although all 20 journals required that each author disclose conflicts of interest, only 5 required disclosure of interests involving spouses or partners and minor or dependent children.

DISCUSSION

Our survey of policies on disclosure of conflicts of interest showed great variability among institutional policies. Many of the policies contained important terms that were not adequately defined. In addition, serious potential conflicts of interest were often neglected. Disclosure was generally made only on an in-trainstitutional basis, with no real external accountability. Even when external disclosure was required, many agencies and journals had no procedures for receiving this information or for supervising the management of conflicts.

These findings are a cause for concern. Particularly troublesome is the finding that 15 institutions ap-

parently had no policy on conflicts of interest, even though the PHS–NSF policy requires every institution that receives funds from these agencies to formulate and administer such a policy.³⁰

Many of the policies contained vague language, which can lead to confusion. For example, some policies stated that financial interests of family members are reportable but did not define “family,” and some referred to “public disclosure” as a possible management technique but without an explanation of the term. All important terms in a policy should be clearly defined.

In many cases, potential conflicts of interest were overlooked — for example, the use of sophisticated estate-planning mechanisms. We were surprised that only 6 percent of policies required disclosure of financial arrangements involving grandchildren or trusts.

Most of the institutions required only internal initial disclosure. Only a small minority required initial disclosure to research sponsors, funding agencies, or journals. Although many institutions had policies that mentioned external disclosure as a possible strategy for managing conflicts of interest after the initial disclosure to the institution, the majority of policies did not mention external disclosure, and only one made it mandatory. Only a handful of institutions required initial disclosure of conflicts to IRBs or research subjects, and none had policies that mentioned such disclosure as a subsequent management strategy. We believe that failing to disclose such information is not ethically justified.

We were disturbed that only 7 percent of the institutions and only 43 percent of the medical and scientific journals that we surveyed required disclosure of financial interests in published reports on research. These findings suggest that readers who assume that financial conflicts will be uniformly disclosed are mistaken. According to the International Committee of Medical Journal Editors, such information should be disclosed to journal editors and made available to readers.³¹ The policies of federal agencies may also contribute to inadequate management of conflicts of interest. Most agencies do not have policies that explicitly address extramural research. The PHS and the NSF, which do have such a policy, require only that the existence of conflicts of interest, but not their substantive details, be reported. Decisions about managing conflicts are totally discretionary. These policies seem inadequate to allow federal agencies to safeguard against substantive conflicts.

Our study is limited by the fact that we did not investigate the actual processes that institutions use to manage conflicts of interest. Such an analysis would have posed practical problems.

On the basis of our findings, we propose revising the federal guidelines again in order to achieve an ethically justified balance between the initial emphasis on a restrictive-prohibition approach and the subsequent

emphasis on a discretionary approach focusing on internal disclosure. This goal could be accomplished through several requirements. First, to address the deficiencies we have described and to achieve greater uniformity among institutional policies, all federal agencies should adopt a common conflict-of-interest rule. Second, research institutions should report to federal agencies the substance of conflicts and strategies for managing them. Third, journals should require disclosure of substantive conflicts of interest from all authors and should publish this information routinely. Finally, both IRBs and research subjects should routinely be informed about conflicts of interest.

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