DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 50

45 CFR Part 94

[Docket Number: NIH–2010–0001]

RIN 0925–AA53

Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding Is Sought and Responsible Prospective Contractors

AGENCY: Department of Health and Human Services.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Department of Health and Human Services (HHS or the Department) and the HHS Public Health Service (PHS), proposes to amend its regulations on the Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought and Responsible Prospective Contractors. Since the promulgation of the regulations in 1995, biomedical and behavioral research and the resulting interactions among Government, research institutions, and the private sector have become increasingly complex. This complexity, as well as a need to strengthen accountability, have led to the proposal of amendments that would expand and add transparency to investigator disclosure of significant financial interests, enhance regulatory compliance and effective institutional oversight and management of investigators' financial conflicts of interests, as well as NIH's compliance oversight.

DATES: Comments must be received on or before July 20, 2010 in order to ensure we will be able to consider the comments when preparing the final rule.

ADDRESSES: Individuals, organizations and institutions interested in submitting comments identified by RIN 0925–AA53 and Docket Number [NIH–2010–0001] may do so by any of the following methods:

Electronic Submissions

You may submit electronic comments in the following way:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the instructions for submitting comments.
- To ensure timely processing of comments, NIH is no longer accepting comments submitted to the agency by e-mail.

Written Submissions

You may submit written comments in the following ways:

- *Fax:* 301–402–0169.
- *Mail:* Jerry Moore, NIH Regulations Officer, Office of Management Assessment, National Institutes of Health, 6011 Executive Boulevard, Suite 601, MSC 7669, Rockville, MD 20852–7669.

Instructions: All submissions received must include the agency name and Regulatory Information Number (RIN) [0925–AA53] and docket number [NIH–2010–0001] for this rulemaking action. All comments may be posted without change, including any personal information provided.

Docket: For access to the docket to read background documents or comments received concerning this rulemaking action, go to the eRulemaking.gov Portal: *http://www.regulations.gov* and follow the instructions provided for conducting a search, using the docket number [NIH–2010–0001].

FOR FURTHER INFORMATION CONTACT: Jerry Moore, NIH Regulations Officer, Office of Management Assessment, National Institutes of Health, 6011 Executive Boulevard, Suite 601, MSC 7669, Rockville, MD 20852–7669, telephone 301–496–4607, fax 301–402–0169, e-mail *jm40z@nih.gov,* concerning questions about the rulemaking process and Dr. Sally Rockey, NIH Deputy Director for Extramural Research, concerning substantive questions about the proposed rule, e-mail *FCOI-NPRM@mail.nih.gov.*

SUPPLEMENTARY INFORMATION: Proper stewardship of Federal funds includes ensuring objectivity of results by protecting Federally-funded research from potential bias due to investigator financial conflicts of interest (FCOI).

I. Background

In 1995, the PHS and the Office of the Secretary of HHS published regulations at 42 CFR Part 50 Subpart F and 45 CFR Part 94 (the regulations), that are designed to promote objectivity in PHS-funded research.[1] The current regulations are applicable to Institutions that apply for or seek PHS funding for research (except for Small Business Innovation Research (SBIR)/Small Business Technology Transfer Research (STTR) Phase I applications) and, through implementation of the regulations by these Institutions, to each Investigator participating in the research. Generally, under the current regulations:

- The Institution [2] is responsible for complying with the regulations, including maintaining a written and enforced policy; managing, reducing, or eliminating identified conflicts; and reporting identified conflicts to the PHS Awarding Component. The reports denote the existence of a conflicting interest and the Institution must assure that it has been managed, reduced, or eliminated.
- Investigators [3] are responsible for complying with their Institution's written FCOI policy and for disclosing their Significant Financial Interests [4] (SFIs) to the Institution.
- The PHS Awarding Components [5] are responsible for overseeing

[1] 48 CFR Subpart 9.1, "Responsible Prospective Contractors," and 48 CFR Subpart 9.5, "Organizational and Consultant Conflicts of Interest," also address conflicts of interest in Federally-funded projects. These provisions apply only to acquisitions, not to grants or cooperative agreements.

[2] "Institution" is currently defined under 42 CFR Part 50, Subpart F, as any domestic or foreign, public or private, entity or organization (excluding a Federal agency), and under 45 CFR Part 94 as any public or private entity or organization (excluding a Federal agency) (1) that submits a proposal for a research contract whether in response to a solicitation from the PHS or otherwise, or (2) that assumes the legal obligation to carry out the research required under the contract. 42 CFR 50.603; 45 CFR 94.3.

[3] "Investigator" is currently defined under the regulations as the principal investigator and any other person who is responsible for the design, conduct, or reporting of research (or, in the case of PHS contracts, a research project) funded by PHS, or proposed for such funding. For purposes of the regulatory requirements relating to financial interests, the term "Investigator" includes the Investigator's spouse and dependent children. 42 CFR 50.603; 45 CFR 94.3.

[4] "Significant Financial Interest" is currently defined under the 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); and intellectual property rights (*e.g.,* patents, copyrights and royalties from such rights). The term does not include: (1) Salary, royalties, or other remuneration from the applicant institution; (2) any ownership interests in the institution, if the institution is an applicant under the SBIR/STTR programs; (3) income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities; (4) income from service on advisory committees or review panels for public or nonprofit entities; (5) an equity interest that when aggregated for the Investigator and the Investigator's spouse and dependent children meets both of the following tests: 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; or (6) 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 (or, in the case of PHS contracts, are not reasonably expected) to exceed $10,000. 42 CFR 50.603; 45 CFR 94.3.

[5] "PHS Awarding Component" is currently defined as the/an organizational unit of the PHS that funds [the] research that is subject to the regulations. 42 CFR 50.603, 45 CFR 94.3.

Institutional compliance with the regulations.

Ensuring objectivity in research requires a commitment from Institutions and their Investigators to:

- Completely disclose,
- Appropriately review, and
- Robustly manage identified conflicts.

The purpose of the existing regulations is to ensure that there is no reasonable expectation that the design, conduct, or reporting of PHS-funded research will be biased by any Investigator FCOI.

Since the publication of these regulations, the pace by which new discoveries are translated from the research bench into effective treatment of patients has accelerated significantly and the biomedical and behavioral research enterprise in the United States has grown in size and complexity. For example, an analysis of financial support of biomedical research from 1994 to 2004 [6] showed that funding increased from $37.1 billion in 1994 to $94.3 billion in 2003. Fifty seven percent of the funding in 2003 came from industry sources. At the same time, relationships between individual academic researchers and industry have also increased from 28% in a 1996 survey [7] to 52.8% in a survey conducted in 2007.[8]

Researchers frequently work in multidisciplinary teams to develop new strategies and approaches for translating basic research into clinical application, thus hastening discovery and advancing human health. In addition, these newer translational strategies often involve complex collaborations between investigators and the private sector.

The growing complexity of biomedical and behavioral research; the increased interaction among Government, research institutions, and the private sector in attaining common public health goals while meeting public expectations for research integrity; as well as increased public scrutiny, all have raised questions as to whether a more rigorous approach to Investigator disclosure, management of financial conflicts, and Federal oversight is required. Consequently, we previously published an Advance Notice of Proposed Rulemaking (ANPRM) in the **Federal Register** on May 8, 2009 (74 FR 21610–21613), inviting public comment on potential changes to the regulations.

The ANPRM invited comment on the following major areas of the regulation:

1. Expanding the scope of the regulation and disclosure of interests
2. Definition of "significant financial interest" (including questions regarding the appropriate de minimis threshold and exemptions to the definition)
3. Identification and management of conflicts by Institutions
4. Assuring institutional compliance
5. Requiring Institutions to provide additional information to the PHS
6. Institutional conflict of interest

After careful consideration of the comments received in response to the ANPRM and further deliberation within the Department, we are proposing substantial revisions to the current regulations, detailed below. The specific comments to the ANPRM are discussed in the relevant sections describing the proposed changes to the regulations. We believe that the proposed revisions would expand and add transparency to investigator disclosure of SFIs as well as enhance regulatory compliance and effective FCOI oversight.

II. Description of Proposed Revisions

The following provides a more detailed discussion of the proposed revisions to the current regulations in the order that they would appear in 42 CFR Part 50, Subpart F and 45 CFR Part 94.

Purpose (42 CFR 50.601; 45 CFR 94.1)

We are proposing minor revisions to the text of this section. These revisions reflect a broader effort to improve internal consistency with regard to the use of various terms and phrases throughout these regulations. As a general matter, along with the more substantive changes to the regulations discussed further below, we are seeking to use this rulemaking proceeding as an opportunity to refine the current text of the regulations to improve clarity and readability for users.

Applicability (42 CFR 50.602, 45 CFR 94.2)

The current regulations at 42 CFR Part 50, Subpart F, are applicable to each Institution that applies for PHS grants or cooperative agreements for research and, through implementation of the regulations by each Institution, to each Investigator participating in such research.[9] The current PHS contracting regulations at 45 Part 94 similarly apply to each Institution that seeks PHS funding for research and, through implementation of the regulations, to each Investigator who participates in such research. In neither case do the regulations currently apply to SBIR/STTR Phase I applications.

When the existing regulations were published as a final rule in 1995, it was acknowledged in the preamble that SBIR/STTR Phase I applications "are for limited amounts." [10] Since that time, the size of these awards has increased and the amounts are not insignificant expenditures of public funds. For example, the median amount of an NIH Phase I award increased from approximately $99,000 in 1995 to approximately $182,000 in 2009. In addition, Phase I awards are often used to leverage Phase II funding or significant outside financial support, and a significant proportion of Institutions receiving Phase I funding from NIH, in particular, already have Phase II awards (approximately 200 Institutions in 2008 and 2009). As a result, it would be reasonable to conclude that many Institutions with Phase I awards will be required to implement these regulations in due course.

In light of these factors, we asked in the ANPRM whether the scope of the regulations should be expanded to cover SBIR/STTR Phase I applications. Many of the respondents to the ANPRM indicated that any and all applications and proposals for PHS funding should be subject to the regulations, including SBIR/STTR Phase I applications. For the reasons stated above and the sentiment expressed in public comments on the ANPRM, we are proposing to broaden the applicability of the regulations by eliminating the current exception for SBIR/STTR Phase I applications.

We also propose to add language in this section clarifying that the regulations continue to apply once the PHS-funded research is underway (*i.e.,* after the application process). Finally, we are proposing to make minor revisions to the text of this section as part of a broader effort to improve internal consistency in the use of various terms and phrases throughout the regulations and, where feasible, consistency between the text of 42 CFR Part 50, Subpart F, and 45 CFR Part 94.

Definitions (42 CFR 50.603, 45 CFR 94.3)

We propose to add several new definitions in this section of the regulations, revise some of the existing

[6] Moses H *et al,* JAMA; 2005; 294:1333–1342

[7] Blumenthal D *et al,* N Engl J Med; 1996; 335:1734–9

[8] Zinner DE *et al, Health Aff;* 2009; 28:1814–25.

[9] In those few cases where an individual, rather than an institution, is an applicant for PHS grants or cooperative agreements for research, PHS Awarding Components will make case-by-case determinations on the steps to be taken to ensure that the design, conduct, and reporting of the research will not be biased by any conflicting financial interest of the individual.

[10] 60 FR 35810, 35814 (July 11, 1995)

definitions, and remove one definition, as follows:

1. *Contractor.* We propose a minor revision to the current definition of "Contractor" in 45 CFR 94.3 that would clarify that the term applies to an entity that provides property or services "under contract" for the direct benefit or use of the Federal Government.

2. *Disclosure of significant financial interests.* This definition would be new and would mean an Investigator's disclosure of significant financial interests to an Institution. We propose to include this definition—along with the definition of "FCOI report" below—because of the confusion that can result from the seemingly interchangeable use of the terms "disclosure" and "report" with regard to communications from an Investigator to an Institution and, correspondingly, from an Institution to the PHS. We propose to use the phrase "disclosure of significant financial interests" to describe the communication that occurs between an Investigator and the Institution requesting SFI information from the Investigator as part of its compliance with these regulations. We intend for the term "FCOI report" to describe communications from an Institution to the PHS regarding FCOI.

3. *FCOI report.* This definition would be new and would mean an Institution's report of a financial conflict of interest to a PHS Awarding Component. We propose to add this new definition for the reasons described above regarding the "disclosure of significant financial interests" definition.

4. *Financial conflict of interest.* This definition would be new and would mean a significant financial interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research. Although this definition would be "new" in the sense that it is not listed in the current definitions sections (42 CFR 50.603 and 45 CFR 94.3), the definition is consistent with language contained elsewhere in the current regulations. Specifically, subsection (a)(1) of the current 42 CFR 50.605 and 45 CFR 94.5 provides 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 PHS-funded research." We propose to incorporate a modified version of this text into a freestanding financial conflict of interest definition in order to improve the clarity and readability of the regulations.

5. *Financial interest.* This definition would be new and would mean anything of monetary value or potential monetary value. We propose adding this new definition as a companion to our proposed revision of the "significant financial interest" definition, described below. In the current regulations, the "significant financial interest" definition incorporates the phrase, "anything of monetary value." In the new definition of "financial interest," we propose adding the phrase "or potential monetary value" to capture financial interests that may not have monetary value currently, but could become valuable in the future. This proposed definition could apply, for example, to an ownership interest that an Investigator may hold in a small start-up company.

6. *Institution.* We propose to revise the current definition of "Institution" in 42 CFR 50.603 to refer specifically to an Institution that is applying for, or that receives, PHS research funding. We propose this revision to clarify the entities and organizations to which the requirements in 42 CFR Part 50, Subpart F would apply. We propose corresponding changes to the current definition of "Institution" in 45 CFR 94.3 to maintain consistency, where feasible, between the text of 42 CFR Part 50, Subpart F, and 45 CFR Part 94.

7. *Institutional responsibilities.* This definition would be new and would mean an Investigator's professional responsibilities on behalf of the Institution including, but not limited to, activities such as research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards. We propose to add this new definition because, as described further below, we are proposing to modify the "significant financial interests" definition and Investigator disclosure obligations such that the SFIs being disclosed are those that reasonably appear to be related to the Investigator's "institutional responsibilities" as defined.

Under the current regulations, an Investigator generally is obligated to disclose SFIs on a project-specific basis (*i.e.,* interests that would reasonably appear to be affected by the research for which PHS funding is sought, or in entities whose financial interests would reasonably appear to be affected by the research). We believe that the proposed shift to a focus on "institutional responsibilities" in the regulations would provide Institutions with a better understanding of the totality of an Investigator's interests and would result in more consistent identification, evaluation, and management of any identified conflicts. We also believe that the revised approach would be consistent with the current practices at many institutions, which require investigators to disclose interests annually and/or on an ongoing basis, regardless of specific research projects that are underway. We welcome public comment on the specific elements that should (or should not) be included in an "institutional responsibilities" definition.

8. *Investigator.* We propose to revise the definition of "Investigator" to clarify that it means the PD/PI as well as any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the PHS, or proposed for such funding, including persons who are subgrantees, contractors, collaborators, or consultants (or, in the case of PHS contracts, subcontractors, collaborators, or consultants). We propose these revisions based on our observations regarding the current regulations and the proper application of the "investigator" definition. Although we have developed regulatory guidance on this issue with regard to grants and cooperative agreements (*see* NIH "Frequently Asked Question" A.7 at *http://grants.nih.gov/grants/policy/coifaq.htm*), we believe that further clarification in the regulations themselves is warranted.

We have also revised this definition to eliminate reference to the Investigator's spouse and dependent children. As described further below, we propose to include reference to an Investigator's spouse and dependent children in the revised "significant financial interest" definition.

9. *Manage.* This definition would be new and would mean to take action to address a financial conflict of interest, which includes reducing or eliminating the financial conflict of interest, to ensure that the design, conduct, or reporting of research is free from bias or the appearance of bias. We propose adding this definition as part of a wider reconsideration of the concepts of managing, reducing, and eliminating a FCOI. In the current regulations, these concepts are typically listed separately (*see, e.g.,* 42 CFR 50.604(g), 45 CFR 94.4(g)), suggesting that reducing or eliminating a FCOI may not be the same as managing a FCOI. We believe that it would be more appropriate to consider the reduction or elimination of a FCOI as alternate means of managing a FCOI, depending on the circumstances. Thus, in a hypothetical example where an Institution has concluded that an Investigator's ownership interest in a company is a FCOI, the Institution

could manage the FCOI by requiring the Investigator to reduce his or her ownership interest by some appropriate amount, or to sell the ownership interest in its entirety.

10. *PD/PI.* This definition would be new and would mean a project director or principal investigator of a PHS-funded research project. We propose to use "PD/PI" in the regulation in circumstances in which we may have traditionally used the term "principal investigator" (*e.g.,* in the proposed "investigator" definition, as revised).

11. *PHS.* We propose to revise the definition of "PHS" to include a specific reference to the National Institutes of Health. NIH is part of the Public Health Service and provides a substantial amount of research funding to Institutions, however, it is not otherwise referenced specifically in these regulations. We want to clarify for Institutions applying for, or receiving, research funding from the NIH that they are subject to these PHS regulations.

12. *Research.* We propose to revise the definition of "research" to include a non-exclusive list of examples of different types of PHS funding mechanisms to which the definition applies. As revised, the definition would include any activity for which research funding is available from a PHS Awarding Component through a grant, cooperative agreement, or contract whether authorized under the PHS Act or other statutory authority, such as a research grant, career development award, center grant, individual fellowship award, infrastructure award, institutional training grant, program project, or research resources award.

13. *Significant Financial Interest.* We propose to revise substantially the definition of "significant financial interest" (SFI). Under the current regulations, a SFI means 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); and intellectual property rights (*e.g.,* patents, copyrights and royalties from such rights). The term does not include: (1) Salary, royalties, or other remuneration from the applicant institution; (2) any ownership interests in the institution, if the institution is an applicant under the SBIR or STTR programs; (3) income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities; (4) income from service on advisory committees or review panels for public or nonprofit entities; (5) an equity interest that when aggregated for the Investigator and the Investigator's spouse and dependent children meets both of the following tests: 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; or (6) 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 (or, in the case of PHS contracts, are not reasonably expected) to exceed $10,000.

We propose to revise the definition of "significant financial interest" as follows, incorporating the proposed definitions of "financial interest" and "institutional responsibilities" described above:

"*Significant financial interest* means, except as otherwise specified in this definition: "(1) A financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:

"(i) With regard to any publicly traded entity, a *significant financial interest* exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (*e.g.,* consulting fees, honoraria, paid authorship, travel reimbursement); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value;

"(ii) With regard to any non-publicly traded entity, a *significant financial interest* exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (*e.g.,* stock, stock option, or other ownership interest); or

"(iii) Intellectual property rights (*e.g.,* patents, copyrights), royalties from such rights, and agreements to share in royalties related to such rights.

"(2) The term *significant financial interest* does not include the following types of financial interests: salary, royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed or otherwise appointed by the Institution; any ownership interest in the Institution held by the Investigator, if the Institution is a commercial or for-profit organization; income from seminars, lectures, or teaching engagements sponsored by a federal, state, or local government agency, or an institution of higher education as defined at 20 U.S.C. 1001(a); or income from service on advisory committees or review panels for a federal, state, or local government agency, or an institution of higher education as defined at 20 U.S.C. 1001(a)."

This revised SFI definition would differ from the current SFI definition in a number of respects.

Institutional responsibilities: As indicated in the discussion of the "institutional responsibilities" definition above, SFIs subject to disclosure by an Investigator to an Institution would be those that reasonably appear to be related to the Investigator's "institutional responsibilities" and would not be specific to a particular PHS-funded research project. As a result, when read in conjunction with the revised Investigator disclosure requirements under 42 CFR 50.604 and 45 CFR 94.4 (discussed below), we anticipate that the revised SFI definition would result in the disclosure by Investigators to Institutions of a wider array of interests on a more frequent basis. This proposed approach is consistent with many of the comments we received in response to the ANPRM, which supported expansion of the SFIs that should be disclosed by Investigators to Institutions.

Monetary threshold: The revised SFI definition also would lower—and, in some circumstances, eliminate—the existing monetary thresholds for disclosure. Under the current regulations, a SFI does not include an equity interest that when aggregated for the investigator and the investigator's spouse and dependent children, meets both of the following tests: Does not exceed $10,000 in value, and does not represent more than a five percent ownership interest in any single entity. Similarly, a SFI does not include payments (*e.g.,* salary) 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. The revised definition would differentiate between remuneration to the Investigator (and the Investigator's spouse and dependent children) from a publicly traded entity and remuneration from a non-publicly traded entity. With regard to a publicly traded entity, a

monetary threshold of $5,000 would apply to the aggregated value of any remuneration received from the entity in the twelve months preceding disclosure and the value of any equity interest as of the date of disclosure. With regard to a non-publicly traded entity, a monetary threshold of $5,000 would apply to any remuneration received from the entity in the twelve months preceding disclosure; in addition, however, a SFI would exist with regard to any equity interest in the entity, regardless of value.

In a hypothetical example, the proposed changes to the monetary threshold would operate as follows. Assume an Institution has required an Investigator, who conducts biomedical research at the Institution, to complete a form disclosing her SFIs. Among the Investigator's financial interests are the following: $3,000 in consulting fees that she has received in the past twelve months from Pharmaceutical Company A; stock in Pharmaceutical Company A held by her husband worth $2,500 as of the date of disclosure; and stock options she holds in Start-Up Company B, a private biotechnology firm whose only products are in the early research and development stage. Assuming that these financial interests reasonably appear to be related to the Investigator's institutional responsibilities, the Investigator would be required to disclose them as SFIs. A SFI in Pharmaceutical Company A would exist because the aggregated value of her remuneration for the past twelve months and her husband's equity interest in the company exceeds $5,000 ($3,000 + $2,500 = $5,500). A SFI in Start-up Company B would exist because the Investigator would have an obligation to disclose any ownership interest in a non-publicly traded entity, even if the interest has only potential monetary value as of the time of disclosure.

We recognize that lowering the monetary threshold, as proposed, is not without cost. In particular, while we believe that certain elements of the revised "significant financial interest" definition would make the disclosure and review obligations of Investigators and Institutions more efficient, we recognize that incorporating a lower monetary threshold is likely to lead to increased administrative burden on Investigators and Institutions because more financial interests are likely to be subject to disclosure and review. For this reason, we considered a variety of alternatives for the proposed regulations including a threshold that would be approximate to the current standard (*i.e.,* $10,000), a significantly lower threshold for all types of financial interests (*e.g.,* $100), as well the current proposal.

We declined to propose a threshold equivalent to the current standard because we do not believe that this approach would be consistent with our statutory mandate to revise the regulations for the purpose of "strengthening Federal and institutional oversight and identifying enhancements, including requirements for financial disclosure to institutions * * *." Public Law 111–117, Div. D, Tit. II, sec. 219, 123 Stat. 3034 (2009). In addition, when we raised this question in the ANPRM, a majority of respondents who addressed this question favored lowering the monetary disclosure threshold. These responses were consistent with our own sense that Institutions would welcome greater transparency regarding Investigator financial interests because additional information would help them to better manage identified FCOI. Thus, for example, even if an Investigator's disclosed SFIs falling below the current monetary threshold would not themselves result in new FCOI determinations, the information could provide context for the Institution's management of higher value SFIs that the Institution determines are FCOI.

Given the arguments in favor of lowering the monetary threshold, we analyzed whether a significantly lower threshold (*e.g.,* $100) would be appropriate for all types of financial interests. Although there has been limited study on the effect of the exact monetary value of an Investigator's financial interests on the integrity of his or her research, the authors of at least one journal article note, "a large body of evidence from the social sciences shows that behavior can be influenced by gifts of negligible value."[11] In addition, recent legislative initiatives have incorporated low monetary thresholds in comparable circumstances. For example, the disclosure provisions that apply to applicable manufacturers of drugs and other covered items with regard to transfers of value to physicians and teaching hospitals under title VI, section 6002, of the recently enacted Patient Protection and Affordable Care Act, Public Law 111–148, generally apply to transfers of value of $10 or more.

Notwithstanding these arguments for a significantly lower monetary threshold, we are concerned that the administrative costs associated with disclosure and review of all but negligible financial interests would outweigh the intended benefit of these regulations in promoting objectivity in research. For example, given the existing (and proposed) obligation on Investigators to update SFI disclosures during the period of award, we believe it would be a challenge for Investigators and Institutions alike to comply with this provision every time a new, all-but-negligible financial interest was obtained by the Investigator.

We welcome comment on all aspects of the proposed "significant financial interest" definition, including comments regarding the appropriate balance between the costs that may be associated with expanding the number of financial interests subject to disclosure as a result of a lower monetary threshold versus the potential benefits that might be expected to result from the lower threshold.

Timing: As indicated in the example above, the revised SFI definition would also change the timing for determining whether remuneration represents a SFI. The current regulations exclude aggregated payments (including salary and royalties) that are "not expected to exceed" (or, in the case of PHS contracts, are "not reasonably expected to exceed") the monetary threshold "over the next twelve months." Under the revised definition, at issue is remuneration (including salary and any payment for services not otherwise identified as salary) received from an entity "in the twelve months preceding the disclosure." We believe this change would help Institutions and Investigators to determine more accurately whether or not a financial interest represents a SFI because the payments have already occurred and are likely to have been documented. Moreover, to the extent an Investigator receives additional remuneration from an entity after completing an initial SFI disclosure, such remuneration would be subject to the Investigator's ongoing disclosure obligations assuming the relevant monetary threshold were exceeded. This issue is addressed further in the discussion of 42 CFR 50.604, 45 CFR 94.4 below.

Examples of payment for services: The current definition references as examples of payments for services, receipt of consulting fees, or honoraria. We propose to add "paid authorship" and "travel reimbursement" as additional examples in the revised definition. With regard to "paid authorship," in particular, although there should be little question that receipt of payment from an entity in exchange for the drafting of a

[11] Dana Katz, Arthur L. Caplan, and Jon F. Merz, "All Gifts Large and Small," Am. J. of Bioethics, summer 2003, vol. 3, no. 3, at 39, 39.

publication constitutes payment for services, we believe it is important to reference this form of payment specifically in the regulations. This practice has come under increasing scrutiny in recent years and we wish to make it clear to Institutions and Investigators that such activity may be subject to the disclosure and reporting requirements depending on the circumstances of a given case, such as the amount of payment.

Royalties & Intellectual Property: Under the existing regulation, royalties are included among the "payments" subject to the $10,000 threshold. Under the proposed regulations, the $5,000 threshold would apply to equity interests and "payment for services," which would include salary but not royalties. Royalties nevertheless would be potentially subject to disclosure, as would other interests related to intellectual property. Specifically, the revised definition would potentially apply to any of the following: Intellectual property rights (*e.g.,* patents, copyrights), royalties from such rights, and agreements to share in royalties related to intellectual property rights. As discussed further below, however, royalties received by the Investigator from the Institution would still be excluded from the SFI definition if the Investigator is currently employed or otherwise appointed by the Institution.

Exclusions: We propose to modify the types of interests that are specifically excluded from the SFI definition. For example, the revised definition would only exclude income from seminars, lectures, teaching engagements, if sponsored by a federal, state, or local government agency, or an institution of higher education as defined at 20 U.S.C. 1001(a). Similarly, income from service on advisory committees or review panels would only be excluded if from a federal, state, or local government agency, or an institution of higher education as defined at 20 U.S.C. 1001(a). Thus, income from non-profit entities other than institutions of higher education for the types of activities described above would be subject to the SFI definition. We are proposing this change due to the growth of non-profit entities that sponsor such activities since the current regulations were promulgated in 1995. Some of these non-profit entities receive funding from for-profit entities that may have an interest in the outcome of the Investigators' research (*e.g.,* foundations supported by pharmaceutical companies or other industrial sectors). As a result, we believe it would promote objectivity in biomedical and behavioral research if income in excess of the relevant monetary threshold received from such non-profit entities for teaching and advisory committee-related activities were included within the SFI definition and disclosed by Investigators to Institutions for their review. Under the current 1995 exclusions to the SFI definition, income from such entities for the above-described activities would not be disclosed.

In developing the proposed exclusions to the SFI definition, we considered various alternatives, including whether the exclusions described above should be limited solely to income from federal, state, or local government agencies (*i.e.,* income from institutions of higher education for such activities would be covered by the SFI definition). However, given that many academic Investigators engage in seminars, lectures, teaching engagements, as well as service on advisory committees or review panels at academic Institutions other than those at which they are employed, we concluded that the burden of requiring disclosure of the income from these activities outweighed the potential benefit to be gained from such disclosures.

With regard to the current exclusion for any ownership interests in the institution if the institution is an applicant under the SBIR or STTR programs, we propose to broaden this exclusion to include any ownership interest in the Institution held by the Investigator if the Institution is a commercial or for-profit organization (whether or not an SBIR/STTR applicant). This proposed change is based primarily on the recognition that ownership in one's own company not only is generally an inherent and understood financial interest, but also is an interest that the Institution is already in a position to know without having to request an Investigator to include it in a disclosure of SFIs.

For similar reasons, we do not propose to make substantive changes to the current exclusion for salary, royalties, or other remuneration paid by the Institution to the Investigator, other than to limit the exception to circumstances in which the Investigator is currently employed or otherwise appointed by the Institution. With regard to current employees and appointees, we believe not only that these financial interests are inherent and understood, but also that an Institution is in a position to know this information without having to request Investigators to include it in a disclosure of SFIs. However, other Investigators (*e.g.,* subrecipient Investigators) may be involved with a PHS-funded research project who were previously affiliated with an Institution (*e.g.,* former employees) but who still receive remuneration from the Institution (*e.g.,* royalty payments). Although an Institution presumably maintains information regarding payments to all third parties, it may not be obvious to institutional officials reviewing a SFI disclosure from a subrecipient Investigator under these circumstances that recent payments have been made to the subrecipient Investigator. By limiting the exclusion to Investigators who are currently employed or otherwise appointed by the Institution, as proposed, an Institution could avoid having to investigate, as a matter of course, possible Institution payments to every subrecipient Investigator participating in a PHS-funded research project.

We welcome comment on the proposed exclusions to the SFI definition, including, for example, whether the proposed exclusion for income from teaching and advisory committee-related activities should be expanded to apply to all public or non-profit entities (similar to the current regulations) or to specific categories of public or non-profit entities, or further narrowed to apply solely to federal, state, or local government agencies. We are particularly interested in comments about the balance between the cumulative burden of the inclusion of non-profits (or certain categories of non-profits) in conjunction with defining SFIs to include institutional responsibilities and the potential benefit to be gained from such disclosures.

14. *Small Business Innovation Research (SBIR) Program.* We propose to remove the current definition for the SBIR Program. In light of the proposed removal of reference to the SBIR program from the "Applicability" section and the "significant financial interests" definition, discussed above, the SBIR definition would no longer be necessary in the revised regulations, as proposed.

Responsibilities of Institutions Regarding Investigator Financial Conflicts of Interest (42 CFR 50.604, 45 CFR 94.4)

We propose to revise substantially the regulation addressing the responsibilities of Institutions regarding Investigator FCOI.

Subsection (a) of the current regulation provides, in part, that each Institution must maintain an appropriate written, enforced policy on conflict of interest that complies with the regulations. We propose to revise this provision to require an Institution

not only to maintain an up-to-date, written, enforced policy on FCOI that complies with the regulations, but also to make such policy available via a publicly accessible Web site. We believe these revisions would foster greater transparency and accountability with regard to institutional policies. The revised provision would also clarify that if an Institution's policy on FCOI includes standards that are more stringent than the regulations, the Institution shall adhere to its policy and shall provide FCOI reports regarding identified FCOI to the PHS Awarding Component in accordance with the Institution's own standards. Although we have developed regulatory guidance on this issue with regard to grants and cooperative agreements (*see* NIH "Frequently Asked Question" B.4 at *http://grants.nih.gov/grants/policy/coifaq.htm),* we believe that further clarification in the regulation itself is warranted.

The current subsection (a) also requires, in part, that each Institution must inform each Investigator of its policy on conflict of interest, the Investigator's disclosure responsibilities, and of these regulations. We propose to address this requirement as a new subsection (b), and to add to this new subsection an Investigator training requirement. Specifically, we propose that Institutions shall require Investigators to complete training regarding the Institution's FCOI policy, the Investigator's responsibilities regarding disclosure of FCOI, and the regulations, prior to engaging in PHS-funded research and, thereafter, at least once every two years. This proposal is consistent with the comments of a majority of the respondents to the ANPRM, who supported adding an Investigator FCOI training requirement.

The current subsection (a) also states that if the Institution carries out the PHS-funded research through subgrantees, contractors, or collaborators (or, in the case of PHS contracts, subcontractors or collaborators), the Institution must take reasonable steps to ensure that Investigators working for such entities comply with the regulations, either by requiring those Investigators to comply with the Institution's policy or by requiring the entities to provide assurances to the Institution that will enable the Institution to comply with the regulations. We propose to create a new subsection (c) that would provide a substantially expanded clarification of an Institution's obligations with regard to PHS-funded research carried out through a subrecipient (*e.g.,* subgrantee, contractor, or collaborator or, in the case of a PHS contract, a subcontractor or collaborator). In the ANPRM, we included a question that asked whether specific requirements related to FCOI identification, management, and reporting should be established for subrecipients. This question was based, at least in part, on the concern that awardee and subrecipient Institutions may not fully recognize their responsibilities related to the regulations. Many ANPRM respondents stated that they comply with the current version of subsection (a) by requiring a subrecipient to certify to the awardee Institution that its FCOI policy complies with the applicable Federal regulations and, in those cases when a subrecipient cannot provide a certification, requiring the subrecipient to comply with the awardee Institution's policy. We believe that this type of approach provides a useful means of reinforcing compliance with the regulations.

Therefore, we propose to include as part of the new subsection (c) the following requirements: An Institution that carries out the PHS-funded research through a subrecipient must incorporate as part of a written agreement with the subrecipient legally enforceable terms that establish whether the FCOI policy of the awardee Institution or that of the subrecipient applies to the subrecipient's Investigators. If the subrecipient's FCOI policy applies to subrecipient Investigators, the subrecipient shall certify as part of the agreement that its policy complies with the regulations. If the subrecipient cannot provide such certification, the agreement shall state that subrecipient Investigators are subject to the FCOI policy of the awardee Institution. If the subrecipient's FCOI policy applies to subrecipient Investigators, the agreement shall specify time period(s) for the subrecipient to report all identified FCOI to the awardee Institution. Such time period(s) shall be sufficient to enable the awardee Institution to provide timely FCOI reports, as necessary, to the PHS. If subrecipient Investigators are subject to the awardee Institution's FCOI policy, the agreement shall specify time period(s) for the subrecipient to submit all Investigator disclosures of SFIs to the awardee Institution. Such time period(s) shall be sufficient to enable the awardee Institution to comply timely with its review, management, and reporting obligations under the regulations. Subsection (c) would also require that the Institution must provide FCOI reports to the PHS regarding all FCOI of all subrecipient Investigators consistent with the regulations. We believe that the addition of the above text in the new subsection (c) would help clarify for Institutions and their subrecipients the requirements of both parties in these relationships and promote greater compliance with the regulations.

Subsection (b) of the current regulation requires that an Institution must designate an institutional official(s) to solicit and review financial disclosure statements from each Investigator who is planning to participate in PHS-funded research. In the ANPRM, we asked whether large Institutions (defined as greater than 50 employees) should 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. After considering the responses, we weighed the complexity of the issues that can arise in reviewing financial interests and evaluating conflicts, as well as the potential practical difficulty in determining which Institutions would fall within a "large" Institution definition and which would not. As a result, we do not propose to change the redesignated subsection (d). That being said, however, we strongly encourage each Institution to form a committee of adequate size and scope to review Investigator SFI disclosures and assess comprehensively the potential conflicts that may arise in the Institution. In addition, since reviewing Investigator financial disclosures for potential FCOI can involve many complex issues, we recommend that Institutions consult available resources from the Federal government (*e.g.,* NIH materials posted at *http://grants.nih.gov/grants/policy/coi/*) or other public resources (*e.g.,* materials prepared by academic and professional associations or other scientific organizations).

The current subsection (c) requires that by the time an application is submitted to the PHS, each Investigator who is planning to participate in the PHS-funded research has submitted to the designated official(s) a listing of his/her known SFIs (and those of his/her spouse and dependent children): (i) That would reasonably appear to be affected by the research for which PHS funding is sought; and (ii) in entities whose financial interests would reasonably appear to be affected by the research. All financial disclosures must be updated during the period of award, either on an annual basis or as new reportable SFIs are obtained. In the ANPRM, we asked whether this

requirement should be expanded to require disclosure by Investigators of all SFIs that are related to their institutional responsibilities. Many respondents to the ANPRM were in favor of expanding the SFIs that should be disclosed by the Investigator. As indicated in the above discussion of the "significant financial interest" definition, the proposed revision would capture as part of the definition itself the concept that a "significant financial interest" is one that reasonably appears to be related to the Investigator's "institutional responsibilities." Accordingly, we propose to revise the current subsection (c) language as part of a redesignated subsection (e) with the understanding that the scope of Investigator disclosures would no longer be project specific, but would (consistent with the revised SFI definition) pertain to the Investigator's institutional responsibilities. As part of the new subsection (e), we are also proposing to revise and clarify an Investigator's annual and ongoing *ad hoc* disclosure obligations.

Specifically, in addition to requiring that each Investigator who is planning to participate in the PHS-funded research disclose to the Institution's designated officials the Investigator's SFIs (and those of the Investigator's spouse and dependent children), the Institution also would have to require that each Investigator who is participating in the PHS-funded research submit an updated SFI disclosure: (1) At least annually during the period of the award, including disclosure of any information that was not disclosed initially to the Institution or in a subsequent SFI disclosure, and disclosure of updated information regarding any previously-disclosed SFI (*e.g.,* the updated value of a previously-disclosed equity interest); and (2) within thirty days of acquiring a new SFI (*e.g.,* through purchase, marriage, or inheritance). Although the current regulations include a requirement regarding the updating of financial disclosures (see current subsection (c)(2)), we believe that the revisions proposed above will provide Institutions and Investigators with greater specificity as to the timing of disclosures that are required after an Investigator's initial SFI disclosure to the Institution.

The existing subsection (d) requires an Institution to provide guidelines consistent with the regulations for the designated official(s) to identify conflicting interests and take such actions as necessary to ensure that such conflicting interests will be managed, reduced, or eliminated. We propose to reorganize and expand this requirement in a redesignated subsection (f) to clarify an Institution's obligations. First, the guidelines to be provided by an Institution for the designated institutional officials would be required to address two related tasks, specifically, determination of whether an Investigator's SFI is related to PHS-funded research and, if so related, whether the SFI is a FCOI. Under the current regulations, the Investigator bears the responsibility for determining the relatedness of a SFI to the PHS-funded research as part of the disclosure process (42 CFR 50.604(c), 45 CFR 94.4(c)). As discussed above, however, the proposed regulations would revise the definition of "significant financial interest" to address "institutional responsibilities" and, as a result, SFIs subject to disclosure by an Investigator to an Institution would not be specific to a particular PHS-funded research project. Consistent with these proposed changes, the responsibility for determining whether an Investigator's SFI is related to PHS-funded research would shift to the Institution. This subsection would provide that an Investigator's SFI is related to PHS-funded research when the Institution, through its designated officials, reasonably determines that the SFI: (1) Appears to be affected by the PHS-funded research; or (2) is in an entity whose financial interest appears to be affected by the research.

To provide clarification regarding the determination of whether an Investigator's SFI is a FCOI, the redesignated subsection (f) would incorporate modified language moved from subsection (a)(1) of the current 42 CFR 50.605 and 45 CFR 94.5. Specifically, this subsection would provide that a FCOI exists when the Institution, through its designated officials, reasonably determines that the SFI could directly and significantly affect the design, conduct, or reporting of the PHS-funded research. As discussed above, the proposed regulations would also incorporate a definition of "financial conflict of interest" that is similarly based on this language.

With regard to the current requirement in subsection (d) regarding FCOI management responsibilities, we propose to include this requirement in a separate subsection (g) and clarify that the requirement includes management of any financial conflicts of a subrecipient Investigator pursuant to the new subsection (c), described above. We also propose to cross-reference the Institution's revised management responsibilities that we propose in 42 CFR 50.605(a), 45 CFR 94.5(a), including development and implementation of a management plan and, if necessary, a mitigation plan. Additional discussion of these proposed revisions is addressed below. As a related matter, we propose to include a new subsection (h) that cross-references the Institution's revised and expanded reporting requirements in the proposed new subsection 42 CFR 50.605(b), 45 CFR 94.5(b).

Subsection (e) of 42 CFR 50.604 currently requires an Institution to maintain records of all financial disclosures and all actions taken by the Institution with respect to each conflicting interest for at least three years from the date of submission of the final expenditures report or, where applicable, from other dates specified in 45 CFR 74.53(b) for different situations. Correspondingly, subsection (e) of 45 CFR 94.4 currently requires an Institution to maintain records of all financial disclosures and all actions taken by the Institution with respect to each conflicting interest for three years after final payment or, where applicable, for the other time periods specified in 48 CFR part 4, subpart 4.7. We propose to revise this requirement in a redesignated subsection (i) of both 42 CFR 50.604 and 45 CFR 94.4 to include a responsibility to maintain records relating to all Investigator disclosures of financial interests and the Institution's review of, or response to, such disclosures (whether or not a disclosure resulted in the Institution's determination of a FCOI). We believe that this proposed revision would help clarify for Institutions our intent for the record retention obligation to apply not only in cases in which the Institution has identified a FCOI, but to all Investigator SFI disclosures whether or not such disclosure generated a response by the Institution.

The existing regulations require at subsection (f) that Institutions establish adequate enforcement mechanisms and provide for sanctions where appropriate. We propose to revise this obligation in a redesignated subsection (j) to require an Institution to establish not only adequate enforcement mechanisms and provide for employee sanctions, but also to provide for other administrative actions to ensure Investigator compliance as appropriate.

We propose to revise and, in some respects, shorten the certification requirement currently set forth in subsection (g). In a redesignated subsection (k), the revised requirement would require an Institution to certify that the Institution (1) has in effect at that Institution an up-to-date, written,

and enforced administrative process to identify and manage FCOI with respect to all research projects for which funding is sought or received from the PHS; (2) shall promote and enforce Investigator compliance with the regulations' requirements including those pertaining to disclosure of SFIs; (3) shall manage FCOI and provide initial and ongoing FCOI reports to the PHS consistent with the regulations; (4) agrees to make information available, promptly upon request, to the HHS relating to any Investigator disclosure of financial interests and the Institution's review of, or response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of a FCOI; and (5) shall fully comply with the requirements of the regulations. Notably, this revised subsection would eliminate much of the current certification language regarding an Institution's reporting obligations. In the existing regulations, the certification requirement in subsection (g) essentially provides the primary source of an Institution's reporting responsibilities regarding FCOI. As described further below, we propose a substantial revision and expansion of the reporting requirements and, thus, propose to move the discussion of such requirements to a newly revised subsection 42 CFR 50.605(b), 45 CFR 94.5(b).

Management and Reporting of Financial Conflicts of Interest (42 CFR 50.605, 45 CFR 94.5)

We propose to revise and expand substantially the current regulation regarding management of FCOI to address requirements for both management and reporting of FCOI.

The existing regulations require, at subsection (a), that an Institution's designated official(s) review all financial disclosures and determine whether a conflict of interest exists. If so, the official(s) must determine what actions should be taken by the institution to manage, reduce or eliminate such conflict of interest. Under the existing regulation, a conflict of interest exists when the designated official(s) reasonably determines that a SFI could directly and significantly affect the design, conduct, or reporting of the PHS-funded research. Subsection (a) also provides examples of conditions or restrictions that might be imposed to manage conflicts of interest, specifically, public disclosure of SFIs, monitoring of research by independent reviewers, modification of the research plan, disqualification from participation in all or a portion of the research funded by the PHS, divestiture of SFIs, or severance of relationships that create actual or potential conflicts.

We propose to revise the above language as part of a redesignated subsection (a)(1) to require that, prior to the Institution's expenditure of any funds under a PHS-funded research project, the designated officials of an Institution shall, consistent with subsection (f) of the preceding section (42 CFR 50.604 or 45 CFR 94.4): Review all Investigator disclosures of SFIs; determine whether any SFIs relate to PHS-funded research; determine whether a FCOI exists; and, if so, develop and implement a management plan that shall specify the actions that have been, and shall be, taken to manage such FCOI. The most significant change in the above proposed text is the introduction of a management plan requirement. Although the existing regulations require Institutions to manage FCOI, the term "management plan" is not used. While many Institutions currently may develop and implement management plans as a means of fulfilling their FCOI management responsibilities, we believe that explicitly incorporating this requirement into the regulations would further help to prevent the introduction of bias into PHS-funded research across the research community. We have not proposed to specify comprehensively in this subsection what elements must be included in a management plan, however, as indicated in the discussion of subsection (b) below, the expanded reporting requirements that we propose would include an obligation to report a description of certain "key elements" of the Institution's management plan in certain FCOI reports. Another change in this subsection would be the deletion of the current sentence that describes when a financial conflict of interest exists. As discussed above, a modified version of this sentence would be moved to the redesignated subsection (f) of 42 CFR 50.604 and 45 CFR 94.4, as well as incorporated into a definition of "financial conflict of interest" in 42 CFR 50.603 and 45 CFR 94.3.

The revised subsection (a)(1) would also include the following updated and expanded list of examples of conditions or restrictions that might be imposed to manage a FCOI: Public disclosure of FCOI (*e.g.,* when presenting or publishing the research); for research projects involving human subjects research, disclosure of FCOI directly to participants; appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of the research against bias, or the appearance of bias, resulting from the FCOI; modification of the research plan; change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research; reduction or elimination of a financial interest (*e.g.,* sale of an equity interest); or severance of relationships that create actual or potential financial conflicts. Among the differences from the current text would be the addition of a specific example in the human subjects research context. The ANPRM posed a number of questions related to the issue of whether the regulations should be amended to require specific approaches to management of FCOI related to certain types of research or alternatively, specific types of financial interests or FCOI. After considering the comments, we agree with the majority of the respondents that this approach would not account for the full range of research projects as well as the large contextual variation in circumstances in which FCOI may arise. As a result, the proposed revised regulations would impose uniform FCOI management responsibilities, regardless of the type of research, financial interest, or identified FCOI at issue.

In addition to revising the current regulation as described above, we also propose to introduce two new subsections that clarify an Institution's obligations in situations in which an Institution becomes aware of a SFI after the PHS-funded research is already underway. Specifically, new subsection (a)(2) would require that whenever, in the course of an ongoing PHS-funded research project, a new Investigator participating in the research project discloses a SFI or an existing Investigator discloses a new SFI to the Institution, the designated officials of the Institution shall, within sixty days: Review the SFI disclosure; determine whether it is related to PHS-funded research; determine whether a FCOI exists; and, if so, implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage the FCOI. This subsection would additionally provide that, depending on the nature of the SFI, an Institution may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date of disclosure and the completion of the Institution's review.

A new subsection (a)(3) would provide that whenever an Institution identifies a SFI that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by the Institution during an ongoing PHS-funded research project

(*e.g.,* was not timely reviewed or reported by a subrecipient), the designated officials shall, within sixty days: Review the SFI; determine whether it is related to PHS-funded research; determine whether a FCOI exists; and, if so: (A) Implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage such FCOI going forward; and (B) implement, on at least an interim basis, a mitigation plan which shall include review and determination as to whether any PHS-funded research, or portion thereof, conducted prior to the identification and management of the FCOI was biased in the design, conduct, or reporting of such research. This subsection would additionally provide that, depending on the nature of the SFI, an Institution may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date that the SFI is identified and the completion of the Institution's review.

Our interest in proposing new subsections (a)(2) and (a)(3) is based, at least in part, on our experience working with awardee Institutions and our general impression that some Institutions may be more diligent about addressing potential FCOI at the onset of a PHS-funded research project than after the work is already underway. We also believe it is important to address in the regulations circumstances in which an Institution, for whatever reason, has not timely reviewed a SFI, particularly when such SFI is later determined to be a FCOI. In such circumstances, it is of course important for an Institution to manage the FCOI going forward, however, there is also a critical need to review and determine whether any bias was introduced into the research during the period of time prior to review and management of the FCOI. We have proposed to address this need in subsection (a)(3) by introduction of a "mitigation plan" requirement. We have not proposed the specific elements of a mitigation plan because we believe different circumstances may necessitate different measures. In some instances, for example, it may be sufficient to review a matter internally within a given research department, while in other instances it may be appropriate to have individuals outside the department or outside the Institution review and determine whether the design, conduct, or reporting of the research in question was biased by a belatedly-identified or belatedly-reviewed FCOI.

New subsection (a)(4) would require that whenever an Institution implements a management plan pursuant to the regulations, the Institution must monitor Investigator compliance with the management plan on an ongoing basis until the completion of the PHS-funded research project. This subsection would dovetail with the new subsections (a)(2) and (a)(3), described above, by ensuring that the management actions taken by an Institution at the time a FCOI is identified continue to be followed by the Investigator(s) involved going forward through the duration of the project.

We propose to introduce at subsection (a)(5) an important and significant new requirement to help the biomedical and behavioral research community monitor the integrity and credibility of PHS-funded research and underscore our commitment to fostering transparency, accountability, and public trust. Specifically, we are proposing to amend the regulations to require that, prior to the Institution's expenditure of any funds under a PHS-funded research project, the Institution shall make available via a publicly accessible Web site information concerning any SFI that meets the following three criteria: (A) The SFI was disclosed and is still held by the PD/PI or any other Investigator who has been identified by the Institution as senior/key personnel for the PHS-funded research project in the grant application, contract proposal, contract, progress report, or other required report submitted to the PHS; (B) the Institution determines that the SFI is related to the PHS-funded research; and (C) the Institution determines that the SFI is a FCOI.

As part of this new subsection, we would require that the information posted include, at a minimum, the following: The Investigator's name; the Investigator's position with respect to the research project; the nature of the SFI; and the approximate dollar value of the SFI (dollar ranges would be permissible; less than $20,000; less than $50,000; less than $100,000; less than or equal to $250,000; greater than $250,000), or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value. We propose to require the Institution to update the posted information at least annually. We would also require the Institution to update the Web site within sixty days of the Institution's receipt or identification of information concerning any additional SFI that was not previously disclosed by the PD/PI or senior/key personnel for the PHS-funded research project, or upon the disclosure of a SFI by a new PD/PI or new senior/key personnel for the PHS-funded research project, if the Institution determines that the SFI is related to the PHS-funded research and is a FCOI. We would also require that information concerning the SFIs of an individual subject to this subsection (a)(5) shall remain available via the Institution's publicly accessible Web site for at least five years from the date that the information was most recently updated.

We are aware that this proposed public disclosure requirement was not discussed in the ANPRM. However, given the number and scope of public disclosure initiatives that have emerged since the ANPRM was developed, we believe it is appropriate to include such a provision in this Notice of Proposed Rulemaking. For example, similar disclosure initiatives already are underway at some Institutions and pharmaceutical companies, and some states have implemented similar disclosure requirements legislatively. In addition, at the federal level, the recently enacted Patient Protection and Affordable Care Act (Affordable Care Act), Public Law 111–148, includes several public disclosure provisions. Of greatest relevance, title VI, section 6002, of the Affordable Care Act generally requires designated manufacturers of covered drugs, devices, biological or medical supplies to submit certain information to HHS regarding certain payments made to designated physicians and teaching hospitals annually beginning March 31, 2013, and generally requires the Secretary of HHS to make such information publicly available through an Internet Web site annually beginning not later than September 30, 2013. This section of the Affordable Care Act includes similar provisions that generally apply to information concerning ownership or investment interests held by designated physicians in designated manufacturers and group purchasing organizations. In addition to these institutional and legislative initiatives, many scientific journals require authors to publicly disclose information regarding their research-related financial relationships, and many scientific organizations impose similar requirements with regard to speakers at scientific meetings and conferences.

We recognize that the proposed public disclosure requirement would place an additional administrative burden on Institutions, and would also impact the privacy of Investigators who have information related to their personal financial interests posted publicly to the extent such interests are

determined to be FCOI. Consequently, it is important to identify the optimal balance between these more onerous impacts and the imperative to preserve the integrity of the public's investment in biomedical and behavioral research.

Therefore, we considered several alternatives to the proposed text of subsection (a)(5), including:

1. No requirement that Institutions publicly disclose Investigators' SFI.

2. A requirement that an Institution shall make available via a publicly accessible Web site information concerning any SFI disclosed to the Institution and still held by the PD/PI or any other Investigator who has been identified by the Institution as senior/key personnel for the PHS-funded research project in the grant application, contract proposal, contract, progress report, or other required report submitted to the PHS.

The first alternative—i.e., no requirement for public disclosure—has the advantage of reducing the burden on Institutions and the privacy impact on Investigators. However, this alternative would not promote as much increased transparency or accountability and, given the increasing number of other public sources of at least some of this information, we are unconvinced that this alternative would be sufficient to assist the PHS in strengthening oversight and ensuring proper management of potential bias from FCOI. *The second alternative—i.e.,* requiring public disclosure of all SFIs held by certain Investigators—has the advantage of providing the public with more complete information that aligns and harmonizes with information other sources (*e.g.,* disclosures in journals, at meetings, and in accordance with the Affordable Care Act). Expanding the public disclosure requirement in this manner, however, could increase the administrative burden on the Institutions in some respects (due to an increase in volume of posted information) and raise privacy concerns among impacted Investigators given the increased scope of financial interest information, not all of which is related to PHS-funded research, that would be made publicly available. This requirement also risks strengthening the misperception that all SFI constitute FCOI.

The text proposed in subsection (a)(5) is an attempt to balance the concerns presented by these and other alternatives by including a public disclosure requirement, but limiting it to public disclosure of SFIs determined by the Institution to be related to the PHS-funded research and to be FCOI. We believe that including a public disclosure requirement in these regulations would be advantageous because, among other reasons, the information would derive directly from the Investigator and the Institution (as opposed to a third party not involved in the PHS-funded research) and the information can be updated timely. In addition, confining the public disclosure requirement solely to those SFIs determined by the Institution to be related to the PHS-funded research and to be FCOI limits the amount of Investigator financial information that is made publicly available. We recognize, however, that limiting the requirement for public disclosure in this manner does risk strengthening the misperception that any FCOI necessarily causes bias, which should not be the case if the FCOI is sufficiently managed by the Institution.

We welcome comment on the proposed requirement set forth in the new subsection (a)(5) and the alternatives described above, as well as suggestions for modifying the proposed regulation language or suggestions for other alternative approaches.

Subsection (b) of the current regulation provides that, in addition to the types of conflicting financial interests described in this paragraph that must be managed, reduced, or eliminated, an Institution may require the management of other conflicting financial interests, as the Institution deems appropriate. We propose to maintain this requirement using slightly modified language in a new redesignated subsection (a)(6).

In place of the existing subsection (b), we propose to include a substantial revision and expansion of Institutions' existing FCOI reporting requirements. As indicated above, the certification requirement in the existing 42 CFR 50.604(g), 45 CFR 94.4(g), essentially provides the primary source of an Institution's FCOI reporting responsibilities under the current regulations. The existing provision requires—as part of the Institution's certification in each contract proposal or application for funding to which the regulations apply—that, prior to the Institution's expenditure of any funds under the award, the Institution will report to the PHS Awarding Component the existence of a conflicting interest (but not the nature of the interest or other details) found by the Institution and assure that the interest has been managed, reduced, or eliminated in accordance with the regulation; and, for any interest that the Institution identifies as conflicting subsequent to the Institution's initial report under the award, the report will be made and the conflicting interest managed, reduced, or eliminated, at least on an interim basis, within sixty days of that identification.

A new subsection (b)(1), as proposed, would continue the existing regulation's requirement with regard to the timing of initial FCOI reports and reference the proposed management plan requirements addressed in the above discussion of subsection (a). Specifically, an Institution would be required, prior to the Institution's expenditure of any funds under a PHS-funded research project, to provide to the PHS Awarding Component a FCOI report regarding any Investigator SFI found by the Institution to be conflicting and ensure that the Institution has implemented a management plan in accordance with the regulations.

Similarly, a new subsection (b)(2) would continue the existing regulation's requirement with regard to timing of follow-up FCOI reports with examples of when such reports may be required as well as reference to the proposed management plan and mitigation plan requirements addressed above in the discussion of subsection (a). Specifically, the regulation would require that for any SFI that the Institution identifies as conflicting subsequent to the Institution's initial FCOI report during an ongoing PHS-funded research project (*e.g.,* upon the participation of a new Investigator in the research project), the Institution shall provide to the PHS Awarding Component, within sixty days, a FCOI report regarding the FCOI and ensure that the Institution has implemented a management plan in accordance with the regulations. Where such FCOI report involves a SFI that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by the Institution (*e.g.,* was not timely reviewed or reported by a subrecipient), the Institution also would be required to provide with its FCOI report the mitigation plan implemented by the Institution to determine whether any PHS-funded research, or portion thereof, conducted prior to the identification and management of the FCOI was biased in the design, conduct, or reporting of such research.

In the ANPRM, we requested comment on whether Institutions should be required to report additional information to the PHS Awarding Component and if so, what kind of information would provide valuable data to the PHS Awarding Component in evaluating these reports and the potential risk of bias in the conduct of research. Many respondents supported such a requirement and indicated that

reporting additional information would allow for enhanced oversight by the PHS Awarding Component.

Consistent with these public comments, we are proposing a new subsection (b)(3) that would identify the information that must be included in the FCOI reports required under subsections (b)(1) and (b)(2), described above. Specifically, any FCOI report required under these subsections would be required to include sufficient information to enable the PHS Awarding Component to understand the nature and extent of the financial conflict, and to assess the appropriateness of the Institution's management plan. As proposed, elements of the FCOI report shall include, but are not limited to the following:

- Project/Contract number;
- PD/PI or Contact PD/PI if multiple PD/PI model is used;
- Name of the Investigator with the FCOI;
- Nature of the financial interest (*e.g.,* equity, consulting fee, travel reimbursement, honorarium);
- Value of the financial interest (dollar ranges would be permissible: $0–$4,999; $5,000–$9,999; $10,000–$19,999; amounts between $20,000–X$100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000), or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value;
- A description of how the financial interest relates to the PHS-funded research and the basis for the Institution's determination that the financial interest conflicts with such research;
- A description of the key elements of the Institution's management plan, including:
  - The role and function of the conflicted Investigator in the research project;
  - The rationale for including the conflicted Investigator in the research project;
  - The conditions of the management plan;
  - How the management plan will safeguard objectivity in the research project;
  - Confirmation of the Investigator's agreement to the management plan;
  - How the management plan will be monitored to ensure Investigator compliance;
  - Other information as needed.

We welcome public comment on the FCOI report elements that we propose to include in the new subsection (b)(3).

We propose to introduce in a new subsection (b)(4) a new requirement to provide follow-up reports in cases in which an FCOI has been previously identified and reported. Specifically, the regulation would require that for any FCOI previously reported by the Institution with regard to an ongoing PHS-funded research project, the Institution shall provide an annual FCOI report that addresses the status of the FCOI and any changes to the management plan to the PHS Awarding Component for the duration of the PHS-funded research project. The annual FCOI report would be required to specify whether the financial conflict is still being managed or explain why the FCOI no longer exists. The regulations would require the Institution to provide annual FCOI reports to the PHS Awarding Component for the duration of the project period (including extensions with or without funds) in the time and manner specified by the PHS Awarding Component. If this provision were to be implemented as part of a Final Rule, we anticipate that PHS Awarding Components would provide guidance to Institutions regarding the specific mechanics for filing annual FCOI reports.

Finally, we propose in a new subsection (b)(5) language with regard to FCOI reporting that is similar to the language for FCOI management proposed in the redesignated subsection (a)(5), described above. Namely, we propose that in addition to the types of financial conflicts of interest as defined in the regulations that must be reported pursuant to this section, an Institution may require the reporting of other FCOI, as the Institution deems appropriate.

Remedies (42 CFR 50.606, 45 CFR 94.6)

We propose limited revisions to the existing regulation regarding remedies. Subsection (a) currently provides that if the failure of an Investigator to comply with the conflict of interest policy of the Institution has biased the design, conduct, or reporting of the PHS-funded research, the Institution must promptly notify the PHS Awarding Component of the corrective action taken or to be taken. We propose to revise this requirement such that it applies if an Investigator's failure to comply with an Institution's FCOI policy or a FCOI management plan appears to have biased the design, conduct, or reporting of the PHS-funded research.

In subsection (b), we propose to incorporate language regarding the Department's right of inquiry and access to records that is consistent with the proposed certification provision in 42 CFR 50.604(k)(4), 45 CFR 94.4(k)(4), discussed above. Specifically, subsection (b) would provide that the HHS may inquire at any time (*i.e.,* before, during, or after award) into any Investigator disclosure of financial interests and the Institution's review of, or response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of a FCOI. Similar to the existing regulations, an Institution would be required to submit, or permit on site review of, all records pertinent to compliance with the regulations.

Subsection (b) would also be revised to clarify the types of actions that may be taken if a PHS Awarding Component decides that a particular FCOI will bias the objectivity of the PHS-funded research to such an extent that further corrective action is needed or that the Institution has not managed the FCOI in accordance with the regulations. With regard to grants and cooperative agreements, in particular, subsection 50.606(b) would specify that the PHS Awarding Component may determine that imposition of special award conditions under 45 CFR 74.14 or suspension of funding or other enforcement action under 45 CFR 74.62 is necessary until the matter is resolved. Correspondingly, subsection 94.6(b) would specify for PHS contracts that the PHS Awarding Component may determine that issuance of a Stop Work Order by the Contracting Officer or other enforcement action is necessary until the matter is resolved.

We propose to revise subsection (c) to add that in any case in which the HHS determines that a PHS-funded project of clinical research whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment has been designed, conducted, or reported by an Investigator with a FCOI that was not managed or reported by the Institution as required by the regulations, the Institution must not only require the Investigator involved to disclose the FCOI in each public presentation of the results of the research, but also to request an addendum to previously published presentations.

We propose additional minor revisions to this section as part of a broader effort to improve internal consistency with regard to the use of various terms and phrases throughout these regulations and, where feasible, consistency between the text of 42 CFR Part 50, Subpart F, and 45 CFR Part 94.

Other HHS Regulations That Apply (42 CFR 50.607)

We propose minor revisions to the list of other HHS regulations that apply to

update changes that have been made in the CFR location or title of the existing references in this section. In the course of our review, we considered whether this section was necessary, or whether it should be deleted as potentially confusing to readers with regard to the scope of additional regulations that may apply to a given Institution or Investigator. We welcome comment on whether the regulations should be further revised to delete this section.

III. Institutional Conflict of Interest

Institutional conflict of interest is a subject that is not specifically addressed in the current regulations. Because this is a topic of increasing interest to the Department as well as in the research community, we invited public comment in the ANPRM on the possible revision of the regulations to address institutional conflict of interest. In particular, we asked (a) how "institutional conflict of interest" would be defined, and (b) what an institutional conflict of interest policy would address in order to assure the PHS of objectivity in research.

The comments that we received in response to these questions demonstrated a variety of viewpoints on this complex issue and, in particular, the extensive differences in administrative structure among Institutions that receive PHS funding. As a result, we believe that further careful consideration is necessary before PHS regulations could be formulated that would address the subject of institutional conflict of interest in the same comprehensive manner as the proposed regulations regarding Investigator FCOI. Because we believe it is important to revise the existing regulations regarding Investigator FCOI in a timely manner, our proposed revisions to the text of the regulations are limited to the subject of Investigator FCOI.

Notwithstanding this limitation, we welcome comment on whether the regulations should be further revised to require Institutions, at a minimum, to adopt some type of policy on institutional conflict of interest, even if the scope and elements of the policy remain undefined in the regulations. For example, in addition to the changes we have proposed herein to subsection (a) of 42 CFR 50.604 and 45 CFR 94.4, discussed above, this subsection could be further revised to require that each Institution shall maintain up-to-date, written, enforced policies on Investigator financial conflicts of interest and institutional conflict of interest that comply with this subpart, and make such policies available via a publicly accessible Web site. If this additional revision to subsection (a) were to be incorporated, further corresponding revisions to the regulations would be made as necessary, *e.g.,* to the Purpose section (42 CFR 50.601, 45 CFR 94.1).

Whether or not final regulations includes further revisions to address institutional conflict of interest, the Department will continue to consider the issue carefully and may propose in the future more comprehensive revisions to the regulations to address this subject.

IV. Regulatory Impact Analyses (RIA)

The following is provided as public information.

Analysis of Impacts

We have examined the impacts of the proposed amendments to 42 CFR Part 50 Subpart F and 45 CFR Part 94 under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4). Executive Order 12866, Regulatory Planning and Review, directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The Executive Order defines an economically significant regulatory action as one that would have an annual effect on the economy of $100 million or more. Based on our analyses, we believe that the proposed amendments to the regulations do not constitute an economically significant regulatory action under this definition.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of the rule on small entities. For the purposes of this analysis, small entities include small business concerns as defined by the SBA, usually businesses with fewer than 500 employees. Approximately 2800 [12] such organizations apply for research funding annually, of which approximately 1300 [13] are awarded funds. The only proposed change to the current regulations that pertains to applicant organizations is the proposed removal of the exemption for SBIR/STTR Program Phase I applications in sections 50.602 and 94.4, respectively. This would affect approximately 2000 small business concerns that apply for SBIR/STTR Program Phase I funding. All other proposed changes to the regulations apply only to the approximately 1200 small business concerns that receive PHS funding (under both the SBIR/STTR Program Phase I and Phase II programs). The cost of implementing the amended regulations is an allowable cost eligible for reimbursement as a Facilities and Administrative cost on PHS-supported grants, cooperative agreements and contracts. This generally offsets the cost burdens of implementation. Therefore, we do not believe that the proposed changes to the regulations would have a significant economic impact on a substantial number of small entities. Our analysis is further supported by the small number of FCOI reports submitted to NIH by small business concerns—four reports were submitted in FY2008 and ten in FY2009. Finally, we considered the impact of the proposed requirement for Investigator training every two years on small entities. For the current regulation, NIH developed training materials that Institutions, including those that small businesses, can use which are available on the NIH Web site at *http://grants.nih.gov/grants/policy/coi/index.htm.* NIH will continue to update the training materials when the Final Rule is published to ameliorate the burden on Institutions, including small businesses.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation with base year of 1995) in any one year." The current inflation-adjusted statutory threshold is approximately $142 million.[14] The agency does not expect that the proposed amendments to the regulations will result in any 1-year expenditure that would meet or exceed this amount.

Though the proposed amendments will not result in the expenditures listed above, we do discuss the effects of the amendments elsewhere in this preamble.

[12] All applicant Institution numbers are based on the number of Institutions that applied for NIH funding in FY2008.

[13] All awardee Institution numbers are based on the number of Institutions that were awarded NIH funding in FY2008.

[14] Bureau of Labor Statistics inflation calculator.

Benefits

The proposed amendments to the regulations on the Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought (42 CFR Part 50, Subpart F) and Responsible Prospective Contractors (45 CFR Part 94) would expand and add transparency to investigator disclosure of Significant Financial Interests as well as enhance regulatory compliance and effective oversight of financial conflicts of interest.

Costs

Approximately 5000 Institutions that apply for PHS funding annually would be subject to the amended regulations. The only proposed change to the current regulations that pertains to applicant organizations, however, pertains to a subset of applicant organizations and that is the proposed removal of the exemption for SBIR/STTR Program Phase I applications in sections 50.602 and 94.4, respectively, which would affect approximately 2000 small business concerns. The remaining proposed amendments would affect the approximately 2800 organizations (of all types, including small businesses) that are awarded PHS funding annually and, through the implementation of the regulations by the Institutions, to the estimated 40,500 Investigators participating in PHS-funded research that have Significant Financial Interests. The cost of implementing the amended regulations is an allowable cost eligible for reimbursement as a Facilities and Administrative cost on PHS supported grants, cooperative agreements and contracts. This generally offsets the cost burdens of implementation for the affected Institutions and through their implementation of the regulations, to the Investigators. That said, we are including a description of the projected costs of the proposed amendments to the regulations for general information.

42 CFR Part 50 Subpart F/45 CFR Part 94	New proposed requirement?	Number of respondents	Frequency of response (annual)	Estimated cost per response [15]	Estimated annual cost [16]
50.602/94.2	Only for SBIR/STTR Phase I applicants.	Total: ~5,000 applicant Institutions and 2,800 awardee institutions [17] and an estimated 40,500 investigators. New: Approximately 2,000 applicant Institutions and 700 awardee Institutions.[18]	NA	NA	Total estimated annual cost $$12,047,525.[19]
50.604/94.4					
(a)	Only making the policy public.	2,800 [20]	1	$665	$1,862,000.
(b)	Only the training component is new.	Institutions: 2,800 [21] Investigators: 40,500.[22]	Institutions: 1 Investigators: 0.5	Institutions: $105 Investigators: $17.5 Total: $122.5	Institutions: $294,000. Investigators: $708,750. Total: $1,002,750.
(c)(1)	n—clarification of current requirements.	700 [23]	1	$35.00	$24,500.
(d)	y	2,800 [24]	1	$35	$98,000.
(e)(1)	n but scope has changed.	40,500 [25]	1	$70	$2,835,000.
(e)(2)	n	40,500	1	$17.50 [26]	$708,750.
(e)(3)	n	1,000 [27]	1	$17.50	$17,500.
(f)	n but scope has changed.	2,800 awardee Institutions.	1	$35.00	$98,000.
(i)	n	2,800 awardee Institutions.	1	$140	$392,000.
50.605/94.5					
(a)(1)	Requirement to develop a management plan.	2,800 awardee institutions.[28]	1	$35 for review of 40,500 disclosures and $2,800 for developing management plan for 1,000 identified FCOI.	$4,217,500.[29]
(a)(2)	n	1,000 [30]	NA [31]	NA	NA.
(a)(3)	y	500 [32]	1	$105	$52,200.
(a)(3)(i)	n	50 [33]	1	$2,800 [34]	$140,000.
(a)(3)(ii)	y	50 [35]	1	$280 [36]	$14,000.
(a)(4)	y	1,000 [37]	12	$35	$420,000.
(a)(5)	y	2,800	1	$35 [38]	$98,000.
(b)(1)	n but amount of information reported has changed.	Included in 50.605(b)(3)/94.5 (b)(3) below.	NA	NA	NA.
(b)(2)	y	100 [39]	1	$70	$7,000.
(b)(3)	y	1,000	1	$35	$35,000.[40]
(b)(4)	n but scope has been clarified.	1,000	1	$17.50 [41]	$17,500.
50.606/94.6					

42 CFR Part 50 Subpart F/45 CFR Part 94	New proposed requirement?	Number of respondents	Frequency of response (annual)	Estimated cost per response [15]	Estimated annual cost [16]
(a)	n—but scope has been clarified.	20 [42]	1	$350	$7,000.
(c)	n—only the addendum to previously published presentations is new.	50 [43]	3 [44]	$10.50	$525.

Alternatives

The key alternative to the proposed amendment of these regulations would be to continue to operate under the current regulations. In the intervening years since the regulation was promulgated, Investigator collaborations have become more complex and public scrutiny has increased significantly creating an environment that would benefit from a regulation with more effective means for management and oversight. If we continue to operate under the current regulations, we would then lose the opportunity to implement enhanced institutional management of Investigator financial conflicts of interests related to PHS-funded research, increased oversight by the PHS funding component, and enhanced transparency. We believe that the incremental increase in the cost of implementing the proposed regulation is outweighed by the benefits of these changes and that the proposed regulation will strengthen public trust in PHS-funded research. With regard to alternative approaches to particular requirements in the regulations, we have indicated in various provisions of the preamble to this Notice of Proposed Rulemaking the basis for the Department's proposed approach versus alternatives. (*See, e.g.,* section III regarding institutional conflicts of interest.)

Paperwork Reduction Act

This proposed rule contains requirements that are subject to OMB approval under the Paperwork Reduction Act of 1995, as amended (44 U.S.C. chapter 35). Sections 50.604(a), 50.604(b), 50.604(c)(1), 50.604(d), 50.604(e)(1), 50.604(e)(2), 50.604(e)(3), 50.604(f), 50.605(a)(1), 50.605(a)(3), 50.605(a)(3)(i), 50.605(a)(3)(ii), 50.605(a)(4), 50.605(a)(5), 50.605(b)(1), 50.605(b)(2), 50.605(b)(3), 50.605(b)(4), 50.606(a), 50.606(c); 94.4(a), 94.4(b), 94.4(c)(1), 94.4(d), 94.4(e)(1), 94.4(e)(2), 94.4(e)(3), 94.4(f), 94.5(a)(1), 94.5 (a)(3), 94.5(a)(3)(i), 94.5(a)(3)(ii), 94.5(a)(4), 94.5(a)(5), 94.5(b)(1), 94.5(b)(2), 94.5(b)(3), 94.5(b)(4), 94.6(a), and 94.6(c) contain reporting and information collection requirements that are subject to OMB approval under the Paperwork Reduction Act.

Sections 50.604(i), and 94.4(i), contain recordkeeping requirements that are subject to OMB review under the Paperwork Reduction Act. The title, description, and respondent description of the information collection and recordkeeping requirements contained in this proposed rule have been submitted to OMB for review. Other organizations and individuals desiring to submit comments on the information collection and recordkeeping requirements should send their comments to: (1) Mikia Currie, Project Clearance Officer, National Institutes of Health, Rockledge Center 1, 6705 Rockledge Drive, Room 3509, Bethesda, MD 20817, telephone 301–594–7949 (not a toll-free number); and (2) the Office of Information and Regulatory Affairs, OMB, *OIRA_submission@omb.eop* or by fax to 202–395–6974, and mark "*Attention:* Desk Officer for the National Institutes of Health, Department of Health and Human Services." After we obtain OMB

[15] Average burden hours × $35/hour based on recent NIH cost analyses.

[16] Number of respondents × estimated cost per response.

[17] Based on FY2008 numbers.

[18] Will be newly covered by the regulations under the proposed expansion to include the SBIR/STTR phase I program.

[19] Sum of all the columns below.

[20] Assumes 2,800 awardee Institutions and 19 hours per institution for formulating and maintaining the policy. Also assumes that all awardee Institutions already maintain a public Web site. Therefore, posting the policy to the Web site is an incremental cost.

[21] Assumes that 2,800 awardee institutions: 1. Inform investigators about the policy on an annual basis by sending a notification to all investigators = 1 hour and 2. Annually adapt NIH-provided training materials to Institutional needs = 2 hours.

[22] Assumes 40,500 Investigators undergo 1 hour of training every two years. This refers to FCOI training only and is based on the use of training materials developed by the NIH and adapted to the Institution's needs.

[23] An estimated maximum 25% of Institutions may have sub-recipients in any one year—assuming 1 hour per Institution to incorporate the requirement of the regulations into an already existing written agreement.

[24] Assumes that 2,800 awardee institutions solicit disclosures on an annual basis by sending a notification to all investigators.

[25] The financial disclosure burden estimate is based upon an investigator figure of 40,500 with an average response time of 2 hours.

[26] Assumes that updating a disclosure takes less time/effort and therefore costs less than creating a new one.

[27] Assumes that only a small number of the 40,500 investigators will have a new SFI in any year.

[28] Although not more than 1,000 reports of Conflict of Interest are expected annually, the 2,800 responding institutions must review all financial disclosures associated with PHS-funded awards to determine whether any conflicts of interest exist. Thus, the review cost of $1,417,500 is based upon estimates that it will take on the average 1 hour to review each of 40,500 financial disclosures associated with PHS-funded awards. The cost for developing a management plan for identified FCOI is estimated at 80 hours × 1,000 cases × $35/hour = $2,800,000.

[29] $4,252,500 for review plus $2,800,000 for developing management plans = $7,052,500.

[30] Based on 50.604/94.4 (e)(3) above.

[31] The cost is included in 50.605/94.5 (b)(2) below.

[32] Assumes that this is a rare occurrence, based on prior experience.

[33] Assumes only a fraction of the newly identified SFIs will constitute FCOI.

[34] Development of management plan.

[35] Assumes only a fraction of the newly identified SFIs will constitute FCOI.

[36] Assumes the mitigation plan will be adapted from the management plan developed in 50.605/94.5 (a)(3)(i) above and therefore will cost less than developing an entirely new plan.

[37] Based on previous assumption of 1,000 FCOI reports annually.

[38] Assumes that all awardee Institutions already maintain a public Web site. Adding the required information is an incremental cost. However, updating annually does have a cost.

[39] The cost of subsequent reports of conflicts is significantly less, because we do not expect many additional reportable conflicts and there will be only a limited number of disclosures to review.

[40] Assumes 1,000 FCOI reports annually × 1 hour × $35/hour to prepare the report/complete an NIH-provided web form.

[41] Assumes it takes less time to update a report than to create a new one.

[42] This was originally estimated in the 1995 Final Rule to be no more than 5 instances that the failure of an investigator to comply with the institution's conflict of interest policy has biased the design, conduct or reporting of the research. "Objectivity in Research, Final Rule" 60 FR 132 (July 11, 1995) pps. 35810–35819. This estimate, and others were increased in 2002 "due to increased numbers of institutions and investigators."

[43] Number based on 50.605/94.5 (a)(3)(i)—of those only a fraction will relate to a project of clinical research whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment, but we are calculating the maximum assumed cost.

[44] Assumes an average of 3 publications annually.

approval, we will publish the OMB control number in the **Federal Register**.

Following are details of the estimated burden of implementing the proposed regulations.

42 CFR Part 50 Subpart F/45 CFR Part 94	New proposed requirement?	Number of respondents	Frequency of response (annual)	Average burden hours	Annual burden hours[45]
50.602/94.2	Only for SBIR/STTR Phase I applicants.	Total: ~5,000 applicant Institutions and 2,800 awardee institutions[46] and an estimated 40,500 investigators. New: Approximately 2,000 applicant Institutions and 700 awardee Institutions.[47]	NA	NA	Total estimated burden hours: 344,215.[48]
50.604/94.4					
(a)	Only making the policy public.	2,800[49]	1	19	53,200.
(b)	Only the training component.	Institutions: 2,800[50] .. Investigators: 40,500.[51]	Institutions: 1 ..... Investigators: 0.5	Institutions: 3 ..... Investigators: 1	Institutions: 8,400. Investigators: 20,250.
(c)(1)	n-clarification of current requirements.	700[52]	1	1	700.
(d)	y	2,800[53]	1	1	2,800.
(e)(1)	n but scope has changed.	40,500[54]	1	2	81,000.
(e)(2)	n	40,500	1	0.5[55]	20,250.
(e)(3)	n	1,000[56]	1	0.5	500.
(f)	n but scope has changed.	2,800 awardee Institutions.	1	1	2,800.
(i)	n	2,800 awardee Institutions.	1	4	11,200.
50.605/94.5					
(a)(1)	Requirement to develop a management plan.	2,800 awardee institutions.[57]	1	1 hour per disclosure to review plus 80 hours per identified FCOI to develop management plan.	120,500.[58]
(a)(2)	n	1,000[59]	NA[60]	NA	NA.
(a)(3)	y	500[61]	1	3	1500.
(a)(3)(i)	n	50[62]	1	80[63]	4,000.
(a)(3)(ii)	y	50[64]	1	8[65]	400.
(a)(4)	y	1,000[66]	12	1	12,000.
(a)(5)	y	2,800	1[67]	1	2,800.
(b)(1)	n but amount of information reported has changed.	Included in 50.605(b)(3)/94.5 (b)(3) below.	NA	NA	NA.
(b)(2)	y	100[68]	1	2	200.
(b)(3)	y	1,000	1	1	1,000.[69]
(b)(4)	n-scope has been clarified.	1,000	1	0.5[70]	500.
50.606/94.6					
(a)	n-scope has been clarified.	20[71]	1	10	200.
(c)	n-only the addendum to previously published presentations.	50[72]	3[73]	0.3	15.

Environmental Impact

We have determined that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

[45] Number of respondents × average burden hours × frequency of response.

[46] Based on FY2008 numbers.

[47] Will be newly covered by the regulations under the proposed expansion to include the SBIR/STTR phase I program.

[48] Sum of all the columns below.

[49] Assumes 2,800 awardee Institutions and 19 hours per institution for formulating and maintaining the policy. Also assumes that all awardee Institutions already maintain a public Web site. Therefore, posting the policy to the Web site is an incremental burden.

[50] Assumes that 2,800 awardee institutions: 1. Inform investigators about the policy on an annual basis by sending a notification to all investigators

Continued

= 1 hour, and 2. Annually adapt NIH-provided training materials to Institutional needs = 2 hours.

[51] Assumes 40,500 Investigators undergo 1 hour of training every two years. This refers to FCOI training only and is based on the use of training materials developed by the NIH and adapted to the Institution's needs.

[52] An estimated maximum 25% of Institutions may have sub-recipients in any one year—assuming 1 hour per Institution to incorporate the requirement of the regulations into an already existing written agreement.

[53] Assumes that 2,800 awardee institutions solicit disclosures on an annual basis by sending a notification to all investigators.

[54] The financial disclosure burden estimate is based upon an investigator figure of 40,500 with an average response time of 2 hours.

[55] Assumes that updating a disclosure takes less time/effort than creating a new one.

[56] Assumes that only a small number of the 40,500 investigators will have a new SFI in any year.

[57] Although not more than 1,000 reports of Conflict of Interest are expected annually, the 2,800 responding institutions must review all financial disclosures associated with PHS-funded awards to determine whether any conflicts of interest exist. Thus, the review burden of 40,500 hours is based upon estimates that it will take on the average 1 hour for an institutional official to review each of 40,500 financial disclosures associated with PHS funded awards.. The burden for developing a management plan for identified FCOI is estimated at 80 hours × 1,000 cases = 80,000 hours.

[58] 40,500 for reviewing disclosures from 40,500 Investigators plus 80,000 for developing management plans for 1,000 identified FCOI.

[59] Based on 50.604/94.4 (e)(3) above.

[60] The burden is included in 50.605/94.5 (b)(2) below.

[61] Assumes that this is a rare occurrence, based on prior experience.

[62] Assumes only a fraction of the newly identified SFIs will constitute FCOI.

[63] Development of management plan.

[64] Assumes only a fraction of the newly identified SFIs will constitute FCOI.

[65] Assumes the mitigation plan will be adapted from the management plan developed in 50.605/94.5(a)(3)(i) above and therefore will take less time/effort than developing an entirely new plan.

[66] Based on previous assumption of 1,000 FCOI reports annually.

[67] Assumes that all awardee Institutions already maintain a public Web site. Adding the required information is an incremental burden. However, updating annually does have a burden.

[68] The burden for subsequent reports of conflicts is significantly less, because we do not expect many additional reportable conflicts and there will be only a limited number of disclosures to review.

[69] Assumes 1,000 FCOI reports annually × 1 hour to prepare the report/complete an NIH-provided Web form.

[70] Assumes it takes less time to update a report than to create a new one.

[71] This burden was originally estimated in the 1995 Final Rule to be no more than 5 instances that the failure of an investigator to comply with the institution's conflict of interest policy has biased the design, conduct or reporting of the research. "Objectivity in Research, Final Rule" 60 FR 132 (July 11, 1995) pps. 35810–35819. This burden estimate and others was increased in 2002 "due to increased numbers of institutions and investigators."

[72] Number based on 50.605/94.5(a)(3)(i)—of those only a fraction will relate to a project of clinical research whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment, but we are calculating the maximum assumed burden/cost.

[73] Assumes an average of 3 publications annually.

Catalogue of Federal Domestic Assistance

The Catalogue of Federal Domestic Assistance numbered programs applicable to this proposed rule are:

93.113—Environmental Health
93.121—Oral Diseases and Disorders Research
93.142—NIEHS Hazardous Waste Worker Health and Safety Training
93.143—NIEHS Superfund Hazardous Substances—Basic Research and Education
93.172—Human Genome Research
93.173—Research Related to Deafness and Communication Disorders
93.187—Undergraduate Scholarship Program for Individuals from Disadvantaged Backgrounds
93.209—Contraception and Infertility Research Loan Repayment Program
93.213—Research and Training in Complementary and Alternative Medicine
93.220—Clinical Research Loan Repayment Program for Individuals from Disadvantaged Backgrounds
93.233—National Center on Sleep Disorders Research
93.242—Mental Health Research Grants
93.271—Alcohol Research Career Development Awards for Scientists and Clinicians
93.272—Alcohol National Research Service Awards for Research Training
93.273—Alcohol Research Programs
93.279—Drug Abuse and Addiction Research Programs
93.280—National Institutes of Health Loan Repayment Program for Clinical Researchers
93.281—Mental Health Research Career/Scientist Development Awards
93.282—Mental Health National Research Service Awards for Research Training
93.285—National Institutes of Health Pediatric Research Loan Repayment Program
93.286—Discovery and Applied Research for Technological Innovations to Improve Human Health
93.307—Minority Health and Health Disparities Research
93.310—Trans-NIH Research Support
93.361—Nursing Research
93.389—National Center for Research Resources
93.393—Cancer Cause and Prevention Research
93.394—Cancer Detection and Diagnosis Research
93.395—Cancer Treatment Research
93.396—Cancer Biology Research
93.397—Cancer Centers Support Grants
93.398—Cancer Research Manpower
93.399—Cancer Control
93.701—Trans-NIH Recovery Act Research Support RECOVERY
93.702—National Center for Research Resources, Recovery Act Construction Support Recovery
93.837—Cardiovascular Diseases Research
93.838—Lung Diseases Research
93.839—Blood Diseases and Resources Research
93.846—Arthritis, Musculoskeletal and Skin Diseases Research
93.847—Diabetes, Digestive, and Kidney Diseases Extramural Research
93.853—Extramural Research Programs in the Neurosciences and Neurological Disorders
93.855—Allergy, Immunology and Transplantation Research
93.856—Microbiology and Infectious Diseases Research
93.859—Biomedical Research and Research Training
93.865—Child Health and Human Development Extramural Research
93.866—Aging Research
93.867—Vision Research
93.879—Medical Library Assistance
93.891—Alcohol Research Center Grants
93.989—International Research and Research Training

List of Subjects

42 CFR Part 50
45 CFR Part 94

Colleges and universities, Conflict of interests, Contracts, Financial disclosure, Grants-health, Grants programs, Non-profit organizations, Research, Scientists, Small businesses.

For the reasons set forth in the preamble, the Department proposes to amend 42 CFR chapter I, subchapter D, part 50, subpart F and 45 CFR subtitle A, subchapter A, part 94 as follows:

TITLE 42—GRANTS AND AGREEMENTS

PART 50—POLICIES OF GENERAL APPLICABILITY

1. Revise Subpart F to read as follows:

Subpart F—Promoting Objectivity in Research

Sec.
50.601 Purpose.
50.602 Applicability.
50.603 Definitions.
50.604 Responsibilities of Institutions regarding Investigator financial conflicts of interest.
50.605 Management and reporting of financial conflicts of interest.
50.606 Remedies.
50.607 Other HHS regulations that apply.

Subpart F—Promoting Objectivity in Research

Authority: 42 U.S.C. 216, 289b–1, 299c–4; Sec. 219, Tit. II, Div. D, Pub. L. 111–117, 123 Stat. 3034.

§ 50.601 Purpose.

This subpart promotes objectivity in research by establishing standards that provide a reasonable expectation that

the design, conduct, and reporting of research funded under PHS grants or cooperative agreements is free from bias resulting from Investigator financial conflicts of interest.

§ 50.602 Applicability.

This subpart is applicable to each Institution that is applying for, or that receives, PHS research funding by means of a grant or cooperative agreement and, through the implementation of this subpart by the Institution, to each Investigator participating in such research. In those few cases where an individual, rather than an Institution, is applying for, or receives, PHS research funding, PHS Awarding Components will make case-by-case determinations on the steps to be taken, consistent with this subpart, to provide a reasonable expectation that the design, conduct, and reporting of the research will be free from bias resulting from a financial conflict of interest of the individual.

§ 50.603 Definitions.

As used in this subpart:

Disclosure of significant financial interests means an Investigator's disclosure of significant financial interests to an Institution.

FCOI report means an Institution's report of a financial conflict of interest to a PHS Awarding Component.

Financial conflict of interest means a significant financial interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research.

Financial interest means anything of monetary value or potential monetary value.

HHS means the United States Department of Health and Human Services, and any components of the Department to which the authority involved may be delegated.

Institution means any domestic or foreign, public or private, entity or organization (excluding a Federal agency) that is applying for, or that receives, PHS research funding.

Institutional responsibilities means an Investigator's professional responsibilities on behalf of the Institution including, but not limited to, activities such as research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards.

Investigator means the PD/PI and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the PHS, or proposed for such funding, including persons who are subgrantees, contractors, collaborators, or consultants.

Manage means to take action to address a financial conflict of interest, which includes reducing or eliminating the financial conflict of interest, to ensure that the design, conduct, or reporting of research is free from bias or the appearance of bias.

PD/PI means a project director or principal investigator of a PHS-funded research project.

PHS means the Public Health Service, an operating division of the U.S. Department of Health and Human Services, and any components of the PHS to which the authority involved may be delegated, including the National Institutes of Health.

PHS Awarding Component means the organizational unit of the PHS that funds the research that is subject to this subpart.

Public Health Service Act or *PHS Act* means the statute codified at 42 U.S.C. 201 *et seq.*

Research means a systematic investigation designed to develop or contribute to generalizable knowledge relating broadly to public health, including behavioral and social-sciences research. The term encompasses basic and applied research and product development. As used in this subpart, the term includes any such activity for which research funding is available from a PHS Awarding Component through a grant, cooperative agreement, or contract, whether authorized under the PHS Act or other statutory authority, such as a research grant, career development award, center grant, individual fellowship award, infrastructure award, institutional training grant, program project, or research resources award.

Significant financial interest means, except as otherwise specified in paragraph (1) of this definition:

(1) A financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:

(i) With regard to any publicly traded entity, a *significant financial interest* exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (*e.g.,* consulting fees, honoraria, paid authorship, travel reimbursement); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value;

(ii) With regard to any non-publicly traded entity, a *significant financial interest* exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (*e.g.,* stock, stock option, or other ownership interest); or

(iii) Intellectual property rights (*e.g.,* patents, copyrights), royalties from such rights, and agreements to share in royalties related to such rights.

(2) The term *significant financial interest* does not include the following types of financial interests: Salary, royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed or otherwise appointed by the Institution; any ownership interest in the Institution held by the Investigator, if the Institution is a commercial or for-profit organization; income from seminars, lectures, or teaching engagements sponsored by a federal, state, or local government agency, or an institution of higher education as defined at 20 U.S.C. 1001(a); or income from service on advisory committees or review panels for a federal, state, or local government agency, or an institution of higher education as defined at 20 U.S.C. 1001(a).

§ 50.604 Responsibilities of Institutions regarding Investigator financial conflicts of interest.

Each Institution shall:

(a) Maintain an up-to-date, written, enforced policy on financial conflicts of interest that complies with this subpart, and make such policy available via a publicly accessible Web site. If an Institution maintains a policy on financial conflicts of interest that includes standards that are more stringent than this subpart (*e.g.,* that require a more extensive disclosure of financial interests), the Institution shall adhere to its policy and shall provide FCOI reports regarding identified financial conflicts of interest to the PHS Awarding Component in accordance with the Institution's own standards.

(b) Inform each Investigator of the Institution's policy on financial conflicts of interest, the Investigator's responsibilities regarding disclosure of significant financial interests, and of

these regulations, and require each Investigator to complete training regarding same prior to engaging in PHS-funded research and, thereafter, at least once every two years.

(c) If the Institution carries out the PHS-funded research through a subrecipient (*e.g.,* subgrantee, contractor, or collaborator):

(1) Incorporate as part of a written agreement with the subrecipient legally enforceable terms that establish whether the financial conflicts of interest policy of the awardee Institution or that of the subrecipient applies to the subrecipient's Investigators.

(i) If the subrecipient's financial conflicts of interest policy applies to subrecipient Investigators, the subrecipient shall certify as part of the agreement that its policy complies with this subpart. If the subrecipient cannot provide such certification, the agreement shall state that subrecipient Investigators are subject to the financial conflicts of interest policy of the awardee Institution;

(ii) If the subrecipient's financial conflicts of interest policy applies to subrecipient Investigators, the agreement shall specify time period(s) for the subrecipient to report all identified financial conflicts of interest to the awardee Institution. Such time period(s) shall be sufficient to enable the awardee Institution to provide timely FCOI reports, as necessary, to the PHS;

(iii) If subrecipient Investigators are subject to the awardee Institution's financial conflicts of interest policy, the agreement shall specify time period(s) for the subrecipient to submit all Investigator disclosures of significant financial interests to the awardee Institution. Such time period(s) shall be sufficient to enable the awardee Institution to comply timely with its review, management, and reporting obligations under this subpart.

(2) Provide FCOI reports to the PHS regarding all financial conflicts of interest of all subrecipient Investigators consistent with this subpart.

(d) Designate an institutional official(s), to solicit and review disclosures of significant financial interests from each Investigator who is planning to participate in the PHS-funded research.

(e)(1) Require that each Investigator who is planning to participate in the PHS-funded research disclose to the Institution's designated official(s) the Investigator's significant financial interests (and those of the Investigator's spouse and dependent children).

(2) Require that each Investigator who is participating in the PHS-funded research submit an updated disclosure of significant financial interests at least annually during the period of the award. Such disclosure shall include any information that was not disclosed initially to the Institution pursuant to paragraph (e)(1) of this section, or in a subsequent disclosure of significant financial interests, and shall include updated information regarding any previously-disclosed significant financial interest (*e.g.,* the updated value of a previously-disclosed equity interest).

(3) Require that each Investigator who is participating in the PHS-funded research submit an updated disclosure of significant financial interests within thirty days of acquiring a new significant financial interest (*e.g.,* through purchase, marriage, or inheritance).

(f) Provide guidelines consistent with this subpart for the designated institutional officials to determine whether an Investigator's significant financial interest is related to PHS-funded research and, if so related, whether the significant financial interest is a financial conflict of interest. An Investigator's significant financial interest is related to PHS-funded research when the Institution, through its designated officials, reasonably determines that the significant financial interest: Appears to be affected by the PHS-funded research; or is in an entity whose financial interest appears to be affected by the research. A financial conflict of interest exists when the Institution, through its designated officials, reasonably determines that the significant financial interest could directly and significantly affect the design, conduct, or reporting of the PHS-funded research.

(g) Take such actions as necessary to manage financial conflicts of interest, including any financial conflicts of a subrecipient Investigator pursuant to paragraph (c) of this section. Management of an identified financial conflict of interest requires development and implementation of a management plan and, if necessary, a mitigation plan pursuant to § 50.605(a).

(h) Provide initial and ongoing FCOI reports to the PHS as required pursuant to § 50.605(b).

(i) Maintain records relating to all Investigator disclosures of financial interests and the Institution's review of, or response to, such disclosures (whether or not a disclosure resulted in the Institution's determination of a financial conflict of interest), for at least three years from the date of submission of the final expenditures report or, where applicable, from other dates specified in 45 CFR 74.53(b) for different situations.

(j) Establish adequate enforcement mechanisms and provide for employee sanctions or other administrative actions to ensure Investigator compliance as appropriate.

(k) Certify, in each application for funding to which this subpart applies, that the Institution:

(1) Has in effect at that Institution an up-to-date, written, and enforced administrative process to identify and manage financial conflicts of interest with respect to all research projects for which funding is sought or received from the PHS;

(2) Shall promote and enforce Investigator compliance with this subpart's requirements including those pertaining to disclosure of significant financial interests;

(3) Shall manage financial conflicts of interest and provide initial and ongoing FCOI reports to the PHS consistent with this subpart;

(4) Agrees to make information available, promptly upon request, to the HHS relating to any Investigator disclosure of financial interests and the Institution's review of, or response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of a financial conflict of interest; and

(5) Shall fully comply with the requirements of this subpart.

§ 50.605 Management and reporting of financial conflicts of interest.

(a) Management of financial conflicts of interest.

(1) Prior to the Institution's expenditure of any funds under a PHS-funded research project, the designated officials of an Institution shall, consistent with § 50.604(f): Review all Investigator disclosures of significant financial interests; determine whether any significant financial interests relate to PHS-funded research; determine whether a financial conflict of interest exists; and, if so, develop and implement a management plan that shall specify the actions that have been, and shall be, taken to manage such financial conflict of interest. Examples of conditions or restrictions that might be imposed to manage a financial conflict of interest include, but are not limited to:

(i) Public disclosure of financial conflicts of interest (*e.g.,* when presenting or publishing the research);

(ii) For research projects involving human subjects research, disclosure of financial conflicts of interest directly to participants;

(iii) Appointment of an independent monitor capable of taking measures to

protect the design, conduct, and reporting of the research against bias, or the appearance of bias, resulting from the financial conflict of interest;

(iv) Modification of the research plan;

(v) Change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research;

(vi) Reduction or elimination of the financial interest (*e.g.,* sale of an equity interest); or

(vii) Severance of relationships that create actual or potential financial conflicts.

(2) Whenever, in the course of an ongoing PHS-funded research project, a new Investigator participating in the research project discloses a significant financial interest or an existing Investigator discloses a new significant financial interest to the Institution, the designated officials of the Institution shall, within sixty days: Review the disclosure of significant financial interests; determine whether it is related to PHS-funded research; determine whether a financial conflict of interest exists; and, if so, implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage such financial conflict of interest. Depending on the nature of the significant financial interest, an Institution may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date of disclosure and the completion of the Institution's review.

(3) Whenever an Institution identifies a significant financial interest that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by the Institution during an ongoing PHS-funded research project (*e.g.,* was not timely reviewed or reported by a subrecipient), the designated officials shall, within sixty days: Review the significant financial interest; determine whether it is related to PHS-funded research; determine whether a financial conflict of interest exists; and, if so:

(i) Implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage such financial conflict of interest going forward;

(ii) Implement, on at least an interim basis, a mitigation plan which shall include review and determination as to whether any PHS-funded research, or portion thereof, conducted prior to the identification and management of the financial conflict of interest was biased in the design, conduct, or reporting of such research. Depending on the nature of the significant financial interest, an Institution may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date that the significant financial interest is identified and the completion of the Institution's review.

(4) Whenever an Institution implements a management plan pursuant to this subpart, the Institution shall monitor Investigator compliance with the management plan on an ongoing basis until the completion of the PHS-funded research project.

(5)(i) Prior to the Institution's expenditure of any funds under a PHS-funded research project, the Institution shall make available via a publicly accessible Web site information concerning any significant financial interest disclosed to the Institution that meets the following three criteria:

(A) The significant financial interest was disclosed and is still held by the PD/PI or any other Investigator who has been identified by the Institution as senior/key personnel for the PHS-funded research project in the grant application, contract proposal, contract, progress report, or other required report submitted to the PHS;

(B) The Institution determines that the significant financial interest is related to the PHS-funded research; and

(C) The Institution determines that the significant financial interest is a financial conflict of interest.

(ii) The information that the Institution makes available via a publicly accessible Web site shall include, at a minimum, the following: The Investigator's name; the Investigator's position with respect to the research project; the nature of the significant financial interest; and the approximate dollar value of the significant financial interest (dollar ranges are permissible: Less than $20,000; less than $50,000; less than $100,000; less than or equal to $250,000; greater than $250,000), or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value.

(iii) The information that the Institution makes available via a publicly accessible Web site shall be updated at least annually. In addition, the Institution shall update the Web site within sixty days of the Institution's receipt or identification of information concerning any additional significant financial interest that was not previously disclosed by the PD/PI or senior/key personnel for the PHS-funded research project, or upon the disclosure of a significant financial interest by a new PD/PI or new senior/key personnel for the PHS-funded research project, if the Institution determines that the significant financial interest is related to the PHS-funded research and is a financial conflict of interest.

(iv) Information concerning the significant financial interests of an individual subject to this paragraph (a)(5) shall remain available via the Institution's publicly accessible Web site for at least five years from the date that the information was most recently updated.

(6) In addition to the types of financial conflicts of interest as defined in this subpart that must be managed pursuant to this section, an Institution may require the management of other financial conflicts of interest, as the Institution deems appropriate.

(b) Reporting of financial conflicts of interest.

(1) Prior to the Institution's expenditure of any funds under a PHS-funded research project, the Institution shall provide to the PHS Awarding Component a FCOI report regarding any Investigator significant financial interest found by the Institution to be conflicting and ensure that the Institution has implemented a management plan in accordance with this subpart.

(2) For any significant financial interest that the Institution identifies as conflicting subsequent to the Institution's initial FCOI report during an ongoing PHS-funded research project (*e.g.,* upon the participation of a new Investigator in the research project), the Institution shall provide to the PHS Awarding Component, within sixty days, a FCOI report regarding the financial conflict of interest and ensure that the Institution has implemented a management plan in accordance with this subpart. Where such FCOI report involves a significant financial interest that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by the Institution (*e.g.,* was not timely reviewed or reported by a subrecipient), the Institution shall also provide with its FCOI report the mitigation plan implemented by the Institution to determine whether any PHS-funded research, or portion thereof, conducted prior to the identification and management of the financial conflict of interest was biased in the design, conduct, or reporting of such research.

(3) Any FCOI report required under paragraphs (b)(1) or (b)(2) of this section shall include sufficient information to enable the PHS Awarding Component to

understand the nature and extent of the financial conflict, and to assess the appropriateness of the Institution's management plan. Elements of the FCOI report shall include, but are not limited to the following:

(i) Project/Contract number;

(ii) PD/PI or Contact PD/PI if a multiple PD/PI model is used;

(iii) Name of the Investigator with the financial conflict of interest;

(iv) Nature of the financial interest (*e.g.,* equity, consulting fee, travel reimbursement, honorarium);

(v) Value of the financial interest (dollar ranges are permissible: $0–$4,999; $5,000–$9,999; $10,000–$19,999; amounts between $20,000–$100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000), or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value;

(vi) A description of how the financial interest relates to the PHS-funded research and the basis for the Institution's determination that the financial interest conflicts with such research;

(vii) A description of the key elements of the Institution's management plan, including:

(A) The role and function of the conflicted Investigator in the research project;

(B) The rationale for including the conflicted Investigator in the research project;

(C) The conditions of the management plan;

(D) How the management plan will safeguard objectivity in the research project;

(E) Confirmation of the Investigator's agreement to the management plan;

(F) How the management plan will be monitored to ensure Investigator compliance;

(G) Other information as needed.

(4) For any financial conflict of interest previously reported by the Institution with regard to an ongoing PHS-funded research project, the Institution shall provide an annual FCOI report that addresses the status of the financial conflict of interest and any changes to the management plan to the PHS Awarding Component for the duration of the PHS-funded research project. The annual FCOI report shall specify whether the financial conflict is still being managed or explain why the financial conflict of interest no longer exists. The Institution shall provide annual FCOI reports to the PHS Awarding Component for the duration of the project period (including extensions with or without funds) in the time and manner specified by the PHS Awarding Component.

(5) In addition to the types of financial conflicts of interest as defined in this subpart that must be reported pursuant to this section, an Institution may require the reporting of other financial conflicts of interest, as the Institution deems appropriate.

§ 50.606 Remedies.

(a) If the failure of an Investigator to comply with an Institution's financial conflicts of interest policy or a financial conflict of interest management plan appears to have biased the design, conduct, or reporting of the PHS-funded research, the Institution shall promptly notify the PHS Awarding Component of the corrective action taken or to be taken. The PHS Awarding Component will consider the situation and, as necessary, take appropriate action, or refer the matter to the Institution for further action, which may include directions to the Institution on how to maintain appropriate objectivity in the funded project.

(b) The HHS may inquire at any time (*i.e.,* before, during, or after award) into any Investigator disclosure of financial interests and the Institution's review of, or response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of a financial conflict of interest. An Institution is required to submit, or permit on site review of, all records pertinent to compliance with this subpart. To the extent permitted by law, HHS will maintain the confidentiality of all records of financial interests. On the basis of its review of records or other information that may be available, the PHS Awarding Component may decide that a particular financial conflict of interest will bias the objectivity of the PHS-funded research to such an extent that further corrective action is needed or that the Institution has not managed the financial conflict of interest in accordance with this subpart. The PHS Awarding Component may determine that imposition of special award conditions under 45 CFR 74.14 or suspension of funding or other enforcement action under 45 CFR 74.62 is necessary until the matter is resolved.

(c) In any case in which the HHS determines that a PHS-funded project of clinical research whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment has been designed, conducted, or reported by an Investigator with a financial conflict of interest that was not managed or reported by the Institution as required by this subpart, the Institution shall require the Investigator involved to disclose the financial conflict of interest in each public presentation of the results of the research and to request an addendum to previously published presentations.

§ 50.607 Other HHS regulations that apply.

Several other regulations and policies apply to this subpart. They include, but are not necessarily limited to:

2 CFR Part 376—Nonprocurement Debarment and Suspension (HHS)

42 CFR Part 50, Subpart D—Public Health Service Grant Appeals Procedure

45 CFR Part 16—Procedures of the Departmental Grant Appeals Board

45 CFR Part 74—Uniform Administrative Requirements for Awards and Subawards to Institutions of Higher Education, Hospitals, Other Nonprofit Organizations, and Commercial Organizations

45 CFR Part 79—Program Fraud Civil Remedies

45 CFR Part 92—Uniform Administrative Requirements for Grants and Cooperative Agreements to State, Local, and Tribal Governments

TITLE 45—PUBLIC WELFARE

2. Revise Part 94 to read as follows:

PART 94—RESPONSIBLE PROSPECTIVE CONTRACTORS

Sec.

94.1 Purpose.
94.2 Applicability.
94.3 Definitions.
94.4 Responsibilities of Institutions regarding Investigator financial conflicts of interest.
94.5 Management and reporting of financial conflicts of interest.
94.6 Remedies.

Authority: 42 U.S.C. 216, 289b–1, 299c–4.

§ 94.1 Purpose.

This part promotes objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct, and reporting of research performed under PHS contracts is free from bias resulting from Investigator financial conflicts of interest.

§ 94.2 Applicability.

This part is applicable to each Institution that solicits, or that receives, PHS research funding by means of a contract and, through the implementation of this part by the Institution, to each Investigator participating in such research.

§ 94.3 Definitions.

As used in this part:

Contractor means an entity that provides property or services under contract for the direct benefit or use of the Federal Government.

Disclosure of significant financial interests means an Investigator's disclosure of significant financial interests to an Institution.

FCOI report means an Institution's report of a financial conflict of interest to a PHS Awarding Component.

Financial conflict of interest means a significant financial interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research.

Financial interest means anything of monetary value or potential monetary value.

HHS means the United States Department of Health and Human Services, and any components of the Department to which the authority involved may be delegated.

Institution means any domestic or foreign, public or private, entity or organization (excluding a Federal agency) that solicits, or that receives, PHS research funding.

Institutional responsibilities means an Investigator's professional responsibilities on behalf of the Institution including, but not limited to, activities such as research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards.

Investigator means the PD/PI and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the PHS, or proposed for such funding, including persons who are subcontractors, collaborators, or consultants.

Manage means to take action to address a financial conflict of interest, which includes reducing or eliminating the financial conflict of interest, to ensure that the design, conduct, or reporting of research is free from bias or the appearance of bias.

PD/PI means a project director or principal investigator of a PHS-funded research project.

PHS means the Public Health Service, an operating division of the U.S. Department of Health and Human Services, and any components of the PHS to which the authority involved may be delegated, including the National Institutes of Health.

PHS Awarding Component means the organizational unit of the PHS that funds the research that is subject to this subpart.

Public Health Service Act or *PHS Act* means the statute codified at 42 U.S.C. 201 *et seq.*

Research means a systematic investigation designed to develop or contribute to generalizable knowledge relating broadly to public health, including behavioral and social-sciences research. The term encompasses basic and applied research and product development. As used in this part, the term includes any such activity for which research funding is available from a PHS Awarding Component through a grant, cooperative agreement, or contract, whether authorized under the PHS Act or other statutory authority, such as a research grant, career development award, center grant, individual fellowship award, infrastructure award, institutional training grant, program project, or research resources award.

Significant financial interest means, except as otherwise specified in this definition:

(1) A financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:

(i) With regard to any publicly traded entity, a *significant financial interest* exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (*e.g.,* consulting fees, honoraria, paid authorship, travel reimbursement); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value;

(ii) With regard to any non-publicly traded entity, a *significant financial interest* exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (*e.g.,* stock, stock option, or other ownership interest); or

(iii) Intellectual property rights (*e.g.,* patents, copyrights), royalties from such rights, and agreements to share in royalties related to such rights.

(2) The term *significant financial interest* does not include the following types of financial interests: Salary, royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed or otherwise appointed by the Institution; any ownership interest in the Institution held by the Investigator, if the Institution is a commercial or for-profit organization; income from seminars, lectures, or teaching engagements sponsored by a federal, state, or local government agency, or an institution of higher education as defined at 20 U.S.C. 1001(a); or income from service on advisory committees or review panels for a federal, state, or local government agency, or an institution of higher education as defined at 20 U.S.C. 1001(a).

§ 94.4 Responsibilities of Institutions regarding Investigator financial conflicts of interest.

Each Institution shall:

(a) Maintain an up-to-date, written, enforced policy on financial conflicts of interest that complies with this part, and make such policy available via a publicly accessible Web site. If an Institution maintains a policy on financial conflicts of interest that includes standards that are more stringent than this part (*e.g.,* that require a more extensive disclosure of financial interests), the Institution shall adhere to its policy and shall provide FCOI reports regarding identified financial conflicts of interest to the PHS Awarding Component in accordance with the Institution's own standards.

(b) Inform each Investigator of the Institution's policy on financial conflicts of interest, the Investigator's responsibilities regarding disclosure of significant financial interests, and of these regulations, and require each Investigator to complete training regarding same prior to engaging in PHS-funded research and, thereafter, at least once every two years.

(c) If the Institution carries out the PHS-funded research through a subrecipient (*e.g.,* subcontractor or collaborator):

(1) Incorporate as part of a written agreement with the subrecipient legally enforceable terms that establish whether the financial conflicts of interest policy of the awardee Institution or that of the subrecipient applies to the subrecipient's Investigators.

(i) If the subrecipient's financial conflicts of interest policy applies to subrecipient Investigators, the subrecipient shall certify as part of the agreement that its policy complies with this part. If the subrecipient cannot

provide such certification, the agreement shall state that subrecipient Investigators are subject to the financial conflicts of interest policy of the awardee Institution;

(ii) If the subrecipient's financial conflicts of interest policy applies to subrecipient Investigators, the agreement shall specify time period(s) for the subrecipient to report all identified financial conflicts of interest to the awardee Institution. Such time period(s) shall be sufficient to enable the awardee Institution to provide timely FCOI reports, as necessary, to the PHS;

(iii) If subrecipient Investigators are subject to the awardee Institution's financial conflicts of interest policy, the agreement shall specify time period(s) for the subrecipient to submit all Investigator disclosures of significant financial interests to the awardee Institution. Such time period(s) shall be sufficient to enable the awardee Institution to comply timely with its review, management, and reporting obligations under this part.

(2) Provide FCOI reports to the PHS regarding all financial conflicts of interest of all subrecipient Investigators consistent with this part.

(d) Designate an institutional official(s) to solicit and review disclosures of significant financial interests from each Investigator who is planning to participate in the PHS-funded research.

(e)(1) Require that each Investigator who is planning to participate in the PHS-funded research disclose to the Institution's designated official(s) the Investigator's significant financial interests (and those of the Investigator's spouse and dependent children).

(2) Require that each Investigator who is participating in the PHS-funded research submit an updated disclosure of significant financial interests at least annually during the period of the award. Such disclosure shall include any information that was not disclosed initially to the Institution pursuant to paragraph (e)(1) of this section, or in a subsequent disclosure of significant financial interests, and shall include updated information regarding any previously-disclosed significant financial interest (*e.g.,* the updated value of a previously-disclosed equity interest).

(3) Require that each Investigator who is participating in the PHS-funded research submit an updated disclosure of significant financial interests within thirty days of acquiring a new significant financial interest (*e.g.,* through purchase, marriage, or inheritance).

(f) Provide guidelines consistent with this part for the designated institutional officials to determine whether an Investigator's significant financial interest is related to PHS-funded research and, if so related, whether the significant financial interest is a financial conflict of interest. An Investigator's significant financial interest is related to PHS-funded research when the Institution, through its designated officials, reasonably determines that the significant financial interest: Appears to be affected by the PHS-funded research; or is in an entity whose financial interest appears to be affected by the research. A financial conflict of interest exists when the Institution, through its designated officials, reasonably determines that the significant financial interest could directly and significantly affect the design, conduct, or reporting of the PHS-funded research.

(g) Take such actions as necessary to manage financial conflicts of interest, including any financial conflicts of a subrecipient Investigator pursuant to paragraph (c) of this section. Management of an identified financial conflict of interest requires development and implementation of a management plan and, if necessary, a mitigation plan pursuant to § 94.5(a).

(h) Provide initial and ongoing FCOI reports to the PHS as required pursuant to § 94.5(b).

(i) Maintain records relating to all Investigator disclosures of financial interests and the Institution's review of, or response to, such disclosures (whether or not a disclosure resulted in the Institution's determination of a financial conflict of interest), for at least three years from the date of final payment or, where applicable, for the time periods specified in 48 CFR part 4, subpart 4.7.

(j) Establish adequate enforcement mechanisms and provide for employee sanctions or other administrative actions to ensure Investigator compliance as appropriate.

(k) Certify, in each contract proposal to which this part applies, that the Institution:

(1) Has in effect at that Institution an up-to-date, written, and enforced administrative process to identify and manage financial conflicts of interest with respect to all research projects for which funding is sought or received from the PHS;

(2) Shall promote and enforce Investigator compliance with this part's requirements including those pertaining to disclosure of significant financial interests;

(3) Shall manage financial conflicts of interest and provide initial and ongoing FCOI reports to the PHS consistent with this part;

(4) Agrees to make information available, promptly upon request, to the HHS relating to any Investigator disclosure of financial interests and the Institution's review of, or response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of a financial conflict of interest; and

(5) Shall fully comply with the requirements of this part.

§ 94.5 Management and reporting of financial conflicts of interest.

(a) Management of financial conflicts of interest.

(1) Prior to the Institution's expenditure of any funds under a PHS-funded research project, the designated officials of an Institution shall, consistent with § 94.4(f): Review all Investigator disclosures of significant financial interests; determine whether any significant financial interests relate to PHS-funded research; determine whether a financial conflict of interest exists; and, if so, develop and implement a management plan that shall specify the actions that have been, and shall be, taken to manage such financial conflict of interest. Examples of conditions or restrictions that might be imposed to manage a financial conflict of interest include, but are not limited to:

(i) Public disclosure of financial conflicts of interest (*e.g.,* when presenting or publishing the research);

(ii) For research projects involving human subjects research, disclosure of financial conflicts of interest directly to participants;

(iii) Appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of the research against bias, or the appearance of bias, resulting from the financial conflict of interest;

(iv) Modification of the research plan;

(v) Change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research;

(vi) Reduction or elimination of the financial interest (*e.g.,* sale of an equity interest); or

(vii) Severance of relationships that create actual or potential financial conflicts.

(2) Whenever, in the course of an ongoing PHS-funded research project, a new Investigator participating in the research project discloses a significant financial interest or an existing Investigator discloses a new significant

financial interest to the Institution, the designated officials of the Institution shall, within sixty days: Review the disclosure of significant financial interests; determine whether it is related to PHS-funded research; determine whether a financial conflict of interest exists; and, if so, implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage such financial conflict of interest. Depending on the nature of the significant financial interest, an Institution may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date of disclosure and the completion of the Institution's review.

(3) Whenever an Institution identifies a significant financial interest that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by the Institution during an ongoing PHS-funded research project (*e.g.,* was not timely reviewed or reported by a subrecipient), the designated officials shall, within sixty days: Review the significant financial interest; determine whether it is related to PHS-funded research; determine whether a financial conflict of interest exists; and, if so:

(i) Implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage such financial conflict of interest going forward;

(ii) Implement, on at least an interim basis, a mitigation plan which shall include review and determination as to whether any PHS-funded research, or portion thereof, conducted prior to the identification and management of the financial conflict of interest was biased in the design, conduct, or reporting of such research. Depending on the nature of the significant financial interest, an Institution may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date that the significant financial interest is identified and the completion of the Institution's review.

(4) Whenever an Institution implements a management plan pursuant to this part, the Institution shall monitor Investigator compliance with the management plan on an ongoing basis until the completion of the PHS-funded research project.

(5)(i) Prior to the Institution's expenditure of any funds under a PHS-funded research project, the Institution shall make available via a publicly accessible Web site information concerning any significant financial interest disclosed to the Institution that meets the following three criteria:

(A) The significant financial interest was disclosed and is still held by the PD/PI or any other Investigator who has been identified by the Institution as senior/key personnel for the PHS-funded research project in the grant application, contract proposal, contract, progress report, or other required report submitted to the PHS;

(B) The Institution determines that the significant financial interest is related to the PHS-funded research; and

(C) The Institution determines that the significant financial interest is a financial conflict of interest.

(ii) The information that the Institution makes available via a publicly accessible Web site shall include, at a minimum, the following: The Investigator's name; the Investigator's position with respect to the research project; the nature of the significant financial interest; and the approximate dollar value of the significant financial interest (dollar ranges are permissible: Less than $20,000; less than $50,000; less than $100,000; less than or equal to $250,000; greater than $250,000), or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value.

(iii) The information that the Institution makes available via a publicly accessible Web site shall be updated at least annually. In addition, the Institution shall update the Web site within sixty days of the Institution's receipt or identification of information concerning any additional significant financial interest that was not previously disclosed by the PD/PI or senior/key personnel for the PHS-funded research project, or upon the disclosure of a significant financial interest by a new PD/PI or new senior/key personnel for the PHS-funded research project, if the Institution determines that the significant financial interest is related to the PHS-funded research and is a financial conflict of interest.

(iv) Information concerning the significant financial interests of an individual subject to this paragraph (a)(5) of this section shall remain available via the Institution's publicly accessible Web site for at least five years from the date that the information was most recently updated.

(6) In addition to the types of financial conflicts of interest as defined in this part that must be managed pursuant to this section, an Institution may require the management of other financial conflicts of interest, as the Institution deems appropriate.

(b) Reporting of financial conflicts of interest.

(1) Prior to the Institution's expenditure of any funds under a PHS-funded research project, the Institution shall provide to the PHS Awarding Component a FCOI report regarding any Investigator significant financial interest found by the Institution to be conflicting and ensure that the Institution has implemented a management plan in accordance with this part.

(2) For any significant financial interest that the Institution identifies as conflicting subsequent to the Institution's initial FCOI report during an ongoing PHS-funded research project (*e.g.,* upon the participation of a new Investigator in the research project), the Institution shall provide to the PHS Awarding Component, within sixty days, a FCOI report regarding the financial conflict of interest and ensure that the Institution has implemented a management plan in accordance with this part. Where such FCOI report involves a significant financial interest that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by the Institution (*e.g.,* was not timely reviewed or reported by a subrecipient), the Institution shall also provide with its FCOI report the mitigation plan implemented by the Institution to determine whether any PHS-funded research, or portion thereof, conducted prior to the identification and management of the financial conflict of interest was biased in the design, conduct, or reporting of such research.

(3) Any FCOI report required under paragraphs (b)(1) or (b)(2) of this section shall include sufficient information to enable the PHS Awarding Component to understand the nature and extent of the financial conflict, and to assess the appropriateness of the Institution's management plan. Elements of the FCOI report shall include, but are not limited to the following:

(i) Project/Contract number;

(ii) PD/PI or Contact PD/PI if a multiple PD/PI model is used;

(iii) Name of the Investigator with the financial conflict of interest;

(iv) Nature of the financial interest (*e.g.,* equity, consulting fee, travel reimbursement, honorarium);

(v) Value of the financial interest (dollar ranges are permissible: $0–$4,999; $5,000–$9,999; $10,000–$19,999; amounts between $20,000–$100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000), or a statement that the

interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value;

(vi) A description of how the financial interest relates to the PHS-funded research and the basis for the Institution's determination that the financial interest conflicts with such research;

(vii) A description of the key elements of the Institution's management plan, including:

(A) The role and function of the conflicted Investigator in the research project;

(B) The rationale for including the conflicted Investigator in the research project;

(C) The conditions of the management plan;

(D) How the management plan will safeguard objectivity in the research project;

(E) Confirmation of the Investigator's agreement to the management plan;

(F) How the management plan will be monitored to ensure Investigator compliance;

(G) Other information as needed.

(4) For any financial conflict of interest previously reported by the Institution with regard to an ongoing PHS-funded research project, the Institution shall provide an annual FCOI report that addresses the status of the financial conflict of interest and any changes to the management plan to the PHS Awarding Component for the duration of the PHS-funded research project. The annual FCOI report shall specify whether the financial conflict is still being managed or explain why the financial conflict of interest no longer exists. The Institution shall provide annual FCOI reports to the PHS Awarding Component for the duration of the project period (including extensions with or without funds) in the time and manner specified by the PHS Awarding Component.

(5) In addition to the types of financial conflicts of interest as defined in this part that must be reported pursuant to this section, an Institution may require the reporting of other financial conflicts of interest, as the Institution deems appropriate.

§ 94.6 Remedies.

(a) If the failure of an Investigator to comply with an Institution's financial conflicts of interest policy or a financial conflict of interest management plan appears to have biased the design, conduct, or reporting of the PHS-funded research, the Institution shall promptly notify the PHS Awarding Component of the corrective action taken or to be taken. The PHS Awarding Component will consider the situation and, as necessary, take appropriate action, or refer the matter to the Institution for further action, which may include directions to the Institution on how to maintain appropriate objectivity in the funded project.

(b) The HHS may inquire at any time (*i.e.,* before, during, or after award) into any Investigator disclosure of financial interests and the Institution's review of, or response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of a financial conflict of interest. An Institution is required to submit, or permit on site review of, all records pertinent to compliance with this part. To the extent permitted by law, HHS will maintain the confidentiality of all records of financial interests. On the basis of its review of records or other information that may be available, the PHS Awarding Component may decide that a particular financial conflict of interest will bias the objectivity of the PHS-funded research to such an extent that further corrective action is needed or that the Institution has not managed the financial conflict of interest in accordance with this part. The PHS Awarding Component may determine that issuance of a Stop Work Order by the Contracting Officer or other enforcement action is necessary until the matter is resolved.

(c) In any case in which the HHS determines that a PHS-funded project of clinical research whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment has been designed, conducted, or reported by an Investigator with a financial conflict of interest that was not managed or reported by the Institution as required by this part, the Institution shall require the Investigator involved to disclose the financial conflict of interest in each public presentation of the results of the research and to request an addendum to previously published presentations.

Dated: March 26, 2010.

Francis S. Collins,

Director, National Institutes of Health.

Approved: April 14, 2010.

Kathleen Sebelius,

Secretary.

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