



Federation of American Societies for Experimental Biology

— *Quality Life Through Research* —

Member Societies

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American Society for Biochemistry and
Molecular Biology
American Society for Pharmacology and
Experimental Therapeutics
American Society for Investigative
Pathology
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Society for the Study of Reproduction
Teratology Society
The Endocrine Society
The American Society of Human
Genetics
Society for Gynecologic Investigation
Environmental Mutagen Society
International Society for
Computational Biology
American College of Sports Medicine
Biomedical Engineering Society

June 15, 2009

Attention: Jerry Moore
NIH Regulations Officer
Office of Management Assessment
National Institutes of Health
6011 Executive Boulevard
Suite 601, MSC 7669
Rockville, MD 20852-7669

BY ELECTRONIC SUBMISSION VIA <http://www.regulations.gov>

Re: “Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding Is Sought and Responsible Prospective Contractors; Request for Comments”

Dear Mr. Moore:

The Federation of American Societies for Experimental Biology (FASEB) appreciates the opportunity to provide feedback on the Advance notice of proposed rulemaking (ANPRM) “Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding Is Sought and Responsible Prospective Contractors; Request for Comments” issued by the Department of Health and Human Services. FASEB comprises 22 scientific societies involved in basic, translational, and clinical research and represents more than 90,000 scientists, making it the largest coalition of biomedical research associations in the United States. The mission of FASEB is to advance biological science through collaborative advocacy for research policies that promote scientific progress and education and lead to improvements in human health. Any modification in Conflict of Interest (COI) regulations at the Public Health Service (PHS) will significantly affect scientists funded by the NIH, many of whom are members of FASEB societies, as well as the institutions that employ them. However, these comments address issues of greatest concern to the individual investigator and represent our official comment submitted to NIH.

FASEB believes that maintaining public trust in medical research and preventing the introduction of bias is absolutely critical, and we support efforts to preserve the integrity of science. NIH has a mission to fund the best science and encourage the application of that science to develop and promote technologies and techniques that improve human health. In doing so, NIH—and the researchers it funds through its extramural research program—must exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science. Academic-industry relationships (including industry-employed researchers funded by NIH) do not indicate misconduct or conflict of interest. These

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relationships are in fact an essential and beneficial part of modern biomedical science and the NIH mission to promote a healthier America. These collaborations lead to the development of new medical treatments, diagnostic tools, and other practical ramifications of research. Nonetheless, the special status of NIH requires that any activities with the potential for introducing bias into research be avoided where possible and, where allowed, be carefully managed through enforced disclosure and review.

FASEB has developed three guiding principles to help investigators identify and manage potential conflicts of interest. Investigators must: 1) conduct research activities objectively, 2) operate with transparency, and 3) be accountable to all stakeholders, especially when relationships with industry exist. The PHS regulation ought to reflect and promote these principles, while not diverting responsibility for managing financial conflicts of interest from research institutions and their investigators. NIH should also encourage institutions, journals, industry contractors and professional societies to adopt and enforce clearer and more uniform standards for COI. While flexibility in policies and case-by-case assessment is important, the lack of clear and uniform practices may cause confusion and, in turn, reduce compliance.

The principal focus of the regulation should be to encourage disclosure and, if necessary, management of COI and perceived COI. Proscription or prohibition of beneficial relationships between academia and industry should be avoided. The rights to privacy enjoyed by investigators and administrators, as well as the existing regulatory burdens they face, must be considered in crafting a fair and effective regulation. NIH should increase efforts to educate the public and policymakers on the necessity and effectiveness of beneficial relationships between academia and industry in translating basic research to therapies and health improvements. In parallel, both NIH and institutions should increase and formalize better training of extramural investigators as to their obligations in terms of reporting possible COI. Compliance with the current regulation should be addressed as a separate issue through monitoring, robust enforcement, and education.

The increasing complexities of science require knowledge and resource exchanges involving academia, industry, and government. Professional relationships between scientists facilitate the understanding of these complexities, encourage interdisciplinary approaches, and accelerate biological and medical discovery. We encourage PHS and NIH to seek ways to construct appropriate, targeted mechanisms that better protect the integrity of research while minimizing regulatory burden and permitting appropriate industry-academia relationships to the benefit of the research community and the public. We also encourage PHS and NIH to continue to solicit community input on this crucial and timely issue. Your efforts to engage our community are greatly appreciated.

In specific response to the questions set forth in the ANPRM, FASEB offers the enclosed recommendations, directed at the issues and questions which generated a high level of concern and consensus within FASEB.

Sincerely,

A handwritten signature in black ink that reads "Richard B. Marchase". The signature is written in a cursive, flowing style.

Richard B. Marchase, Ph.D.
President

Enclosure: FASEB Responses to “Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding Is Sought and Responsible Prospective Contractors; Request for Comments”

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I. Expanding the Scope of the Regulation & Disclosure of Interests

The regulations are applicable to Institutions that apply for PHS funding for research and, through implementation of the regulations by each Institution, to each Investigator participating in such research. However, the regulations do not apply to Phase I SBIR/STTR applications (42 CFR 50.602, 45 CFR 94.2).

The regulations require that Investigators disclose to the Institution only those Significant Financial Interests (SFI) (1) that would reasonably appear to be affected by the research for which funding is sought from the PHS; and (2) in entities whose financial interests would reasonably appear to be affected by the research (42CFR 50.604(c)(1); 45 CFR 94.4(c)(1)).

a. Should the regulations be expanded so that they also apply to Phase I SBIR/STTR research applications/proposals for PHS funding?

FASEB COMMENTS:

All extramural investigators funded by NIH should be included in the regulation, including those funded through SBIR and STTR.

b. In May 2004, HHS issued a guidance document entitled, “Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection” that raises points to consider in determining whether specific financial interests, including Institutional financial interests, in research affect the rights and welfare of human subjects and if so, what actions could be considered to protect those subjects. In February 2008, the Association of American Medical Colleges (AAMC) and the Association of American Universities (AAU) Advisory Committee on Financial Conflicts of Interest in Human Subjects Research issued a report, “Protecting Patients, Preserving Integrity, Advancing Health: Accelerating the Implementation of COI Policies in Human Subjects Research,” which offered a number of recommendations designed to enhance Institutional conflict of interest policies. One recommendation was that investigators conducting human subjects research should be required to report all of their outside financial interests directly or indirectly related to their professional responsibilities to their Institution, regardless of dollar amount and regardless of whether or not the investigator believes that the reported financial interests might reasonably appear to be affected by his or her current or anticipated research. In light of the above, should Investigators be required to disclose to their Institutions all Significant Financial Interests that are related to their Institutional responsibilities? Would this expanded disclosure allow the Institution to better determine which of these Significant Financial Interests constitute a FCOI?

FASEB COMMENTS:

Generally speaking, non-PHS projects should be reported to institutions by investigators as part of COI disclosure. However, PHS should impose upon investigators no arbitrary ceiling on outside activities. Though human subjects research, and especially clinical trials, foster enhanced concern, all investigators should be subject to comparable standards for reasons of clarity, fairness, and assuring the greatest diligence in protecting the integrity of NIH-funded research and the public trust.

The extent and application of disclosure requirements must be considered judiciously, to prevent both the introduction of bias and unnecessary invasion of privacy. Investigators should be required to disclose to their institutions all financial interests above a certain threshold (described in Question II) that a “reasonable person” would consider “potentially relevant” to the NIH-funded research in question.

II. Definition of “Significant Financial Interest”

A “Significant Financial Interest” is defined by the current regulations as anything of monetary value, including but not limited to:

- *Salary or other payments for services (e.g., consulting fees or honoraria);*
- *Equity interests (e.g., stocks, stock options or other ownership interests);*
- *Intellectual property rights (e.g., patents, copyrights and royalties from such rights).*

The term does not include the following types of financial interests:

- *Salary, royalties, or other remuneration from the Institution;*
- *Any ownership interests in the Institution, if the Institution is an applicant under the SBIR/STTR program;*
- *Income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities;*
- *Income from service on advisory committees or review panels for public or nonprofit entities;*
- *An equity interest that, when aggregated for the Investigator and the Investigator’s spouse and dependent children, does not exceed \$10,000 in value as determined through reference to public prices or other reasonable measures of fair market value, and does not represent more than a five percent ownership interest in any single entity;*
- *Salary, royalties or other payments that when aggregated for the Investigator and the Investigator’s spouse and dependent children over the next twelve months, are not expected to exceed \$10,000. (42 CFR 50.603; 45 CFR 94.3).*

a. Should the current exemptions be maintained?

- *If so, are the current de minimis thresholds (\$10,000 and 5 percent ownership interest in any single entity) reasonable? If not, how should the de minimis thresholds be changed? Should these thresholds be the same for all types of research?*
- *If not, which exemptions should be reconsidered, and why?*

b. Should certain Significant Financial Interests (i.e., Significant Financial Interests received from specific sources or related to certain types of research) automatically be considered a FCOI under the regulations? If so, what types of Significant Financial Interests?

FASEB COMMENTS:

Because aggregate income is imprecise and difficult to estimate, significant financial interest should be calculated on an annual basis. “Significant financial interest” should be defined broadly and on the basis of an annual aggregate, to include any financial or in kind benefit valued in excess of \$200 per source. This threshold comports with the standard set by the Office of Government Ethics (OGE) for government employees including temporary employees serving on advisory boards, etc. Extramural investigators are distinct even from temporary government employees, but the OGE standard is a proven model for a comparable purpose.

Due to enhanced concern about the introduction of bias, lectures and teaching activities sponsored by for-profit entities (other than those included in the core duties at the investigator's primary employer) should be included in disclosure requirements where financial or other compensation is involved. Travel expenses (airfares, lodging, and meals) beyond what is reasonable and customary should be included in the reporting to an institution of what has been received from external sources and in calculating the aggregate size of a relationship. PHS should develop and make available to all investigators a simple, electronic, universal reporting form to ensure compliance with reporting requirements while minimizing regulatory burden. Though human subjects research, and especially clinical trials, foster enhanced concern, all investigators should be subject to comparable standards for reasons of clarity, fairness, and assuring the greatest diligence in protecting the integrity of NIH-funded research and the public trust.

III. Identification and Management of Conflicts by Institutions

The regulations require that an official(s) designated by the Institution review all financial disclosures; determine whether a financial conflict of interest exists; and, if so, determine what actions the Institution should take to manage, reduce, or eliminate the conflict of interest (42 CFR. 50.605; 45 CFR 94.5). The regulations provide that a conflict of interest exists when the designated official(s) reasonably determines that a Significant Financial Interest could directly and significantly affect the design, conduct, or reporting of the research funded by the PHS (42 CFR 50.605; 45 CFR 94.5). The regulations currently do not define the term "designated Institutional official(s)", or mandate specific actions that Institutions must take to manage, reduce or eliminate particular types of FCOIs.

- a. Should large Institutions (defined as greater than 50 employees) be required to establish an independent committee to review financial disclosures, and require that committee to report to an organizational level within the Institution that is not conflicted by the short-term financial interests of the Investigator or Institution? Would a 50 employee threshold reasonably balance the risk of a more relaxed requirement for smaller Institutions against the burden imposed by requiring an independent panel for these evaluations?*
- b. For certain types of research, should the Institution be required to develop a conflict management plan when the Institution decides to manage or reduce, rather than eliminate, the conflict? If so, for which types of research? Should there be prescribed standards for the conflict management plans? Should the Institution be required to submit this plan to the PHS funding component when it reports the existence of a conflict to the component?*
- c. Should Investigators who are involved in participant selection, the informed consent process, and clinical management of a trial, be prohibited from having a Significant Financial Interest in any company whose interests could be affected by their research or clinical trial? If so, what special circumstances would justify waiving this condition, if any?*
- d. Should the regulations prescribe specific approaches for the management, reduction, or elimination of particular types of FCOI? If so, for which types of FCOI? Which approaches?*
- e. Should specific requirements related to the identification, management, and reporting of FCOI be established for subrecipients (i.e., subgrantees, contractors, subcontractors, collaborators)?*
- f. Should amounts received by Investigators from certain kinds of organizations be limited to certain maximum thresholds if an Investigator is supported with PHS research funds? If so, which kinds of organizations? At what thresholds?*

FASEB COMMENTS:

No additional comments on this question.

IV. Assuring Institutional Compliance

Under the current regulations, the PHS funding component may at any time inquire into the Institutional procedures and actions regarding conflicting financial interests in PHS funded research, including a requirement for submission, or review on site, of all records pertinent to compliance with the regulation (42 CFR 50.606; 45 CFR 94.6). On the basis of its review of records and/or other information that may be available, the PHS funding component may decide that a particular conflict of interest will bias the objectivity of the research it funds to such an extent that further corrective action is needed or that the Institution has not managed, reduced, or eliminated the conflict of interest in accordance with the regulation(s) (42 CFR 50.606; 45 CFR 94.6). The PHS funding component may determine that suspension of funding/the issuance of a Stop Work order is necessary until the matter is resolved(42 CFR 50.606; 45 CFR 94.6).

a. Should the regulations enhance existing enforcement options in the event of noncompliance?

b. Should Investigators be required under the regulations to complete routine FCOI training?

c. Should independent confirmation of an Institution's compliance with the regulation be required? If so, what should this confirmation look like (e.g., accreditation by an outside body, an independent audit)?

FASEB COMMENTS:

Investigators and administrators ought to be provided with web-based, portable, simple, and reasonable training for COI compliance. NIH should continue to provide ongoing and broadly targeted education regarding compliance with COI regulations.

While NIH should provide standards and best practices, it should not be primarily responsible for verifying compliance by individual investigators.

VI. Institutional Conflict of Interest

Institutional conflict of interest is currently not addressed by the regulations, although there has been movement in the research community toward incorporating Institutional standards in conflict of interest policies (see, for example, the February 2008 AAMC/AAU report, "Protecting Patients, Preserving Integrity, Advancing Health: Accelerating the Implementation of COI Policies in Human Subjects Research"), and some Institutions have adopted such standards. This is an area of increasing concern. If the regulation were to be amended to address Institutional conflict of interest, how should it address the following issues?

a. How would Institutional conflict of interest be defined?

b. What would an Institutional conflict of Interest policy address in order to assure the PHS of objectivity in research?

FASEB COMMENTS:

FASEB supports processes in this regard that maximize public trust in research.

V. Requiring Institutions to Provide Additional Information to the PHS

Under the current regulations, prior to spending any funds under an award, the Institution must report to the PHS funding component the existence of any conflicting financial interest found by the Institution and assure that the interest has been managed, reduced, or eliminated in accordance with the regulation(s) (42 CFR 50.604(g)(2), 45 CFR 94.4(g)(2)). The regulations do not require the Institution to report to PHS officials the nature of the interest or other details (42 CFR 50.604(g)(2), 45 CFR 94.4(g)(2)).

a. Should Institutions be required to submit to the PHS funding component additional information on any identified conflict? If they should not be required to submit additional information for all identified conflicts, should they be required to submit additional information for identified conflicts involving certain types of research? If so, for which types of research? What kind of information would provide valuable data to the PHS funding component in evaluating these reports and the potential risk of bias in conduct of research?

FASEB COMMENTS:

The PHS regulation ought to reflect and encourage the proper identification and management of COI by institutions. NIH ought to use robust monitoring techniques to ensure compliance, while not diverting responsibility from institutions for managing financial conflicts of interest of their employees (investigators). For example, institutions should not be required to provide CoI management plans to PHS in every case.