



# FEDERAL REGISTER

---

Vol. 76

Thursday,

No. 165

August 25, 2011

---

Part IV

## Department of Health and Human Services

---

42 CFR Part 50

45 CFR Part 94

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

**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:** Final rule.

**SUMMARY:** This final rule implements changes to the regulations on the Responsibility of Applicants for Promoting Objectivity in Research for which Public Health Service 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, led to changes that expand and add transparency to Investigators' disclosure of Significant Financial Interests (SFIs), enhance regulatory compliance and effective institutional oversight and management of Investigators' financial conflicts of interests, as well as increase the Department of Health and Human Services' (HHS) compliance oversight.

**DATES:** *Effective Date:* This final rule is effective as of September 26, 2011.

*Compliance Date:* An Institution applying for or receiving PHS funding from a grant, cooperative agreement, or contract that is covered by this rule must be in full compliance with all of the regulatory requirements herein:

- No later than August 24, 2012; and
- Immediately upon making its institutional Financial Conflict of Interest (FCOI) policy publicly accessible as described herein.

In the interim, Institutions should continue to comply with the 1995 regulations and report Investigator FCOIs to the Public Health Service (PHS) Awarding Component as required in the 1995 regulations.

**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](mailto:jm40z@nih.gov), concerning questions about the rulemaking process; and Dr. Sally Rockey, NIH Deputy Director for Extramural Research, concerning substantive questions about the rule, e-mail [FCOICompliance@mail.nih.gov](mailto:FCOICompliance@mail.nih.gov).

**SUPPLEMENTARY INFORMATION:**

**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 1995 regulations), that are designed to promote objectivity in PHS-funded research. The 1995 regulations cover 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 1995 regulations:

- The Institution<sup>1</sup> is responsible for complying with the regulations, including maintaining a written and enforced FCOI policy; managing, reducing, or eliminating identified conflicts; and reporting identified conflicts to the PHS Awarding Component. The reports denote the existence of an FCOI and the Institution's assurance that it has been managed, reduced, or eliminated.
- Investigators<sup>2</sup> are responsible for complying with their Institution's written FCOI policy and for disclosing their SFIs<sup>3</sup> to the Institution.

<sup>1</sup> "Institution" was 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.

<sup>2</sup> "Investigator" was defined under the 1995 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.

<sup>3</sup> "Significant Financial Interest" was defined under the 1995 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.

• Maintaining objectivity in research requires a commitment from Institutions and their Investigators to completely disclose, appropriately review, and robustly manage identified conflicts.

• The PHS Awarding Components<sup>4</sup> are responsible for overseeing institutional compliance with the regulations.

The purpose of the 1995 regulations was 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 the 1995 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<sup>5</sup> 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<sup>6</sup> to 52.8% in a survey conducted in 2007.<sup>7</sup> 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.

Recent studies from several sources have also highlighted the increasing complexity of the financial relationships

<sup>4</sup> "PHS Awarding Component" was defined as an organizational unit of the PHS that funds research that is subject to these regulations. 42 CFR 50.603, 45 CFR 94.3.

<sup>5</sup> Moses H *et al.*, JAMA; 2005;294:1333-1342.

<sup>6</sup> Blumenthal D *et al.*, N Engl J Med; 1996; 335:1734-9.

<sup>7</sup> Zinner DE *et al.*, Health Aff; 2009;28:1814-25.

between biomedical researchers and industry and the possible ramifications of those relationships. For example, a 2008 report by the Association of American Medical Colleges and the Association of American Universities (AAMC/AAU)<sup>8</sup> states: “The promises of translational research, the challenges of technology transfer, and intense expectations at all levels of government that universities and their academic medical centers function as engines of socio-economic development generate new pressures on institutions and their faculty members to expand their relationships and deepen their engagement with industry. These relationships, now encouraged in many forms, may involve financial linkages that are entirely benign but will in other cases carry the potential to create serious conflicts of interest. Moreover, these financial ties are occurring in a context of dramatically increased public sensitivity to and concern with allegations of financial conflicts of interest more broadly in university business transactions and across diverse sectors of industry.” A recent study of the Institute of Medicine (IOM) on Conflict of Interest in Medical Research, Education, and Practice states: “Physicians and researchers must exercise judgment in complex situations that are fraught with uncertainty. Colleagues, patients, students, and the public need to trust that these judgments are not compromised by physicians’ or researchers’ financial ties to pharmaceutical, medical device, and biotechnology companies. Ties with industry are common in medicine. Some have produced important benefits, particularly through research collaborations that improve individual and public health. At the same time, widespread relationships with industry have created significant risks that individual and institutional financial interests may unduly influence professionals’ judgments about the primary interests or goals of medicine. Such conflicts of interest threaten the integrity of scientific investigations, the objectivity of medical education, and the quality of patient care. They may also jeopardize public trust in medicine.”<sup>9</sup> A 2009 report from the HHS Office of Inspector General (OIG)

stated “Vulnerabilities exist at grantee institutions regarding conflicts.”<sup>10</sup>

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, institutional management of financial conflicts, and Federal oversight is required. HHS decided to explore the need for revisions to the 1995 regulations by publishing an Advance Notice of Proposed Rulemaking on May 8, 2009 (74 FR 21610, hereafter “the ANPRM”).

After analyzing public comments, HHS published a Notice of Proposed Rulemaking (75 FR 28688, hereafter “the NPRM”) on May 21, 2010, to amend the 1995 regulations by expanding and adding transparency to Investigators’ disclosure of SFIs, enhancing regulatory compliance and effective institutional oversight and management of Investigators’ financial conflicts of interests, as well as HHS’ compliance oversight.

Major changes to the 1995 regulations proposed in the NPRM included:

- Expanding the scope of the regulations to include SBIR/STTR Phase I applications.
- Amending the definition of SFI to include a de minimis threshold of \$5,000 for disclosure that generally applies to payments and/or equity interests as well as any equity interest in non-publicly traded entities.
- Excluding income from government agencies or Institutions of higher education for seminars, lectures, teaching, or service on advisory or review panels.
- Expanding Investigator disclosure requirements to include SFIs that are related to an Investigator’s institutional responsibilities, with Institutions responsible for determining whether a disclosed SFI relates to the research for which PHS funding is sought and constitutes an FCOI.

• Enhancing the information on an FCOI reported by the Institution to the PHS Awarding Component to include the information required under the 1995 regulations plus the value of the financial interest or a statement that a value cannot be readily determined, the nature of the FCOI, a description of how

the FCOI relates to PHS-funded research, and key elements of the Institution’s management plan.

- Requiring that before spending funds for PHS-supported research, an Institution shall post on a publicly accessible Web site information on SFIs of senior/key personnel that the Institution determines are related to the PHS-funded research and constitute an FCOI.

In addition to these major proposed changes, the NPRM incorporated minor proposed changes that reflect technical updates from the 1995 regulations (*e.g.*, in the reference to authority for the regulations, 42 U.S.C. 299c–4 replaces 42 U.S.C. 299c–3, and, for the regulations for grants and cooperative agreements, we added section 219, Title II, Division D of Public Law 111–117, the Consolidated Appropriations Act 2010), or that reflect efforts to improve the overall clarity and accuracy of the regulations (*e.g.*, the title of the regulations for grants and cooperative agreements was changed to “Promoting Objectivity in Research,” to reinforce the ongoing nature of the obligations under this subpart). The final rule also incorporates such changes.

On July 21, 2010, HHS published a Notice (75 FR 42362, hereafter “the Extension Notice”) extending the 60 day comment period for the NPRM by another 30 days and seeking comment on whether HHS should clarify its authority to enforce compliance with the regulations by Institutions and Investigators, and whether HHS should clarify how the regulations apply in circumstances in which an Investigator or a PHS-funded research project transfers from one Institution to another.

## II. Discussion of General Public Comments

During the 90 day comment period that ended on August 19, 2010, we received 136 unique comments on the NPRM and the Extension Notice. Many respondents were generally supportive of the overall goal of promoting objectivity in biomedical research. A few cited the importance of such objectivity in maintaining the public’s and particularly patients’ trust in treatments, drugs and devices that result from PHS-funded biomedical research. Responses to comments in this section are of a general nature while comments on specific provisions of the NPRM are addressed in the next section.

### *Balancing the Benefits of Relationships With Industry and Possible Conflicts of Interest*

As stated by several respondents, it is important to emphasize that translating

<sup>8</sup>Protecting Patients, Preserving Integrity, Advancing Health: Accelerating the Implementation of COI Policies in Human Subjects Research, A Report of the AAMC-AAU Advisory Committee on Financial Conflicts of Interest in Human Subjects Research, February 2008 p1.

<sup>9</sup>Lo, B & Field, M.J. (Eds.). (2009) *Conflict of interest in medical research, education, and practice*. Washington, DC: National Academies Press. p2.

<sup>10</sup>HHS OIG report OEI-03-07-00700 “How Grantees Manage Financial Conflicts of Interest in Research Funded by the National Institutes of Health”, November 2009 p12.

basic research into clinical application is critical for advancing human health, and this process requires fruitful collaborations among government, academia, and industry. Some respondents were concerned that the revisions to the regulations will have a negative effect on these collaborations and on the translation of research into cures. We want to emphasize that the revisions are not designed to prevent or hinder relationships among government, academia, and industry. Rather, the revisions are aimed at facilitating such relationships by increasing transparency and accountability so that the resulting research is considered objective and in the interest of the public.

Some respondents were concerned that there has not been sufficient research to document an adverse impact of FCOI on the integrity of PHS-funded research, which makes it difficult to substantiate the effectiveness of the proposed measures, and in particular, one commenter questioned the citation of a specific article in the NPRM (“the Wazana paper”) in that regard. While we did not cite a paper by that author in the NPRM, we understand the limitations of the research on this topic. The 1995 regulations were aimed at preventing bias in PHS-funded research, and as such, were intended to be proactive rather than reactive to specific evidence of bias. Nonetheless, over the past few years, there have been several specific allegations of bias among PHS-funded researchers reported in the press. This has led to increased public concern, as evidenced by statements and correspondence from members of Congress and the language in the Department of Health and Human Services Appropriations Act, 2010, to amend the 1995 regulations “for the purpose of strengthening Federal and institutional oversight and identifying enhancements \* \* \*.”<sup>11</sup> And as mentioned above, the 2009 OIG report: *How Grantees Manage Financial Conflicts Of Interest in Research Funded by the National Institutes of Health* found that “Vulnerabilities exist in grantee Institutions’ identification, management, and oversight of financial conflicts of interest.” It is vital that the public have confidence in the objectivity of PHS-funded research. The revised regulations, with their emphasis on increasing transparency and accountability, as well as providing additional information to the PHS Awarding Component, are aimed at doing just that.

Other respondents requested that, given the complexity of the issues

related to management of Investigator FCOI, HHS fund research to address issues related to the implementation of these regulations. As part of our oversight activities, NIH has developed and conducted a number of initiatives and site visits to evaluate institutional FCOI policies for compliance with the Federal regulations and has publicized on-line “Lessons Learned.” NIH found that the most common compliance issues center around the appropriate definition of “Investigator” and Institutional reporting requirements. NIH observed that there was some confusion about receiving disclosures from Investigators who join a project after it has begun, and identifying and reporting FCOI during the project period. Site visits also reaffirmed that education is key in ensuring that Investigators comply with the FCOI requirements by understanding their responsibilities in the process. Therefore, in light of these observations, the definition of “Investigator” has been revised in the final rule to emphasize that Institutions should consider the roles of those involved in research and the degree of independence with which those individuals work.

In addition, the final rule includes a new requirement for Institutions to require each Investigator to complete training related to the FCOI and/or other FCOI-related requirements at least every four years or immediately under designated circumstances. Information and other resources developed by NIH, which will be updated as appropriate, are available as resources for the new regulatory training requirement and can be accessed through the NIH Web site’s Financial Conflict of Interest page at <http://grants.nih.gov/grants/policy/coi/>.

Several respondents requested that the revised regulations apply only to new or competing PHS awards and newly identified FCOIs. We note that many PHS grants, cooperative agreements, and contracts continue for several years and, particularly in the case of grants and cooperative agreements, a new award can be made every year. Therefore, the revised regulations will apply to each grant or cooperative agreement with an issue date of the Notice of Award that is subsequent to the compliance dates of the final rule (including noncompeting continuations) and to solicitations issued and contracts awarded subsequent to the compliance dates of the final rule that are for research. Through their policies, Institutions may choose to apply the revised regulations to all active PHS awards. For example, Institutions may choose, in their FCOI policy, to implement the regulations on

a single date on all PHS-funded awards rather than implementing the regulations sequentially on the specific award date of each individual project.

#### *Beyond Financial Conflicts of Interest*

A few respondents suggested that the regulations should also address non-financial conflicts of interest. While we acknowledge that non-financial conflicts of interest can influence the scientific process, we chose to retain the focus of these regulations on FCOIs because we believe this is a discrete area in which there is a heightened need to strengthen management and oversight. In addition, legal authority for the regulations references FCOI specifically, e.g. 42 U.S.C. 289b–1.

One respondent suggested that the regulations be revised to restrict recipients of PHS-funded research from entering into agreements that contain a provision restricting the Investigator’s ability to speak, publish, or otherwise undertake activities contrary to a company’s commercial interest. Although we believe this action would go beyond the scope of these regulations, we note that as stated in the HHS and NIH Grants Policy Statements (<http://www.ihs.gov/nonMedicalPrograms/gogp/documents/HHS%20Grants%20Policy%20Statement.pdf> and [http://grants.nih.gov/grants/policy/nihgps\\_2010/nihgps\\_ch8.htm#\\_Toc271264951](http://grants.nih.gov/grants/policy/nihgps_2010/nihgps_ch8.htm#_Toc271264951), respectively), we believe that sharing final research data and other research tools produced or developed by Investigators under PHS-funded grants, such as cell lines, certain types of animals (e.g., transgenic mice), and computer programs, is essential for expedited translation of research results into knowledge, products, and procedures to improve human health. We endorse the sharing of final research data and research tools to serve these and other important scientific goals, and we support the timely release and sharing of final research data and research tools from PHS-supported studies for use by other researchers.

#### *General Comments on Contracts*

One respondent was concerned that by revising the regulations, it appears that HHS is modifying the Public Health Service Act. We want to clarify that, through this final rule, HHS has revised regulations promulgated under the Public Health Service Act, not modified the Public Health Service Act itself. The same respondent also believed that “the PHS Acquisition Regulations were abolished and contents (PHSAR 380—care of lab animals, human subjects and Indian self determination) were folded into HHSAR (approx 1998),” leading the

<sup>11</sup> Sec. 219, Tit. II, Div. D, Pub. L. 111–117

respondent to question whether the regulations set forth in 45 CFR part 94 remain "in force." This concern is unfounded; the regulations at 45 CFR part 94 remain in effect in addition to, and not in conflict with, the HHS Acquisition Regulation (HHSAR) codified at 48 CFR part 301 *et seq.* Additionally, the respondent questioned the authority of NIH/PHS/HHS "to set HHS acquisition policy." As noted in the final rule promulgating the 1995 regulations, published on July 11, 1995 (60 FR 132), the PHS and the Office of the Secretary are acting in accordance with the legislative directive in 42 U.S.C. 289b-1(a). We have also declined this respondent's suggestion to place the revisions to the regulations at 45 CFR part 94 in the HHSAR; the revisions expressly pertain to the regulations at 45 CFR part 94 and not to 48 CFR part 301 *et seq.*

Another respondent suggested that there is a need to develop a specific HHSAR provision and/or standard language in the Request for Proposals (RFP) regarding the requirement of certification by the contractor in the regulations. We disagree; 45 CFR 94.4(k) provides standard language that is appropriate for each contract proposal subject to these regulations.

Another respondent suggested that contractors should be exempt from the regulatory requirements to disclose or report FCOIs, because the respondent believes that contractors are acting as independent vendors and the Institution has no effective means of monitoring their compliance with the policy. We disagree with this comment. All Federal contractors are required to have an effective means of complying with the terms and conditions of their contract, including regulatory obligations designed to promote objectivity in PHS-funded research. The regulation specifically provides for enforcement of these obligations, stating at 94.6(b) that "\* \* \* 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."

One respondent stated that the language under 45 CFR part 94 is confusing because it refers to "applications for research," and "awarding component" which seem more like grant terms than contract

terms; additionally, the respondent noted that the language is inconsistent with HHS regulations which refer to OPDIVs or Agencies. We appreciate the opportunity to clarify that the regulations at 45 CFR part 94 apply to Institutions that solicit or receive PHS research funding by means of a contract for research, as distinguished from the regulations at 42 CFR part 50 subpart F which are applicable to Institutions that apply for or receive PHS research funding by means of a grant or cooperative agreement. The revised regulations under 45 CFR part 94 do not include any references to (grant) applications, but rather to contract proposals. Furthermore, the references to "awarding component" in 45 CFR part 94 are appropriate in the context of research contracts, and such references are not inconsistent with references to "OPDIVs or Agencies" in the HHSAR. These terms have a similar meaning, though the HHSAR applies to all operating divisions within HHS, whereas 45 CFR part 94 only applies to the Public Health Service of HHS.

Another respondent expressed concern about inconsistency between the requirements under 45 CFR part 94 and the treatment of organizational conflicts of interest (OCIs) by the Federal Acquisition Regulation (FAR), Subpart 9.5. We are not aware of any direct conflict(s) between the two sets of regulations at this time; 45 CFR part 94 focuses on financial conflicts of interest of Investigators, whereas Subpart 9.5 of the FAR focuses on organizational conflicts of interest. In response to a related question by the same respondent, we note that neither 45 CFR part 94 nor Subpart 9.5 of the FAR require coordination with legal counsel on conflict of interest issues. The FAR provides only in Part 9.504(b) that "Contracting officers should obtain the advice of counsel" in consideration of OCIs. The use of the word "should" suggests that this step is a matter of policy, and not a legal requirement. To address a final concern by the same respondent, we note that the de minimis reporting level of \$5,000 does not imply that no conflict under that amount exists; as discussed further below, that amount is used only as a monetary threshold for the definition of reportable SFIs under 45 CFR part 94.

#### *General Comments on Cost and Burden*

Several respondents suggested that the analysis of the impact of the proposed revisions in the NPRM underestimated the burden and cost of implementation, particularly regarding the potential number of Investigators, SFI disclosures, and FCOI reports. By

publishing both an ANPRM and an NPRM, we have endeavored to involve the community and carefully consider the public's concerns. This final rule incorporates our best efforts to balance the increased burden that results from any regulatory action with the need to respond to demands for greater transparency and accountability from the public and Congress, including a legislative mandate [Pub. L. 111-117, Div. D, Tit. II, sec. 219, 123 Stat. 3034 (2009)]. We will evaluate the effect of provisions of the regulations such as the de minimis and the public accessibility requirement within three years after implementation of the final rule.

Our burden estimates were based on the current pool of PHS-funded Investigators as well as our experience with FCOI reports under the 1995 regulations. We note that the revised definition of Investigator is not significantly different from that in the 1995 regulations; therefore, the number of Investigators should not change substantially. We recognize that the scope of Investigator SFI disclosures, if not the actual numbers, will increase under the revised regulations, and that the number of FCOI reports may increase as well. We made a good faith estimate in the NPRM as to the extent of these increases. Nonetheless, we have taken these comments into consideration as we revised the Regulatory Impact Analysis in section V to accommodate the content of this final rule. Specifically, we have increased the estimated time for Institutions to adapt NIH training materials to incorporate their policies, the time for Investigator disclosures and updates, and the time for reviewing disclosures. We also added an estimated time for completing a retrospective review, and clarified that the time estimated for Institutions to monitor Investigator compliance with a management plan in the NPRM was calculated on a monthly rather than annual basis.

In addition, several respondents objected to the statement in the NPRM that 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, citing limitations in these reimbursements. We recognize that in some instances current cost principles may limit an Institution's ability to recover costs under the Facilities and Administrative cost mechanism. However, this does not render those costs ineligible for recovery.

### General Comments on Implementation

Several respondents suggested that HHS provide assistance to Institutions for the implementation of new policies and procedures to comply with the revised regulations. HHS recognizes the need to support implementation and is developing implementation guidance, which may include, for example, Frequently Asked Questions and other updates to NIH's Financial Conflicts of Interest Web site, <http://grants.nih.gov/grants/policy/coi/>. General inquiries about the FCOI regulations, and requests to consider additional assistance efforts, may be directed to: [FCOICompliance@mail.nih.gov](mailto:FCOICompliance@mail.nih.gov).

Many respondents requested that the implementation of the revised regulations be staggered and proposed time periods ranging from one to five years. In particular, respondents suggested that the implementation of the public accessibility requirement in 42 CFR 50.605(a)(5) and 45 CFR 94.5(a)(5) should be postponed to October 2013 to coincide with the disclosure provisions under Title VI, Section 6002, of the recently enacted Patient Protection and Affordable Care Act, Public Law 111-148 (hereafter, Affordable Care Act<sup>12</sup>). We agree that it is important to balance the desire to implement the revised regulations as soon as possible with the need to provide sufficient time for Institutions and Investigators to comply. We have done so by providing a compliance date of up to 365 days from publication of this final rule, as described in the Dates section above. We considered a staggered approach but thought this would create added burden for Institutions and Investigators, and confusion for the public.

One respondent suggested that we assemble an advisory board of administrators at Institutions to assist in our deliberations in drafting the final rule. We encouraged all stakeholders including Institutions to submit comments to the ANPRM and to the NPRM; such comments have been instrumental to our deliberations. Additionally, we convened a committee of NIH/HHS staff with expertise in different types of research funded by the PHS to consider the comments to the NPRM and the ANPRM.

<sup>12</sup> The Patient Protection and Affordable Care Act (the Affordable Care Act), Public Law 111-148, was enacted on March 23, 2010; the Health Care and Education Reconciliation Act (the Reconciliation Act), Public Law 111-152, was enacted on March 30, 2010. The Affordable Care Act and the Reconciliation Act reorganize, amend, and add to the provisions of part A of title XXVII of the Public Health Service Act.

A few respondents suggested that we postpone revising the regulations and conduct additional discussion with the research community. Again, we note that by publishing both an ANPRM and an NPRM, and by encouraging public comment through public outreach initiatives, we have involved the community throughout this process, and we have carefully considered the comments that have been raised.

### III. Discussion of Public Comments Related to Specific Provisions of the Revised Regulations

Public comments regarding revisions to specific provisions of the 1995 regulations are summarized below, along with a description of HHS' deliberations and any change made to the final rule in response to the comments.

#### *Purpose (42 CFR 50.601; 45 CFR 94.1)*

As proposed in the NPRM,<sup>13</sup> we have made minor revisions to this section to improve internal consistency with regard to the use of various terms and phrases throughout the regulations. One respondent questioned the removal of the words "to ensure" in the reference to 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 FCOI. We have implemented our proposed language, which focuses on the phrase "reasonable expectation," because we believe it sets a more accurate and realistic objective for the regulations; as another respondent noted, it can be perceived as unrealistic from an enforcement perspective to "ensure" the elimination of bias. The respondent also suggested replacing the phrase "design, conduct, or reporting of research" with "design, conduct, analysis, management, administration, reporting, and distribution of research" throughout the rule. We have not made this change, because we believe that "design, conduct or reporting" covers the major responsibilities related to the PHS-funded research and that the term "conduct" encompasses many of the additional terms suggested by the respondent.

#### *Applicability (42 CFR 50.602, 45 CFR 94.2)*

The 1995 regulations were applicable to each Institution that seeks or receives PHS funding for research and, through implementation of the regulations by each Institution, to each Investigator

participating in such research.<sup>14</sup> However, the 1995 regulations excluded SBIR/STTR Phase I applications because of the expectation that such applications "are for limited amounts."<sup>15</sup> As we discussed in the NPRM, since 1995 the size of these awards has increased, such that the amounts constitute a significant expenditure 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. Therefore, we proposed in the NPRM to include SBIR/STTR Phase I applications in the revised regulations.

We only received a small number of comments on this component of the proposal. While a few respondents agreed that including these applications is reasonable, one respondent suggested that including these applicants in the final rule "could present difficulties for start-up and emerging companies forced to adhere to the rule's extensive requirements for reporting and managing conflicts of interest requirements—the same rules with which large research institutions with substantially more resources will be complying."

We have taken this comment into account in our reevaluation of the proposed inclusion of the SBIR/STTR Phase I program and we ultimately determined that this change from the 1995 regulations could indeed create an undue burden. In particular, SBIR/STTR companies are small in size (eligible companies must have fewer than 500 employees, but, for example, the average NIH SBIR/STTR company has approximately 20 employees and many have only 1–3 employees), and these companies tend to be limited in resources. Accordingly, we found the argument to be compelling that the investment required to comply with the regulations could create a disproportionate burden on small businesses. Moreover, approximately 56% of Phase I awardees will apply for Phase II funding, at which point they will be covered by the regulations. Therefore, the regulations will still capture the benefits of compliance from a significant number of these companies without imposing an undue burden that could create a disincentive to applicants

<sup>14</sup> Consistent with the 1995 regulations, 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.

<sup>15</sup> 60 FR 35814 (July 11, 1995).

<sup>13</sup> 75 FR 28689 (May 21, 2010).

from the small business community, an important part of the biomedical research enterprise. For these reasons, the final rule retains the exemption of Phase I SBIR/STTR applications from the 1995 regulations.

We have also implemented the NPRM's proposal 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).

*Definitions (42 CFR 50.603, 45 CFR 94.3)*

In the NPRM we proposed to add several new definitions, revise some of the existing definitions, and remove one definition. Comments and responses regarding the implementation of those proposed changes in the final rule follow:

1. *Contractor.* We have implemented the NPRM's proposal to revise the definition of "Contractor," to 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 was not included in the 1995 regulations but was proposed in the NPRM to mean an Investigator's disclosure of SFIs to an Institution. We have included this definition in the final rule—along with the definition of "FCOI report" below—because of the confusion that can result from the use of the terms "disclosure" and (FCOI) "report." We intend for the term "disclosure" to capture communication from an Investigator to an Institution regarding SFIs, whereas the term "report" captures communication from an Institution to the PHS Awarding Component regarding FCOI. A few respondents requested that we switch this definition with the one stated below (*i.e.*, FCOI report) in order to align the terminology with a recent report by the AAMC/AAU.<sup>16</sup> We have not made that change because we want to minimize public confusion by keeping our terminology consistent with that used in the 1995 regulations, to the extent possible.

3. *Financial conflict of interest (FCOI).* We proposed this definition in the NPRM to mean an SFI that could directly and significantly affect the design, conduct, or reporting of PHS-funded research. Although this definition was not listed in the

Definitions sections of the 1995 regulations, it is consistent with language contained in other provisions of the 1995 regulations.<sup>17</sup> One respondent suggested that the definition be revised to mean an SFI that could directly or indirectly affect the design, conduct, or reporting of PHS-funded research. We have considered this suggestion and believe that including the term "indirectly" could create ambiguity and extend the definition beyond the scope of the regulations. The term "significantly" in this context means that the financial interest would have a material effect on the research, which we believe appropriately fulfills the intent of the regulations, *i.e.*, to maintain objectivity in PHS-funded research.

Some respondents requested the inclusion of specific examples to illustrate SFIs that could be considered FCOIs. Because conflicts of interest can vary according to the specific context and Institutional policy, we are concerned that providing examples could create public confusion, so we have not made that change to the final rule. Other respondents suggested that Institutions should consider specific criteria, including the stage of the research and its commercial potential, the proximity to possible U.S. Food and Drug Administration (FDA) review, and the magnitude of the potential risk, when determining whether an SFI is an FCOI. Although we disagree that this suggestion should be implemented in the regulations, we note that Institutions may include a variety of criteria in the review of Investigators' SFIs and the determination of whether they constitute an FCOI with the PHS-funded research, including those suggested by respondents.

4. *Financial Conflict of Interest (FCOI) report.* This definition was not included in the 1995 regulations but was proposed in the NPRM to mean an Institution's report of an FCOI to a PHS Awarding Component. We have included this definition in the final rule for the same reasons we have included the "disclosure of SFIs" definition discussed above.

5. *Financial interest.* We proposed this definition in the NPRM, as a companion to the revision of the "SFI" definition, described below, to mean anything of monetary value or potential monetary value. Some respondents agreed with this definition, while others suggested that the phrase "or potential monetary value" is too broad and suggested the stated purpose could be achieved by the phrase: "anything of

monetary value, whether or not the value is readily ascertainable." We agree and have changed the language in the final rule accordingly. Another respondent asked if anything of "potential monetary value" would include patents or patent applications. As discussed below in the definition of SFI, patents and patent applications are included in the definition.

6. *Institution.* Consistent with our proposal in the NPRM, we have revised the definition of "Institution" to refer specifically to an Institution that is applying for, or that receives, PHS research funding. A few respondents questioned whether Federal agencies should be excluded from this definition, as this would exclude Federal researchers such as NIH scientists. One requested that HHS evaluate the revised regulations after a period of time to assess whether Federal researchers ("intramural investigators") should be included. Federal agencies and their employees are subject to conflicts of interest requirements, including disclosure by employees and review by agencies, pursuant to Federal criminal statutes, the Ethics in Government Act as amended, and supplemental agency regulations. Accordingly, we have retained the exclusion of Federal agencies in this definition.

7. *Institutional responsibilities.* We proposed this definition in the NPRM to 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. Some respondents requested that this definition be clarified to specify that the Investigator's responsibilities are defined by the Institution. We agree and have modified the definition accordingly to make clear that the Institution defines the Investigator's responsibilities in its policy on financial conflicts of interests. One respondent suggested that the list of examples should be expanded. In light of the change to the regulatory text noted above, and because the definition indicates that the list is not exhaustive, we have not made further changes.

8. *Investigator.* Consistent with our proposal in the NPRM, we have revised the definition of "Investigator" to clarify that it means the Project Director/Principal Investigator (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

<sup>16</sup> Protecting Patients, Preserving Integrity, Advancing Health: Accelerating the Implementation of COI Policies in Human Subjects Research, A Report of the AAMC-AAU Advisory Committee on Financial Conflicts of Interest in Human Subjects Research, February 2008.

<sup>17</sup> 42 CFR 50.605(a) and 45 CFR 94.5(a).

such funding, which may include, for example, collaborators or consultants. Several respondents suggested that this definition is overly broad and will result in disclosures from people who are only peripherally associated with the PHS-funded research. We note that the definition is not substantially different from the definition in the 1995 regulations<sup>18</sup> and is consistent with regulatory guidance that NIH has issued (e.g., see “Investigator-Specific Questions” section of NIH’s “Frequently Asked Questions” resource at <http://grants.nih.gov/grants/policy/coifaq.htm>). In response to questions about whether this definition includes unfunded collaborators, we note that the definition refers to the function of the individual on the PHS-funded project; i.e., his/her responsibility for the design, conduct, or reporting of the PHS-funded research, and not to his/her title or the amount or source of remuneration.

Other respondents suggested the definition should be expanded to include other types of activities, or to include people in a position to influence the design, conduct, or reporting of the research. We have retained the focus of the definition on Investigators who are responsible for the design, conduct, or reporting of research for the reasons discussed above.

Consistent with our proposal in the NPRM, we have also eliminated the reference to the Investigator’s spouse and dependent children in this definition, as we believe that such reference is more appropriate to include in the SFI definition, below.

9. *Key personnel.* In parallel to the use of the term “senior/key personnel” in making FCOI information publicly accessible for research grants and cooperative agreements under 42 CFR 50.605, the term “key personnel” is used for research contracts under 45 CFR 94.5. Therefore, we thought it would be useful to include a separate definition for this term in the final rule, to clarify the exact meaning: the PD/PI and any other personnel considered to be essential to work performance in accordance with HHSAR subpart 352.242–70 and identified as key personnel in the contract proposal and contract.

10. *Manage.* We proposed this definition in the NPRM to mean taking action to address an FCOI, which includes reducing or eliminating the FCOI, to ensure that the design, conduct, and reporting of research will be free from bias or the appearance of bias. Consistent with our discussion in the NPRM, we have included a modified

version of this definition in the final rule as part of a wider reconsideration of the concepts of managing, reducing, and eliminating an FCOI. In the 1995 regulations, these concepts were typically listed separately;<sup>19</sup> suggesting that reducing or eliminating an FCOI may not be the same as managing an FCOI. We believe that it is more appropriate to consider the reduction or elimination of an FCOI as alternate means of managing an FCOI, depending on the circumstances.

This revision is not intended, as suggested by one respondent, to imply that reduction or elimination is the only acceptable means of managing an FCOI. To address this concern, we have changed the definition in the final rule to read “\* \* \* to take action to address a financial conflict of interest, which can include reducing or eliminating the financial conflict of interest \* \* \*”. Another respondent agreed with the definition, while a third thought it should be expanded to include activities beyond the design, conduct, or reporting of research and to state that the ultimate goal is elimination. Another respondent thought that certain types of SFIs should be specified as requiring elimination or reduction. In response to these related comments, we want to clarify that we do not intend to imply that every FCOI must be eliminated; the goal of the regulations is to ensure appropriate management so as to maintain objectivity of the research. Additionally, as discussed above, we believe “design, conduct, or reporting” covers the major responsibilities related to the PHS-funded research, so we have not expanded the scope of the definition. One respondent suggested that “ensure” is impossible to enforce. To address this concern, we have included the phrase “to the extent possible” in the definition. Finally, respondents suggested the deletion of the phrase “appearance of bias.” We have made this change, as we agree that this phrase can be interpreted as overly broad and ambiguous.

11. *PD/PI.* We proposed this definition in the NPRM to mean a Project Director or Principal Investigator of a PHS-funded research project. In the final rule, to improve clarity, we have noted that the PD/PI is included in the definition of senior/key personnel in 42 CFR 50.603, and in the definition of key personnel in 45 CFR 94.3.

12. *PHS.* Consistent with our proposal in the NPRM, we have revised the definition of “PHS” to include a specific reference to NIH in order to clarify that

Institutions applying for, or receiving, research funding from NIH are subject to the regulations. This language remains unchanged from that proposed in the NPRM; however, as a technical correction to improve clarity and accuracy, we have deleted the reference to “an operating division.”

13. *Research.* Consistent with our proposal in the NPRM, we have revised the definition of “research” to include a non-exhaustive list of examples of different types of PHS funding mechanisms to which the definition applies. As revised, the definition under 42 CFR 50.603 includes any activity for which research funding is available from a PHS Awarding Component through a grant or cooperative agreement, 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. The definition under 45 CFR 94.3 includes any activity for which research funding is available from a PHS Awarding Component through a contract, whether authorized under the PHS Act or other statutory authority. We also added the terms “study or experiment” to enhance clarity. A few respondents requested that the definition exclude certain types of grants such as those for educational activities, training, or construction. We note that PHS funds a wide variety of award types and there may be some research components within award types that are not specifically labeled “research” awards. It is important that the information on SFI related to such activities be provided to the Institution for evaluation of the relatedness to PHS-funded research and the possibility of an FCOI. Therefore, we believe it would not be prudent to limit the types of PHS-funded research activities that are subject to these regulations and we did not make this change.

One respondent suggested the addition of examples for the term “product development” in the definition. We agree that this is useful and have added the examples of product development (a diagnostic test or drug) and of products of basic and applied research (a published article, book, or book chapter). Another respondent suggested that reference to the regulations be included in specific Requests for Applications or Requests for Proposals to clarify exactly when the regulations are applicable. We believe this comment is addressed by the general provision of Web links to and citations of applicable policy

<sup>18</sup> 42 CFR 50.603 and 45 CFR 94.3.

<sup>19</sup> 42 CFR 50.605(a) and 45 CFR 94.5(a).

requirements and terms and conditions of awards on Notices of Award for all PHS funded grants and cooperative agreements and in all contracts awarded by the PHS that are for research.

14. *Senior/key personnel.* The NPRM uses this term in the proposal and discussion of the management and posting of FCOI under 42 CFR 50.605. Therefore, we thought it would be useful to include a separate definition for this term in the final rule, to clarify the exact meaning: the PD/PI and any other person who the Institution identifies as senior/key personnel in the grant application progress report, and any other report submitted to the PHS by the Institution under this subpart. This definition is in parallel to that of the term “key personnel” used in making FCOI information publicly accessible for research contracts under 45 CFR 94.5.

15. *Significant Financial Interest.* In the NPRM, we proposed to revise substantially the SFI definition,<sup>20</sup> incorporating the proposed definitions of “financial interest” and “institutional responsibilities” described above. Below is a discussion of public comments related to the implementation of these changes, using the categories referenced in the NPRM to highlight differences from the 1995 regulations.<sup>21</sup>

*Institutional responsibilities:* Some respondents suggested that the disclosure requirement in the 1995 regulations,<sup>22</sup> *i.e.*, SFIs that Investigators deem related to the PHS-funded research, is sufficient. We note that the NPRM’s proposal to expand the definition of SFI was influenced by the suggestions of many respondents to the

ANPRM who supported this change. A few respondents agreed that expanding SFIs subject to disclosure by an Investigator to an Institution to include those that reasonably appear to be related to the Investigator’s “institutional responsibilities” is warranted. Many others, however, suggested that the SFIs to be disclosed should be limited to those that reasonably appear to be related to the Investigator’s “research responsibilities.” We have considered this suggestion and believe that since the definition of “research responsibilities” is not clear-cut, this change would once again place the responsibility on the Investigator for deciding which SFIs should be disclosed to the Institution (similar to the 1995 regulations) and may not provide the Institutions with the full complement of information needed to evaluate the potential for FCOI. For example, an Investigator is on the board of a pharmaceutical company and believes that this service draws on the Investigator’s clinical expertise rather than research knowledge. If the SFI definition is confined to “research responsibilities”, the Investigator may not disclose the income from this activity to the Investigator’s Institution. Such income definitely would fall under “institutional responsibilities”, however, as the Investigator is on the clinical faculty of the Institution.

Moreover, we note that the scope of activities that need to be disclosed by the Investigator is limited by the fact that the SFI definition excludes income from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education; or income from service on advisory committees or review panels for a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

One respondent proposed that the regulations specify particular relationships and types of interests that should be disclosed. We have considered this suggestion and believe that limiting the scope of SFIs that an Investigator is required to disclose to his or her Institution may exclude SFIs in activities that have the potential to affect the objectivity of PHS-funded

research. Therefore, we have retained the language proposed in the NPRM.

One respondent suggested that PHS funding could change an Investigator’s institutional responsibilities and suggested that SFI disclosures should be based on the anticipated responsibilities if funding is awarded. We have not changed the regulations in this regard, because we believe this concern would be addressed by the Institution’s FCOI policy; *i.e.*, any time there is a significant change in an Investigator’s institutional responsibilities (whether in relation to PHS funding or not), Institutions should consider whether this would require the Investigator to update his or her SFI disclosures.

Other respondents questioned whether specific types of income, such as clinical work within private or university practice or teaching a craft, would need to be disclosed. Income from any activity that is related to the Investigator’s institutional responsibilities as defined by the Institution that meets the monetary threshold must be disclosed. Another suggested that payment related to the accrual of patients to clinical trials should be included in the definition. If the individual receiving the payment meets the definition of “Investigator” under the regulations, such payment would be included in the SFI definition and should be disclosed.<sup>23</sup>

*Monetary threshold:* Respondents submitted a wide range of comments on the monetary threshold proposed in the NPRM. Some supported the \$5,000 threshold; others suggested that the threshold of \$10,000 in the 1995 regulations should be retained; and many suggested that the threshold be lowered even further to \$100 or zero. We have considered all the comments and we believe that the \$5,000 threshold proposed in the NPRM provides the appropriate balance between the administrative burden associated with disclosure and review of SFIs and the intended benefit in promoting objectivity in research.

Some respondents requested that the disclosure thresholds be harmonized with those of other Federal agencies such as the FDA and the National Science Foundation or with the disclosure provisions of the Affordable Care Act. While there may be some similarity in intent, the numerous disclosure requirements of other Federal laws, regulations, or policies are not necessarily comparable to those

<sup>20</sup> 75 FR 28705 (May 21, 2010).

<sup>21</sup> Under the 1995 regulations, an 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/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 12 months, are not expected (or, in the case of PHS contracts, are not reasonably expected) to exceed \$10,000.

<sup>22</sup> 42 CFR 50.604(c)(1) and 45 CFR 94.4(c)(1)

<sup>23</sup> Alternatively, if the commenter is concerned about (improper) payment to an Institution under these circumstances, we note that institutional conflicts of interest are addressed in section IV of this final rule.

specified in these regulations. For example, Title VI, Section 6002 of the Affordable Care Act requires disclosure by the entities providing the payment. FDA, for purposes of financial disclosure by clinical investigators, has defined *significant payment of other sorts* as payments made by the sponsor of a covered study to the investigator or the institution to support activities of the investigator that have a monetary value of more than \$25,000, exclusive of the costs of conducting the clinical study or other clinical studies.<sup>24</sup> Due to the extent of potential differences in the nature, scope, and applicability of Federal disclosure requirements, we do not agree that it is feasible to harmonize all requirements at this time, although we believe these regulations could serve as a basis for ongoing collaboration and coordination regarding the topic of conflicts of interest.

Other respondents suggested that different disclosure thresholds should be instituted for research depending on whether it involves human participants, drugs, or devices. As discussed in the NPRM, we posed a number of questions in the ANPRM on the issue of whether the regulations should be amended to require specific approaches related to certain types of research or alternatively, specific types of financial interests or FCOI.<sup>25</sup> The majority of the respondents to the ANPRM thought that this approach would not account for the full range of research projects as well as the large variation in circumstances in which FCOI may arise. We agree and note that the monetary threshold is the same regardless of the type of research, financial interest, or identified FCOI at issue.

Timing: The NPRM proposed to change the timing for determining whether remuneration represents an SFI. The 1995 regulations excluded 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 12 months.” Under the revised definition proposed in the NPRM, at issue is remuneration (including salary and any payment for services not otherwise identified as salary) received from an entity “in the 12 months preceding the disclosure.” We have included this change in the final rule; we believe it will help Institutions and Investigators to determine more accurately whether or not a financial interest represents an 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 monetary threshold was met or exceeded.

Several respondents suggested that the 1995 regulations’ disclosure period is more consistent with the aim of maintaining objectivity in research. Some suggested that the time period for disclosure include both the preceding and the next 12 months, and one suggested that the period cover the duration of the award. We do not agree with these suggestions. In addition to disclosing SFIs received in the 12 months preceding the disclosure, Investigators are required to disclose new SFIs to the Institution within 30 days, and if payments received after the initial disclosure give rise to an SFI that is determined to be an FCOI by the institutional official(s), the Institution is required to submit an FCOI report to the PHS Awarding Component. Consistent with our proposal in the NPRM, the final rule also includes a requirement for annual updates. We believe this combination of provisions provides reasonable coverage of an Investigator’s SFIs related to the PHS-funded research project, and allows a more accurate listing of SFIs by Investigators. Institutions are free to expand upon these requirements in their institutional policies and when considering whether an SFI is an FCOI with regard to the PHS-funded research.

Some respondents inquired how a payment or reimbursement that occurred before a PHS award should be reviewed in relation to the PHS-funded research. Although such considerations are dependent on the context of the SFI, the regulations do not prevent Institutions from taking into account whether the Investigator has an ongoing financial relationship with the entity providing the payment or reimbursement or whether the payment or reimbursement was limited in duration.

One respondent suggested that different disclosure periods should be instituted for different types of research. As discussed in the NPRM and above, we posed a number of questions in the ANPRM on the issue of whether the regulations should be amended to require specific approaches related to certain types of research or alternatively, specific types of financial interests or FCOI. The majority of the respondents to the ANPRM thought that this approach would not account for the

full range of research projects as well as the large variation in circumstances in which FCOI may arise. As a result, the regulations impose uniform requirements, regardless of the type of research, financial interest, or identified FCOI at issue.

Examples of payment for services: The definition of SFI under the 1995 regulations referenced as examples of payments for services, receipt of consulting fees, or honoraria. In the NPRM, we proposed to add “paid authorship” and “travel reimbursement” as additional examples.<sup>26</sup>

With regard to “paid authorship,” although it should be clear that receipt of payment from an entity in exchange for drafting a publication constitutes payment for services, we believe it is important to reference this form of payment specifically in the regulations. We are particularly concerned about situations in which Investigators may have accepted payment from private entities, in return for allowing their names to be used as authors on publications for which they had very limited input. 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. One respondent noted that remuneration from authorship of textbooks is not considered an FCOI at their Institution. We note that the regulations only require disclosure of such SFI by the Investigator to his or her Institution. The Institution makes the determination as to whether the SFI constitutes an FCOI, based on its review of the specific circumstances. Another respondent suggested that payments to faculty authors from publishers should be excluded from the SFI definition while payments from companies not engaged primarily in publishing should be included. We do not agree with this suggestion, because we believe that it may be difficult to draw a distinction between companies engaged primarily in publishing (*i.e.*, “publishers”) and those that are not, leading to inconsistent disclosures. Therefore, we retained the “paid authorship” example in the definition, as proposed in the NPRM.

With regard to “travel reimbursement,” while one respondent agreed that this should be included in the SFI definition, many objected to its inclusion on the grounds that such

<sup>24</sup> 21 CFR 54.2(f).

<sup>25</sup> 74 FR 21612 (May 8, 2009).

<sup>26</sup> 75 FR 28705 (May 21, 2010).

payments do not constitute income to the Investigator and requiring their disclosure would constitute a burden, as in many cases the Investigator is not aware of the value of the reimbursement. We have considered these comments carefully and appreciate that for Investigators, travel to scientific meetings and to present his/her research to colleagues and other interested parties is an integral part of the scientific research enterprise and affords many important opportunities for forging relationships and collaborations among researchers. The provisions in the revised regulations are not intended to discourage this type of travel. We also appreciate that requiring Investigators to disclose the value of travel reimbursements could be difficult, particularly in the case of sponsored travel, which is paid on behalf of the Investigator and not reimbursed to the Investigator, so that the exact monetary value may not be readily available. Nonetheless, depending on the source of funding and other circumstances (e.g., destination, duration) of specific travel, the Institution may consider whether that sponsored travel could affect the design, conduct, or reporting of PHS-funded research. In order to minimize the burden on the Investigator while providing the Institution with the appropriate level of information, we have added another category (paragraph 2) to the SFI definition that addresses the disclosure of reimbursed and sponsored travel. The Institution's FCOI policy will specify the details of this disclosure, which will include, at a minimum, the purpose of the trip, the identity of the sponsor/organizer, the destination, and the duration. Although the regulations do not require disclosure of the monetary value of the sponsored or reimbursed travel, in accordance with the Institution's FCOI policy, the Institutional official(s) can determine if further information is needed, including a determination or disclosure of monetary value, in order to establish whether the travel constitutes an FCOI with the PHS-funded research. In addition, travel that is reimbursed or sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education is not subject to this disclosure requirement.

We considered the alternative of revising the rule to exclude "reasonable and customary" travel. We did not revise the rule in this manner because

we believe that this puts the responsibility for defining "reasonable and customary" onto the Investigator, which may lead to inconsistency in disclosure.

**Royalties & Intellectual Property:** Under the 1995 regulations, royalties are included among the "payments" subject to the \$10,000 threshold. Under the revisions proposed in the NPRM, which we have implemented, the \$5,000 threshold would apply to equity interests and "payment for services," which would include salary but not royalties. Royalties nevertheless are potentially subject to disclosure, as are other interests related to intellectual property. Specifically, the revised definition applies 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.

One respondent inquired whether Investigators should disclose intellectual property interests when a patent application is submitted or only when the patent is granted. Since income related to an intellectual property interest may be received before a patent is issued we would expect institutional policies to require disclosure upon the filing of a patent application or the receipt of income related to the intellectual property interest, whichever is earlier. We have also clarified our intent that the disclosure requirements include intellectual property interests by adding a specific reference to "interests" to the existing reference to "rights."

Many respondents requested further clarification as to the thresholds associated with these intellectual property interests. The threshold of \$5,000 applies to licensed intellectual property rights (e.g., patents, copyrights), royalties from such rights, and agreements to share in royalties related to licensed intellectual property rights. Several respondents suggested that in the rare cases when unlicensed intellectual property is held by the Investigator instead of flowing through the Institution, it should be excluded from the definition as it is difficult to determine the value of such interests. We agree that it is difficult to determine the value of such interests, and have revised the SFI definition to include intellectual property rights and interests (e.g., patents, copyrights) upon receipt

of income related to such rights and interests. Therefore unlicensed intellectual property that does not generate income is excluded. Nonetheless, such interests have the potential to become significant and generate income, at which point they would become subject to the regulations.

**Exclusions:** Consistent with the NPRM, we have modified the types of interests that are specifically excluded from the SFI definition. For example, the NPRM definition only excludes income from seminars, lectures, and 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, in the NPRM we proposed that 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). We proposed this change due to the growth of non-profit entities that sponsor such activities since the 1995 regulations were promulgated. 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). One respondent suggested that all income should be included in the SFI definition. We believe that the final rule strikes an appropriate balance regarding the income that must be disclosed as an SFI. On the other hand, we received many suggestions for additional types of non-profit Institutions for which income from seminars, lectures, or teaching engagements and from service on advisory committees or review panels could be excluded, e.g., professional or engineering societies, Institutions that provide competitive research grants, academic medical centers, and Institutions that meet the standards of the Accreditation Council for Continuing Medical Education. Other respondents suggested that disclosure be limited to income from non-profit organizations that are primarily supported by for-profit companies. Another suggested the definition exclude activities that primarily support higher education. We have not adopted all these suggestions because we believe that difficulties in identifying the funding sources of many non-profit organizations would pose a greater obstacle to Investigators when deciding which SFI to disclose to their Institution than they would to the Institution when

evaluating such SFI. Therefore, it would seem preferable for the Institution to receive and evaluate the information.

Nonetheless, we agree with respondents that limiting exclusions from disclosure to income from Federal, state, or local government agencies, and Institutions of higher education as defined at 20 U.S.C. 1001(a) is unnecessarily narrow. Therefore, we have revised the SFI definition in the final rule to exclude 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, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education; or income from service on advisory committees or review panels for a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

One respondent inquired whether income received from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency; or income from service on advisory committees or review panels for a Federal, state, or local government agency, but paid by a private contract organization acting for that government agency, is excluded from the SFI definition. If a private organization is acting as a contractor to the Federal, state, or local government agency, for the purposes of these regulations, such income is excluded from the definition.

The 1995 regulations excluded from the SFI definition any ownership interests in the Institution, if the Institution is an applicant under the SBIR Program. As proposed in the NPRM, we have broadened the exclusion to cover any ownership interests in the Institution if the Institution is a commercial or for-profit organization (whether or not the Institution is an applicant under the SBIR Program). A few respondents requested further clarification, of situations in which an Investigator is employed by an Institution and also has equity in a for-profit company. In those cases, his or her equity would only be

excluded from disclosure requirements when the for-profit company is the Institution that is applying for, or that receives, the PHS research funding in which the Investigator is participating.

As proposed in the NPRM, we have also limited the exclusion in the 1995 regulations for salary, royalties, or other remuneration paid by the Institution to the Investigator to circumstances in which the Investigator is currently employed or otherwise appointed by the Institution. In response to questions from a number of respondents, we have also clarified that intellectual property rights assigned to the Institution and agreements to share in royalties related to such rights are also excluded from the SFI definition. Other respondents suggested that royalties and intellectual property rights that are provided by the Institution should not be excluded from the definition as they could affect the objectivity of the PHS-funded research. We do not believe it would be useful to increase the disclosure burden on the Investigator by requiring disclosure to the Institution of information the Institution already has available. However, we note that Institutions have the flexibility to require such disclosures in their own policies. One respondent suggested that such royalties continue to be excluded from the SFI definition if an Investigator transfers to another Institution. In that case, however, the new Institution is not the source of the royalties and the exclusion would not apply; therefore such royalties would be included in the SFI definition.

Many respondents requested that income from mutual funds and retirement accounts be explicitly excluded from Investigator disclosure requirements, to the extent that Investigators do not control the investment decisions made in these vehicles. We have provided guidance in the form of Frequently Asked Questions on the NIH Web site recognizing that interests in a pooled fund such as a diversified mutual fund may be sufficiently remote that it would not reasonably be expected to create a conflict of interest for a PHS-funded Investigator.<sup>27</sup> We have revised the regulations in accordance with this guidance to exclude income from

<sup>27</sup> <http://grants.nih.gov/grants/policy/coiffaq.htm#427>.

Am I required to disclose interests in mutual funds?

Please refer to your Institution's policy. An interest in a pooled fund such as a diversified mutual fund may be sufficiently remote that it would not reasonably be expected to create a conflict of interest for an Investigator funded by the NIH.

investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles.

One respondent requested that the definition cover any "security," as defined by reference to the Securities Act of 1933, as amended, and suggested that there is no reason to exclude debt instruments. Although we have not implemented this suggestion in the final rule, we note that our definition addresses stock, a specific element of the definition of "security" under the Securities Act of 1933, 15 U.S.C. 77a *et seq.*, and that the regulations do not expressly exclude debt instruments. A few respondents suggested that the definition should go beyond the Investigator's spouse and dependent children to include interests held by more distant family members and/or friends. We have not made this change, because we believe that it would expand the scope of the regulations unnecessarily and create ambiguity. Some respondents suggested that the SFI definition include payments from individuals, as well as entities. We have not made this change because we typically would expect individual payors to be acting on behalf of or in connection to entities, and because the source of payment is not the primary focus of the SFI definition.

Several respondents requested that we revise the SFI definition to include "domestic partners." Although we appreciate the interest in identifying individuals who share assets with, or control assets on behalf of, the Investigator through civil unions, powers of attorney, or other arrangements, we have not made that specific change to the final rule because we believe it is beyond the scope of these regulations to define the term "domestic partners." However, we note that Institutions have the flexibility to incorporate this suggestion into their policies.

Finally, as a technical correction to the language proposed in the NPRM, we have deleted the reference to "except as otherwise specified in this definition," to improve the overall clarity of the SFI definition.

**16. Small Business Innovation Research (SBIR) Program.** In the NPRM we removed the definition in the 1995 regulations for the SBIR Program since, in the proposed regulations this program was no longer excluded, and we had not separately defined other HHS research programs that were subject to the proposed regulations. As the SBIR Phase I applications are excluded from the final rule (see

discussion above), we are including the definition in the final rule.

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

Consistent with the NPRM, we have substantially revised the responsibilities of Institutions regarding Investigator FCOI.

The 1995 regulations provided that each Institution must maintain an appropriate written, enforced policy on conflicts of interest that complies with the regulations.<sup>28</sup> In the NPRM we proposed revising this provision to require an Institution not only to maintain an up-to-date, written, enforced FCOI policy that complies with the regulations, but also to make such policy available via a publicly accessible Web site. We have included this requirement in the revised regulations at 42 CFR 50.604(a) and 45 CFR 94.4(a), because we believe that it fosters greater transparency and accountability with regard to institutional policies. Moreover, we have clarified that if an Institution does not have a current presence on a publicly accessible Web site (and only in those cases), the Institution may make the information available in writing within five business days of any request. If, however, the Institution acquires a presence on a publicly accessible Web site during the time of the PHS award, the requirement to post the information on that Web site will apply within 30 calendar days.

One respondent suggested that Institutions' policies should be filed with the PHS. We believe the requirement to make the policies publicly available renders this suggestion unnecessary. One respondent suggested that Institutions should be required to "prominently" post their FCOI policy on the Institution's Web site so that it would be easily accessible. We have not revised the regulations to include this requirement, because we understand that term could create ambiguity. We have used the term "publicly accessible" to communicate our intention that the public can readily obtain the information required under these regulations. In the event of any questions, we encourage members of the public to contact Institutions for instructions as to the location of their policy, and to report any enforcement concerns to the PHS Awarding Component. One respondent inquired as to whether this provision applies to subrecipients. We note that

subrecipients that rely on their own policies would be subject to this requirement. However, if the subrecipient is relying on the policies of the awardee Institution, that Institution would be responsible for posting the policy.

Consistent with the NPRM, we have also revised this section to 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 within the time periods required in the regulations. Many respondents indicated that this provision would provide a substantial disincentive to Institutions to adopt more stringent standards than those set forth in the regulations, and could lead to a lack of consistency in reporting and increased confusion.

We appreciate the concerns raised and discussed them carefully before making the final decision to retain this language in the final rule because of several mitigating factors. For example, the 1995 regulations indicated that the regulations constituted a minimum standard; *i.e.*, the Institution retained flexibility to add requirements to those in the regulations, as long as such requirements are consistent with the regulations. Specifically, 42 CFR 50.605 and 45 CFR 94.5 state: "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 in its policy on financial conflicts of interest, as the Institution deems appropriate." Moreover, in regulatory guidance on this issue with regard to grants and cooperative agreements, NIH stated that Institutions could impose more stringent requirements than those in the regulation as long as the Institution's policies meet the minimum requirements of the regulation and each Investigator is informed of the Institution's policies; of the Investigator's disclosure responsibilities; and of the regulation.<sup>29</sup> In addition, the principle that an Institution must follow its own policies, even if they go beyond—but as long as they are consistent with—Federal policies and regulations, is an established standard of NIH grants policies and applies to the implementation of all terms and

conditions of award for grants and cooperative agreements. Finally, we weighed the possible inconsistency in reporting resulting from implementation of this provision against the possible ramifications of the PHS Awarding Component being unaware of an FCOI related to PHS-funded research that was identified by the Institution. We concluded that full reporting of all Institution-identified FCOIs related to PHS-funded research is necessary for appropriate accountability by the Institution and for robust oversight by the PHS Awarding Component. Although the regulations do not specify a standardized Federal reporting form, as suggested by one respondent, the regulations identify necessary elements of the report (*e.g.*, 42 CFR 50.605(b)(3) and 45 CFR 94.5(b)(3)), and NIH provides a framework for reporting those elements through its online reporting system.

Also consistent with the NPRM, we are incorporating the requirement in the 1995 regulations that each Institution must inform each Investigator of its policy on conflicts of interest, of the Investigator's disclosure responsibilities, and of these regulations. This requirement is addressed as a new paragraph (b), and, as proposed in the NPRM, it includes an Investigator training requirement. However, we have modified the training requirement to accommodate suggestions raised in public comments. Specifically, the NPRM proposed that Institutions require Investigators to complete training regarding the Institution's FCOI policy, the Investigator's responsibilities regarding disclosure of SFI, and the regulations, prior to engaging in PHS-funded research and, thereafter, at least once every two years.

Although some respondents agreed with the training requirements as proposed, many other respondents raised reasonable alternatives. For example, most of the respondents on this topic agreed with the requirement for initial training of Investigators prior to engaging in PHS-funded research but thought that the Institution should determine the training frequency thereafter or that a period longer than two years should be specified. We considered the comments carefully and agree that every two years may be too frequent; however, we believe it is important to ensure that Investigators receive training beyond the initial period in order to maintain objectivity in PHS-funded research over the long term. Therefore, we have revised the provision in 42 CFR 50.604(b) and 45 CFR 94.4(b) to require Institutions to

<sup>28</sup> 42 CFR 50.604(a) and 45 CFR 94.4(a).

<sup>29</sup> NIH "Frequently Asked Question" B.4 at <http://grants.nih.gov/grants/policy/coifaq.htm>.

train Investigators prior to engaging in research related to any PHS-funded grant or contract, and at least every four years (a typical period of a PHS-funded research grant), and immediately when any of the following circumstances apply: (1) The Institution revises its financial conflicts of interest policies or procedures in any manner that affects the requirements of Investigators; (2) an Investigator moves to a new Institution; or (3) an Institution finds that an Investigator is not in compliance with the regulations or with the Institution's financial conflicts of interest policy or management plan.

One respondent proposed that training be required only of those PHS-funded Investigators who have FCOIs. We disagree with this suggestion, as this change would not fulfill the purpose of the training requirement, which is to inform all Investigators conducting PHS-funded research of the Institution's FCOI policy, their responsibilities regarding disclosure of SFI, and the regulations. A few respondents suggested that the mandated training include a discussion of ethical issues surrounding FCOI. We note that as long as the training covers the Institution's FCOI policy, the Investigator's responsibilities regarding disclosure of SFI, and the regulations, Institutions are free to adopt this suggestion, and to include any other issues they deem essential to accomplishing the stated objective of the training. One respondent suggested that the Institution's training materials be submitted to the PHS Awarding Component and that Investigators be required to certify completion of training to the PHS Awarding Component. We believe that this suggestion is addressed by the existing HHS requirement that institutional officials are responsible for ensuring compliance with all applicable Federal laws and regulations, including required certifications and assurances; such officials must provide a certification regarding compliance with the regulation—including the training requirement—with each application for funding.

Finally, several respondents requested that HHS provide training materials that Institutions can use to fulfill this requirement, as well as seminars or workshops that address implementation of the revised regulations. As in the past, NIH/HHS will continue to engage in outreach activities to promote compliance with the regulations, and will make resources available online, including guidance on policy development and a regulatory training module for Institutions and

Investigators. Institutions should adapt these resources to incorporate information related to their specific policies and procedures, as needed.

Consistent with the NPRM, we have also implemented clarifications to the requirement in the 1995 regulations that, if the Institution carries out the PHS-funded research through subrecipients (*e.g.*, subcontractors or consortium members), the Institution must take reasonable steps to ensure that Investigators working for subrecipients comply with the regulations, either by requiring those Investigators to comply with the Institution's policy or by requiring the subrecipients to provide assurances to the Institution that will enable the Institution to comply with the regulations. As proposed in the NPRM, we are addressing these changes in a new subsection (c), though we are implementing minor changes to the proposed language to improve overall clarity as follows: An Institution that carries out the PHS-funded research through a subrecipient must incorporate as part of a written agreement with the subrecipient terms that establish whether the FCOI policy of the awardee Institution or that of the subrecipient will apply to the subrecipient's Investigators. If the subrecipient's Investigator must comply with the subrecipient's FCOI policy, the subrecipient shall certify as part of the agreement referenced above 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 for significant financial interests that are directly related to the subrecipient's work for the awardee Institution.

Additionally, if the subrecipient's Investigators must comply with the subrecipient's FCOI policy, the agreement referenced above 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 as required by the regulations. Alternatively, if the subrecipient's Investigators must comply with the awardee Institution's FCOI policy, the agreement referenced above 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) also requires that the Institution provide FCOI reports to the PHS regarding all FCOIs of all subrecipient Investigators consistent with the regulations. We believe these changes will clarify for Institutions and their subrecipients the requirements of both parties, which will promote greater compliance with the regulations.

Many respondents were concerned that these provisions would be difficult to operationalize as written in the NPRM, particularly in the case of foreign organizations. They suggested that awardee Institutions would not reasonably be able to evaluate the FCOI policies of the subrecipient Institution. We believe that this concern is alleviated by the requirement of a written agreement to reinforce a clear understanding of the expectations of the subrecipient and awardee Institution,<sup>30</sup> depending on whose policy will apply. To address a concern raised by another respondent, we have also added language to limit the SFI reported to the awardee Institution to those that are directly related to the subrecipient's work for the awardee Institution.

Some respondents suggested that the subrecipients report FCOIs identified for their Investigators directly to the PHS Awarding Component. Others proposed that subrecipients that are the direct recipients of other awards from the PHS Awarding Component be exempt from the certification process. We disagree with both suggestions. The PHS Awarding Component has a direct relationship only with the awardee Institution. Therefore, the awardee Institution is responsible for providing FCOI reports to the PHS regarding all financial conflicts of interest of all subrecipient Investigators, consistent with the regulations. These expectations apply whether or not the subrecipient serves as an awardee Institution to the PHS Awarding Component on other awards, as each award is considered separately for purposes of compliance with the regulations.

One respondent noted that there is no timeline specified for Institutions to provide the PHS all FCOI reports of all subrecipient Investigators. We have clarified our expectation that Institutions report subrecipient-identified FCOIs prior to the expenditure of funds and within 60 days of any subsequently identified FCOI by adding this language to subsection (c)(2).

One respondent proposed that the agreement between the awardee and

<sup>30</sup> The term "awardee Institution" is used here to distinguish it from the subrecipient Institution.

subrecipient Institutions, and the subrecipients' FCOI policies should be filed with the PHS. We believe that the submission of this information is not necessary unless specifically requested by the PHS Awarding Component since applicable HHS policy requires Institutions to certify compliance with the requirements of this and other regulations in each application or solicitation for funding. An Institution's failure to comply with the terms and conditions of award, including this regulation, may cause HHS to take one or more enforcement actions, depending on the severity and duration of the noncompliance.

Paragraph (d) of the NPRM required that an Institution designate an institutional official(s) to solicit and review disclosures of SFIs from each Investigator who is planning to participate in PHS-funded research. A few respondents suggested that the regulations be revised to stipulate the requirements for the designated official(s) and how the Institution should ensure that the designated official(s) do not themselves have conflicts of interest. We have not implemented those changes because we believe that the Institution is in the best position to determine the qualifications and characteristics of the designated official(s) in the Institution's policy.

The 1995 regulations required that, by the time an application or contract proposal 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. As discussed above, the revised SFI definition includes SFIs that reasonably appear related to the Investigator's "institutional responsibilities." Therefore, the requirement in the 1995 regulations to disclose SFIs, which we have adopted in paragraph (e) of the final rule, incorporates this revised definition, such that the scope of Investigator disclosures is no longer project specific, but rather pertains to the Investigator's institutional responsibilities. In response to a suggestion from a respondent, we have clarified that Investigators who have not previously disclosed their SFIs to the

Institution's designated official(s) must do so no later than the time of application or date of contract proposal submitted for PHS-funded research.

One respondent suggested that Institutions should establish an internal database for disclosures of Investigator SFI which could be easily updated. We have not included this requirement because we are concerned that it could impose an unnecessary administrative burden and expense to Institutions. As long as Institutions have a process in place to comply fully with all regulatory requirements, they may collect disclosures from Investigators in the manner that is most appropriate for their policies and procedures.

Consistent with our proposal in the NPRM, as part of paragraph (e), we have also revised and clarified an Investigator's annual and ongoing, including *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 official(s) the Investigator's SFIs (and those of the Investigator's spouse and dependent children), the Institution must also require each Investigator who is participating in the PHS-funded research to 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). A number of respondents agreed that annual disclosure by Investigators is necessary but suggested that the Institution should be free to determine the specific timing. We have revised paragraph (e)(2) to adopt this suggestion. Because of this change, we have declined the suggestion of another respondent to link the annual disclosure period to the Fiscal Year calendar. Another respondent suggested that the disclosure period should be event-driven, rather than annual. While we continue to believe that annual disclosure is appropriate, we note that the requirement for disclosing updated SFIs in subsection (e)(3), as described below, should address this concern by providing Institutions with information about Investigator SFIs that arise between the annual disclosure periods.

(2) Within 30 days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new SFI. A few respondents suggested that 30 days is too short a period for disclosure of

new SFIs, and one respondent suggested that this requirement be changed to 60 days, consistent with the time-period specified in other parts of the regulations. After carefully considering the appropriate balance between affording Investigators sufficient time to disclose new SFIs as they arise and the need to review SFIs related to PHS-funded research in a timely manner, we have retained the 30 day period in subsection (e)(3).

A respondent suggested that requiring disclosure when an Investigator is planning to participate in PHS-funded research is too imprecise and requested that this phrase be revised. We have revised subsection (e)(1) to specify that disclosures must occur no later than the time of application or date of contract proposal submitted for PHS-funded research.

The 1995 regulations required 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. Consistent with our proposal in the NPRM, we have reorganized and expanded this requirement in a re-designated paragraph (f), to clarify an Institution's obligations. First, the guidelines must address two related tasks, specifically, determination of whether an Investigator's SFI is related to the PHS-funded research and, if so related, whether the SFI is an FCOI. Under the 1995 regulations, the Investigator bore the responsibility for determining the relatedness of an SFI to the PHS-funded research as part of the disclosure process.

As discussed above, however, we have revised the definition of SFI to address "institutional responsibilities"; consistent with this change, we have shifted the responsibility for determining whether an Investigator's SFI is related to PHS-funded research to the Institution. Specifically, an Investigator's SFI is related to PHS-funded research when the Institution, through its designated official(s), reasonably determines that the SFI: could be affected by the PHS-funded research; or is in an entity whose financial interest could be affected by the research. Although one respondent suggested that this definition is not sufficiently inclusive, we believe it encompasses the range of relationships between an Investigator's SFI and PHS-funded research. We note that this definition has been in effect since the 1995 regulations and remains consistent

with the guidance that NIH/HHS has offered on this issue since that time.

Many respondents agreed that the responsibility for determining whether an Investigator's SFI is related to the PHS-funded research should ultimately rest with the Institution; however, they were concerned that the proposed revisions in the NPRM did not allow Institutions to involve the Investigator in this process. They suggested that requiring Institutions to make this determination without the input of the Investigator would make the decision-making process more challenging. Because this was not the intent of the proposed language, we have revised paragraph (f) to explicitly state that the Institution may involve the Investigator in the designated official(s)'s determination of whether an SFI is related to the PHS-funded research. A few respondents suggested this responsibility should remain with the Investigator. We have weighed this suggestion and believe that the revised language strikes the appropriate balance between the Institution's ultimate responsibility for reviewing Investigator disclosures and the Investigator's responsibility to disclose all SFIs related to his or her institutional responsibilities.

In the Extension Notice, we requested comment as to whether the regulations should further clarify that, as part of the Institution's FCOI determination process, institutional officials must consider whether an Investigator's SFI was previously determined to be an FCOI at another Institution and subject to a management plan with regard to other PHS-funded research project(s). Many respondents suggested that requiring institutional officials to consider information on an FCOI from another Institution is unnecessary, as information regarding FCOIs would be available on a public Web site, as per the proposed revisions in the NPRM. They suggested that Institutions should be free to use their own policies and procedures to comply with the regulations. We have considered these comments and agree. With the expansion of Investigator disclosure to include all SFIs related to their institutional responsibilities and the requirement to ensure public accessibility of information about FCOIs of senior/key personnel for research grants and cooperative agreements and key personnel for research contracts, the likelihood of an Institution not receiving information about a particular SFI or FCOI is minimized.

One respondent suggested the following alternative approach: in a case where an Investigator moves from one

Institution to another, the PHS Awarding Component would mediate the transfer of information related to any identified FCOI from the previous Institution to the new one, and the receiving Institution, while not bound by any previous management plan, would have to advise the PHS Awarding Component of its decision regarding that FCOI. Another suggested that Institutions should be required to notify the PHS Awarding Component of the imposition of a penalty on Investigators that limits their participation in PHS-funded research, and that the PHS Awarding Component should create a registry of these Investigators. In light of these comments, we have specified that updated disclosures should include any FCOI identified on a PHS-funded project that was transferred from another Institution. We also note that, as specified in 42 CFR 50.606(b) and 45 CFR 94.6(b), the HHS may inquire at any time (before, during, or after award) into any Investigator disclosure of financial interests and the Institution's review of, and response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of an FCOI. This would include situations in which an Investigator moves from one Institution to another.

To provide clarification regarding the determination of whether an Investigator's SFI is an FCOI, the re-designated paragraph (f) incorporates modified language moved from paragraph (a)(1) of the 1995 regulations, consistent with the NPRM. Specifically, this paragraph provides that an FCOI exists when the Institution, through its designated official(s), reasonably determines that the SFI could directly and significantly affect the design, conduct, or reporting of the PHS-funded research. As discussed above, the regulations also incorporate a revised definition of FCOI that is based on this language.

Consistent with our proposal in the NPRM, we have included the requirement in the 1995 regulations regarding FCOI management responsibilities in a separate paragraph (g), in which we clarified that the requirement includes management of any financial conflicts of a subrecipient Investigator pursuant to paragraph (c) of the revised regulations described above. We have also cross-referenced the Institution's revised management responsibilities specified in 42 CFR 50.605(a) and 45 CFR 94.5(a), including the development and implementation of a management plan and, if necessary, a retrospective review and a mitigation report regarding how any identified bias

was addressed, as discussed in further detail below. As a related matter, we have included a new paragraph (h) that cross-references the Institution's revised and expanded reporting requirements in the new paragraphs 42 CFR 50.605(b) and 45 CFR 94.5(b).

Consistent with our proposal in the NPRM, we have retained, but re-designated, the requirement of paragraph (e) of the 1995 regulations, *i.e.*, Institutions must maintain records of all financial disclosures and all actions taken by the Institution with respect to each FCOI for at least three years from the date of submission of the final expenditures report or final payment, or where applicable, for the other time periods specified in 45 CFR 74.53(b) or 48 CFR part 4, subpart 4.7. Specifically, in paragraph (i) of 42 CFR 50.604 and 45 CFR 94.4, we have included a responsibility to maintain records relating to all Investigator disclosures of financial interests and the Institution's review of, and response to, such disclosures (whether or not a disclosure resulted in the Institution's determination of an FCOI) and actions under the Institution's policy or retrospective review, if applicable, for that time period. We believe that this revision helps clarify for Institutions our intent for the record retention obligation to apply not only in cases in which the Institution has identified an FCOI, but to all Investigator SFI disclosures, whether or not such disclosure generated a response by the Institution.

One respondent suggested that retaining records for three years is insufficient. We disagree; this requirement is not substantially different from the requirement in the 1995 regulations, and is consistent with the PHS record retention policy. Another suggested that, since some awards continue for many years and disclosures now relate to the institutional responsibilities of Investigator, all records would have to be retained indefinitely. We disagree; as described in the NIH grants policy statement ([http://grants.nih.gov/grants/policy/nihgps\\_2010/nihgps\\_ch8.htm#\\_Toc271264975](http://grants.nih.gov/grants/policy/nihgps_2010/nihgps_ch8.htm#_Toc271264975)), records relating to all Investigator disclosures of financial interests and the Institution's review of, and response to, such disclosures, do not need to be retained indefinitely. Instead, the information must be retained for each competitive segment for a period of three years following the date the final expenditures report or final invoice is submitted to the PHS Awarding Component. In response to another comment, we also note that the record retention requirements in this paragraph

apply to records of all financial disclosures and actions under the Institution's policy, even if the policy is more stringent than the regulations.

Additionally, the 1995 regulations required at paragraph (f) that Institutions establish adequate enforcement mechanisms and provide for sanctions where appropriate. Consistent with our proposal in the NPRM, we have revised this obligation in a re-designated paragraph (j) to require an Institution not only to establish adequate enforcement mechanisms and provide for employee sanctions, but also to provide for other administrative actions to ensure Investigator compliance as appropriate. One respondent suggested that the choice of enforcement mechanisms be left to the discretion of each Institution, and that the PHS should not prescribe specific enforcement mechanisms for use in any type of situation. We note that the revised language strikes a balance between preserving the Institution's discretion in this regard and in enabling the PHS Awarding Component to exercise proper oversight; *e.g.*, the language does not specify particular actions as "adequate" or "appropriate," implicitly recognizing that the Institution and the PHS Awarding Component make those judgments on a case-by-case basis. Another respondent suggested that we consider revising the regulations to specify that FCOI committees, *i.e.*, institutional official(s), can disapprove or suspend PHS funding of Investigators who are not in compliance with these regulations. While this example may indeed account for appropriate action(s) under this provision and/or under the Remedies sections, we have not specified any one action in this particular context because of the need for discretion by the Institutions and the PHS Awarding Components, to account for the specific circumstances at issue. Additionally, providing this example in the regulatory text could create confusion between the suspension of an Investigator by an Institution under these regulations and the suspension or debarment of an Investigator by the PHS Awarding Component under 2 CFR part 376.

One respondent suggested that the PHS/HHS should be given enforcement power over any disclosure of significant financial interest that, although in technical compliance with the regulations is part of a plan or scheme to avoid the disclosure requirements, and referenced the Securities Act of 1933, as amended. We have not implemented this suggestion because we believe this concern is mitigated by

the aforementioned revisions to this section and by the ability of the HHS to inquire at any time (before, during, or after award) into any Investigator disclosure of financial interests and the Institution's review of, and response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of an FCOI.

Finally, consistent with the NPRM, we have revised the certification requirement that was set forth in paragraph (g) of the 1995 regulations. Re-designated paragraph (k) requires 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, and response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of an FCOI; and (5) shall fully comply with the requirements of the regulations. Notably, this revised paragraph eliminates much of the certification language in the 1995 regulations regarding an Institution's reporting obligations. This change is consistent with other critical changes to the regulations that we have implemented; specifically, we have substantially revised and expanded the reporting requirements, and included a discussion of such requirements in the revisions to 42 CFR 50.605(b) and 45 CFR 94.5(b), as discussed below.

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

Consistent with the NPRM, we have revised and expanded substantially the provisions of the 1995 regulations regarding management of FCOI to address requirements for both management and reporting of FCOI.

The 1995 regulations require at paragraph (a), that an Institution's designated official(s) review all financial disclosures and determine whether a conflict of interest exists; *i.e.*, the designated official(s) reasonably determines that an SFI could directly and significantly affect the design, conduct, or reporting of the PHS-funded

research. If a conflict is identified, the official(s) must determine what actions should be taken by the Institution to manage, reduce, or eliminate it. Paragraph (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.

Per our proposal in the NPRM, we have revised the above language as part of a re-designated paragraph (a)(1) to require that, prior to the Institution's expenditure of any funds under a PHS-funded research project, the designated official(s) of an Institution shall, consistent with paragraph (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 an 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. As noted in the preceding section, the Institution may involve the Investigator in determining whether an SFI is related to PHS-funded research.

One respondent suggested that this provision would require an Institution to identify and manage FCOI in advance of the Notice of Award and suggested a transition period of 60 days after award for the implementation of this provision, with an interim management plan in place during that time. In response, we note that this requirement refers to actions that need to be taken prior to expenditure of funds, not necessarily in advance of the award itself. In addition, development and implementation of an interim management plan for all identified FCOIs (instead of only those identified after the retrospective review discussed below) would seem to place an additional burden on the process of managing an identified FCOI, so we have declined that suggestion.

Some respondents suggested that the PHS Awarding Component or some other outside agency, but not Institutions, should have the responsibility for reviewing Investigator SFIs and identifying and managing FCOI, citing possible conflicts of interest of the designated institutional official(s), or the Institutions themselves. After considering this, we believe that the revisions that we have made to the regulations strike the

appropriate balance between the responsibilities of the Institution for determining and managing Investigator FCOI and the oversight responsibilities of the PHS Awarding Component. We believe that our revisions will strengthen the roles of all involved in this process. Additionally, we have included a discussion of institutional conflicts of interest in section IV of this final rule.

The most significant change that we have made to this section is the management plan requirement that we introduced in the NPRM. Although the 1995 regulations required Institutions to manage FCOI, the term "management plan" was not used. As we noted in the NPRM, many Institutions already have been developing and implementing management plans as a means of fulfilling their FCOI management responsibilities; explicitly incorporating this requirement in the regulations acknowledges the value of this practice as an important means to maintain objectivity in PHS-funded research across the research community. As indicated in the discussion of paragraph (b) below, the expanded reporting requirements include an obligation to report, at a minimum, a description of "key elements" of the Institution's management plan in certain FCOI reports.

As discussed in the NPRM, and for reasons explained above, we also have deleted the sentence in this section from the 1995 regulations that describes when an FCOI exists. A modified version of this sentence has been moved to the re-designated paragraph (f) of 42 CFR 50.604 and 45 CFR 94.4, as well as incorporated into a definition of FCOI in 42 CFR 50.603 and 45 CFR 94.3.

In the revised paragraph (a)(1), we have also included the following updated and expanded list of examples of conditions or restrictions that might be imposed to manage an FCOI: public disclosure of FCOI (*e.g.*, when presenting or publishing the research); disclosure of FCOI directly to participants in research projects involving human subjects research; appointment of an independent monitor capable of taking measures to protect the design, conduct, or reporting of the research against 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 financial conflicts.

One respondent suggested that disclosure alone is not sufficient for management of FCOI. Others suggested that the regulations should define a specific standard for acceptable conduct of research when an FCOI with PHS-funded research has been identified (*e.g.*, adopting the guidelines for conducting medical research published by AAMC and AAU), which could include defining the SFI that would preclude an Investigator from being a PD/PI on PHS-funded projects or requiring the Institution to consider the interests of patients explicitly. Another suggested that the risk of advancing potentially conflicted research should be weighed against the risk of not advancing the research. Given the wide range of contexts in which a conflict with PHS-funded research may arise, we believe that specifying particular standards or specific criteria may not cover all types of FCOI. Therefore, we have declined these suggestions, though we note that Institutions may choose a variety of measures, including those proposed by the respondents, in their evaluation of SFIs and in any specific management plan. In addition, as discussed in the NPRM and above, we posed a number of questions in the ANPRM on 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. Many of the respondents to the ANPRM thought that this approach would not account for the full range of research projects as well as the large variation in circumstances in which FCOI may arise. Moreover, the regulations do not include specific provisions related to the type of research, financial interest, or identified FCOI at issue.

Finally, respondents were concerned that the flexibility afforded to Institutions in determining how to manage SFIs that were determined to be FCOIs will lead to a lack of consistency across Institutions in the evaluation and management of Investigator FCOIs. Given the wide variety of contexts in which FCOIs can arise and the differences among Institutions, some variation across Institutions is expected. We believe that Institutions are in the best position to evaluate the circumstances and determine the most appropriate management strategies for specific cases.

Additionally, we have included the two paragraphs that we introduced in the NPRM (paragraphs (a)(2) and (a)(3)), with modifications, to clarify an Institution's obligations in situations in

which an Institution becomes aware of an SFI after the PHS-funded research is already underway. Specifically, paragraph (a)(2) states that whenever, in the course of an ongoing PHS-funded research project, a new Investigator participating in the research project discloses an SFI or an existing Investigator discloses a new SFI to the Institution, the designated official(s) of the Institution shall, within 60 days: Review the SFI disclosure; determine whether it is related to PHS-funded research; determine whether an 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. 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.

Paragraph (a)(3) states that whenever an Institution identifies an 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 official(s) shall, within 60 days: review the SFI; determine whether it is related to PHS-funded research; determine whether an FCOI 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 FCOI going forward; and (ii) In addition, whenever an FCOI is not identified or managed timely including:

- Failure by the Investigator to disclose an SFI that is determined by the Institution to constitute an FCOI;
  - Failure by the Institution to review or manage such an FCOI; or
  - Failure by the Investigator to comply with an FCOI management plan;
- the Institution shall, within 120 days of the Institution's determination of noncompliance, complete a retrospective review of the Investigator's activities and the PHS-funded research project to determine whether any PHS-funded research, or portion thereof, conducted during the time period of the noncompliance, was biased in the design, conduct, or reporting of such research.

The Institution is required to document the retrospective review; such documentation shall include, but not necessarily be limited to, all of the following key elements:

1. Project number;
2. Project title;
3. PD/PI or contact PD/PI if a multiple PD/PI model is used;
4. Name of the Investigator with the FCOI;
5. Entity with which the Investigator has a financial conflict of interest;
6. Reason(s) for the retrospective review;
7. Detailed methodology used for the retrospective review (*e.g.*, methodology of the review process, composition of the review panel, documents reviewed);
8. Findings of the review (*i.e.*, facts and observations); and
9. Conclusions of the review (*i.e.*, determination and recommended actions).

If bias is found, the Institution is required to notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component. The mitigation report must include, at a minimum, the key elements documented in the retrospective review above and a description of the impact of the bias on the research project and the Institution's plan of action or actions taken to eliminate or mitigate the effect of the bias (*e.g.*, impact on the research project; extent of harm done, including any qualitative and quantitative data to support any actual or future harm; analysis of whether the research project is salvageable). Thereafter, the Institution will submit FCOI reports annually, as specified elsewhere in the regulations. Depending on the nature of the FCOI, 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 FCOI or the Investigator's noncompliance is determined and the completion of the Institution's retrospective review.

As we explained in the NPRM,<sup>31</sup> these revisions are based, at least in part, on our experience working with Institutions and our observation 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 an SFI, particularly when such SFI is later determined to be an 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. In the NPRM we proposed to address this need in paragraph (a)(3) by the introduction of a "mitigation plan" requirement,<sup>32</sup> which we have clarified in the revised regulations as a "retrospective review" and "mitigation report," as provided above.

While one respondent agreed with the requirement for a mitigation plan in the case of a newly identified SFI that the Institution determines is an FCOI, many suggested that the proposed requirement for a mitigation plan was unnecessary. They thought that the goal of such a plan would be achieved by the review and management plan that Institutions are required to implement when they determine that an Investigator's SFI constitutes an FCOI, and that determining if there was bias in the design, conduct, or reporting of the PHS-funded research would be very difficult. Some respondents agreed, however, that it seems reasonable to expect the Institution to determine whether a mitigation plan is necessary. We have considered the comments and agree that the requirement for a mitigation plan may have been stated too broadly in the NPRM. Mitigation reports should only be used in cases where the Institution determines that a newly identified FCOI has resulted in bias in the design, conduct, or reporting of PHS-funded research. Respondents also suggested that the elements of the mitigation plan in the NPRM were unclear and requested additional guidance. To address these comments, we have revised the requirement, as provided above.

Paragraph (a)(4) requires the Institution to monitor Investigator compliance with the management plan on an ongoing basis until the completion of the PHS-funded research project. This paragraph dovetails with the new paragraphs (a)(2) and (a)(3), described above, by ensuring that the management actions taken by an Institution at the time an FCOI is identified continue to be followed by the Investigator(s) involved for the duration of the project.

In the NPRM we proposed to introduce at paragraph (a)(5) a new requirement to help the biomedical and behavioral research community as well as the public, Congress, and other interested parties monitor the integrity and credibility of PHS-funded research, and underscore our commitment to fostering transparency, accountability, and public trust. Specifically, we

proposed a new requirement 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 an FCOI.

We proposed to 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 proposed a requirement that the Institution update the posted information at least annually, and update the Web site within 60 days of the Institution's receipt or identification of information concerning any additional SFI that was not previously disclosed by the senior/key personnel for the PHS-funded research project, or upon the disclosure of an SFI by new senior/key personnel, if the Institution determines that the SFI is related to the PHS-funded research and is an FCOI. We proposed that information concerning the SFIs of an individual subject to this requirement 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 received many comments on this proposed requirement. Some respondents did not support this requirement, as they were concerned about privacy issues. A few respondents suggested that posting information about Investigator FCOI without the appropriate context would foster a negative perception of FCOI, and a couple of comments indicated that the requirements might conflict with state laws. Others suggested this requirement is unnecessary, given the disclosure

<sup>31</sup> 75 FR 28697 (May 21, 2010).

<sup>32</sup> 75 FR 28707 (May 21, 2010).

provisions required under the recently enacted Affordable Care Act. One respondent proposed that this information should be included in applications or proposals for PHS-funded research but not posted on a publicly accessible Web site. Several suggested that additional discussion of this provision is needed and requested that this requirement be omitted from the final rule at this time.

We are strongly committed to the value of transparency to the public, and we also appreciate the concerns raised by these respondents. In keeping with the increasing number and range of public disclosure initiatives, including those in the aforementioned Affordable Care Act, we believe it is important to make available to the public critical information affecting PHS-funded research. Consistent with statutory goals and Executive Order 13563, we believe the language that we have finalized in this rule strikes a reasonable balance of the public and private interests at issue.

Some respondents suggested that the information be made available upon request, rather than posted on a publicly available Web site. We carefully considered this suggestion and agree that making the information available upon request is in accordance with the overall goal of enhanced transparency. The chosen approach promotes such transparency without imposing undue burdens. Therefore, we have revised the regulations to state that the Institution must make the information publicly accessible and may do so by posting the information on a public Web site or by making the information available in writing within five business days of any request.

Several respondents thought that the requirement would constitute a substantial burden and cited the necessity of setting up a database structure. We note that the final rule does not require the information to be provided in a specific format. Therefore, an Institution could choose to provide the information as a simple document or spreadsheet.

A few respondents suggested that all Investigator SFIs or all payments from pharmaceutical companies, not only those that were determined to constitute an FCOI with PHS-funded research, should be provided. We disagree; we continue to believe that providing information on only those SFIs determined to be FCOIs with PHS-funded research provides the appropriate level of transparency, particularly as not all SFIs are determined to relate to PHS-funded research. However, Institutions are free to expand upon this requirement by

providing information on all SFIs of their Investigators. One respondent suggested that there should be a grading system to denote levels of conflicts of interest. We note that the determination of an FCOI by an Institution requires an assessment of how an SFI may cause an FCOI with the PHS-funded research, and how any such FCOI must be managed. It is at that point the Institution is judging the SFI and its potential to create an FCOI; there is no gradient associated with an FCOI itself. Additionally, we are concerned that this suggestion would undermine the premise that an Investigator's FCOI with PHS-funded research is not necessarily negative or prohibitive; the intent of the regulations is to ensure the appropriate management of such FCOIs in order to protect the objectivity of the research.

Other respondents supported the requirement for making information about Investigator's SFIs that were determined to be FCOIs with PHS-funded research publicly accessible. Many suggested that the PHS should host the information on a central Web site. Although we considered this suggestion at length, we continue to believe that Institutions are in a better position to provide and maintain this information. For example, the Institution will be able to put the information into context, as suggested by some respondents, e.g., by relating the information to the Institution's FCOI policies or to other information about the Investigator, as the Institution deems appropriate.

Several respondents requested that the regulations provide additional guidance as to exactly which Investigators are covered by this provision. Consistent with our proposal in the NPRM, we have applied the requirement to senior/key personnel for research grants and cooperative agreements and key personnel for research contracts. To provide further clarity, we also have included a new definition of senior/key personnel in 42 CFR 50.603 and of key personnel in 45 CFR 94.3. Because these definitions of "senior/key personnel" and "key personnel" include the PD/PI, we have limited the references in this section to "senior/key personnel" or "key personnel" to avoid confusion and redundancy. Others requested that this provision apply only to Investigators and not to their spouse or dependent children, or at least that the names of the spouse and dependent children not be posted. We note that, consistent with the proposal in the NPRM, the information provided must include the name of the Investigator and the nature of the SFI. Any SFIs of the Investigator's

spouse and dependent children will be attributed to the Investigator, such that only the Investigator's name would be provided.

Some respondents suggested that the dollar ranges included in this provision be the same as those required in reports of FCOI to the PHS Awarding Component. We agree with this suggestion and have revised the language accordingly. Although one respondent requested that no dollar amounts should be provided, while another suggested that the top range of \$250,000 is too low, we believe that the revised ranges provide the appropriate level of information. Respondents made several suggestions as to the length of time the information should remain available, ranging from two to three years. We agree with the specific comments that it would be useful to align the duration of the requirement for providing this information with the PHS records retention policy. Accordingly, we have revised the regulations to require that information concerning the SFIs that were determined to constitute FCOIs shall remain available for at least three years from the date that the information was most recently updated.

One respondent asked for clarification of how the criterion for providing information on an SFI that is still held by the Investigator would apply to payments or reimbursements. We note that the requirements for making information publicly accessible relate to those SFIs that were determined to be FCOIs. The regulations do not prevent Institutions from taking into account, during that evaluation process, whether the Investigator has an ongoing financial relationship with the entity providing the payment or reimbursement or whether the payment or reimbursement was limited in duration.

Finally, several respondents suggested that time is needed to allow Institutions to set up systems required to comply with the requirements in this paragraph. In particular, many suggested that implementation should be delayed to October 2013 to coincide with the implementation of the disclosure provisions of the Affordable Care Act. As specified in the "Compliance Date" paragraph in the Dates section above, we have provided time for implementation of the revised regulations such that 365 days after publication of the final rule, Institutions receiving PHS funding will be required to ensure public accessibility of information on FCOIs of senior/key personnel on research grants and cooperative agreements and of key personnel on research contracts via a publicly accessible Web site or by

making the information available in writing within five business days of any request, as required by 42 CFR 50.605 (a)(5) and 45 CFR 94.5 (a)(5).

Additionally, as proposed in the NPRM and discussed above, we have maintained the requirement of paragraph (b) of the 1995 regulations but restated it as follows: "In addition to the types of conflicting financial interests as defined in this subpart that must be managed pursuant to this section, an Institution may require the management of other financial conflicts of interests in its policy on financial conflicts of interest, as the Institution deems appropriate."

As we also proposed in the NPRM, we have included a substantial revision and expansion of Institutions' existing FCOI reporting requirements. Specifically, paragraph (b)(1) discusses the timing of initial FCOI reports and references the proposed management plan requirements addressed in the above discussion of paragraph (a): Prior to the Institution's expenditure of any funds under a PHS-funded research project, the Institution shall provide to the PHS Awarding Component an FCOI report regarding any Investigator's SFI found by the Institution to be an FCOI and ensure that the Institution has implemented a management plan in accordance with this subpart. We have clarified that, in cases in which the Institution identifies an FCOI and eliminates it prior to the expenditure of PHS-awarded funds, the Institution shall not submit an FCOI report to the PHS Awarding Component.

Similarly, paragraph (b)(2) discusses the timing of follow-up FCOI reports, with examples of when such reports may be required as well as references to the proposed management plan and retrospective review requirements addressed above in the discussion of paragraph (a): 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 an Investigator who is new to the research project), the Institution shall provide to the PHS Awarding Component, within 60 days, a report regarding the FCOI and ensure that the Institution has implemented a management plan in accordance with the regulations. Where such an FCOI report involves an 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 is required to complete a retrospective review 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. Additionally, if bias is found, the Institution is required to notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component.

Consistent with our proposal in the NPRM, paragraph (b)(3) discusses information that must be included in the FCOI reports required under paragraphs (b)(1) and (b)(2), described above. Specifically, such FCOI reports must 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. In addition to the minimum specific elements of the FCOI report that we proposed in the NPRM,<sup>33</sup> we have included a requirement to name the entity with which the Investigator has a financial conflict of interest, to enhance transparency and accountability.

The majority of respondents supported the requirement that Institutions provide this additional information to the PHS Awarding Component, although one respondent thought this was unnecessary. Another respondent thought that requiring Institutions to report key elements of the management plan would include information that Investigators might want to keep private. We have retained this requirement because we believe that receiving information on specific aspects of the management plan is necessary to ensure appropriate oversight by the PHS Awarding Component. We note that the regulations state under 42 CFR 50.606(b) and 45 CFR 94.6(b) that to the extent permitted by law, HHS will maintain the confidentiality of all records of financial interests. Another suggested the regulations require reporting of the exact dollar amount of the financial interest, rather than ranges. We did not make this change; the exact amount of some types of financial interests, such as equity, may change frequently, which could create ambiguity and intensify the administrative burden.

One respondent inquired as to whether the rationale for including the conflicted Investigator in the research project should include application of the "rebuttable presumption standard as articulated by AAMC" (i.e., "Institutional policies should establish the rebuttable presumption that an individual who holds a significant

financial interest in research involving human subjects may not conduct such research." <sup>34</sup>) We note that Institutions have the flexibility to use this standard in their evaluations of Investigator SFI, as long as they comply with the regulations. Other respondents questioned why the FCOI report should contain a rationale for including the conflicted Investigator in the research project since the credentials of the Investigator are included in the research application or proposal and were considered during the peer review process. Although our intent was to include the justification for permitting the Investigator with an FCOI to remain on the project, as opposed to the scientific rationale for the Investigator's involvement in the project, we have removed this element from the minimum requirements of the FCOI report to minimize confusion.

One respondent suggested it would be more efficient for Institutions to describe their monitoring measures annually for all FCOI reports rather than on a report-specific basis. We disagree; because the monitoring measures may differ depending on the requirements of the specific management plan, we believe that retaining that element in each report is important. Several respondents recommended deleting the requirement for a description of how the management plan will safeguard objectivity in the research project, as that is inherent in the management plan and should be apparent from the other information provided. We believe that documenting this element is important to ensure proper oversight; however, to address this comment, we have clarified this element to describe how the management plan is designed to safeguard objectivity in PHS-funded research.

One respondent suggested that this requirement be retained only for research involving human participants. As discussed in the NPRM and above, we posed a number of questions in the ANPRM on 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. The majority of the respondents to the ANPRM thought that this approach would not account for the full range of research projects as well as the

<sup>33</sup> 75 FR 28708 (May 21, 2010).

<sup>34</sup> AAMC Task Force on Financial Conflicts of Interest in Clinical Research: *Protecting Subjects, Preserving Trust, Promoting Progress—Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research*, December 2001 <https://www.aamc.org/download/75302/data/firstreport.pdf>.

large variation in circumstances in which FCOIs may arise. As a result, the regulations, including the provisions in this paragraph, impose uniform FCOI management responsibilities, regardless of the type of research, financial interest, or identified FCOI at issue. Nonetheless, we note that Institutions are free to differentially manage FCOI depending on the nature of the research as long as they remain in full compliance with the regulations.

A few respondents requested that the regulations include additional examples of appropriate elements of a management plan, such as the use of independent monitors or a description of circumstances in which eliminating an FCOI is necessary. Given the wide range of circumstances in which FCOI may occur and the importance of tailoring institutional review and determination to each specific case, we believe that including additional examples may be interpreted as prescriptive and may be misconstrued as the only means of managing a particular type of conflict. Nonetheless, as described above, a list of examples of conditions or restrictions that might be imposed to manage an FCOI is described in 42 CFR 50.605(a)(1) and 45 CFR 94.5(a)(1). One respondent requested that the HHS develop templates for reporting FCOIs to the PHS Awarding Component. Because the regulations describe the basic information required in these reports, we believe that templates are unnecessary.

One respondent noted that the regulations do not state how the PHS Awarding Component will respond to the FCOI reports submitted by Institutions and recommended that HHS establish a policy on the responsibilities of the PHS Awarding Component, while another requested that agency staff receive training in the review of FCOI reports submitted to the PHS Awarding Component to ensure consistency. In response to these comments, we want to assure stakeholders that we have in place procedures and guidance on how staff should respond to FCOI reports submitted by Institutions, and we provide training on the evaluation of information that we receive from Institutions about FCOIs with PHS-funded research. We have taken and are continuing to take steps to increase oversight of the FCOI regulations. For example, NIH has:

- Conducted a thorough review of its system of oversight and compliance with respect to the FCOI regulations with the purpose of ensuring that a vigorous and effective oversight system is in place.

- Developed an FCOI Reporting Module as a tool for Institutions to electronically manage and submit FCOI reports to NIH. This module provides consistent reporting of FCOIs to the NIH. The system interfaces with the Web-based reporting tool for NIH staff already in use and will provide a full spectrum of tracking and oversight capabilities for NIH extramural staff. Mandatory use of the FCOI Module went into effect during FY 2009.<sup>35</sup>

- Developed an FCOI review protocol for use by staff in evaluating institutional FCOI reports and conducted mandatory training for extramural program and grants management staff on the use of the protocol and other FCOI issues.

- Routinely conduct in-depth reviews of cases of alleged FCOI involving extramural grantees and will continue to do so as new allegations arise.

- Evaluate and analyze grantee Institutions' FCOI policies and practices on an ongoing basis.

- Formed an FCOI Liaison group consisting of representatives from each of the NIH Institutes and/or Centers (IC) to discuss FCOI issues and guide FCOI activities in their respective ICs, with assistance from the Office of Extramural Research.

- Developed and included new language for NIH's "Notice of Award" template that highlights FCOI requirements.

- Developed and conducted a number of initiatives and site visits to evaluate institutional FCOI policies for compliance with the regulation. These initiatives include:

- NIH Pilot Compliance Program on FCOI.

- NIH Targeted Site Reviews.

- Following evaluation of the institutional FCOI policies, publicized on-line "Lessons Learned" to encourage enhanced compliance in the grantee community.

- Issued a number of communications to remind extramural grant recipients of their FCOI compliance responsibilities. These communications include:

- Articles (NIH OER "Nexus" newsletter).

- NIH Guide Notices.

- E-mails to Institutional officials.

- Continue to respond to grantee questions directed to the OER FCOI mailbox concerning compliance with the Federal regulation.

- Provide education and outreach activities aimed at raising awareness of the issues surrounding FCOI at the institutional and Investigator levels (e.g., NIH Regional Seminars;

presentations at professional organizations and meetings).

These policies and guidance will be updated to incorporate all revisions implemented in this final rule, and we will continue to train the relevant staff, as necessary.

As proposed in the NPRM, paragraph (b)(4) includes a requirement to provide follow-up reports in cases in which an FCOI has been previously identified and reported. Specifically, for any FCOI previously reported by the Institution with regard to an ongoing PHS-funded research project, the Institution shall provide to the PHS Awarding Component an annual FCOI report that addresses the status of the FCOI and any changes to the management plan for the duration of the PHS-funded research project. The annual FCOI report must specify whether the financial conflict is still being managed or explain why the FCOI no longer exists. The Institution must 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.

A few respondents suggested that providing a report annually when there has been no change to the FCOI or its management is unnecessary. We have considered this suggestion but believe that annual notification, even if there are no changes, is necessary to provide appropriate assurance to the PHS Awarding Component that an identified FCOI continues to be managed throughout the period of the PHS-funded research. One respondent suggested that the regulations allow the Institution to determine the frequency of reporting on identified FCOIs, depending on the type of PHS-funded research and the nature of the conflict. As discussed above, the regulations impose uniform FCOI management responsibilities, regardless of the type of research, financial interest, or identified FCOI at issue to account for the full range of circumstances in which FCOI may arise. Finally, while several respondents requested that the timing of the annual reports be determined by the Institution rather than the PHS Awarding Component, we have determined that the reports need to be provided in the time and manner specified by the PHS Awarding Component in order to facilitate appropriate and efficient oversight.

Finally, as proposed in the NPRM, paragraph (b)(5) includes language with regard to FCOI reporting that is similar to the language for FCOI management in the re-designated paragraph (a)(6), described above. Namely, in addition to

<sup>35</sup> OMB No. 0925-0417.

the types of financial conflicts of interest that must be reported pursuant to this section, an Institution may require the reporting of other FCOI in its policy on financial conflicts of interest, as the Institution deems appropriate.

*Remedies (42 CFR 50.606, 45 CFR 94.6)*

In both the NPRM and the Extension Notice, we welcomed public comments regarding the need to further revise and clarify this section, with respect to PHS' enforcement authority in the event of noncompliance with the regulations. Although we did not receive a high volume of comments on this topic, we took all feedback into consideration when finalizing the rule. We appreciate this opportunity to emphasize our commitment to effective oversight, which requires a partnership between the PHS Awarding Components and the Institutions. The regulations make clear that Institutions are responsible for ensuring Investigator compliance with institutional policies and procedures, and it is necessary for Institutions to establish appropriate consequences for noncompliance. However, it is equally essential that the PHS Awarding Components consider appropriate enforcement action. We believe that the revised regulations strike an appropriate balance of responsibilities in this regard.

In general, several respondents supported our proposal to refine the discussion of remedies in the 1995 regulations. Although one respondent expressed concern that the regulations seem to lack meaningful enforcement mechanisms and remedies, we believe that the Remedies section supports a range of possible corrective and remedial actions for the PHS Awarding Components and the Institutions to consider. Additionally, we believe it is important to weigh the specific circumstances of each particular case when pursuing such action(s) and to retain a full range of available options. For that reason, we have declined to incorporate some of the additional "penalties" that a few respondents suggested, such as monetary fines, dismissals, or jail times for Investigators; fines for Institutions; or, as one respondent suggested, "referrals to the FDA \* \* \* to bar participation by the individual in any clinical study designed to seek marketing approval." Likewise for that reason, we have not incorporated the suggestion of another respondent to include a specific requirement that if an Institution takes enforcement action against an Investigator, PHS should automatically "impose penalties directly on an Investigator."

We did, however, agree with one respondent that it would be helpful to clarify, in the grants context in particular, that institutional sanctions against an Investigator can travel with the Investigator upon his or her transfer to another Institution. Specifically, we have revised 42 CFR 50.606, paragraph (a), as follows: "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 PHS-funded research project. The PHS may, for example, require Institutions employing such an Investigator to enforce any applicable corrective actions prior to a PHS award or when the transfer of a PHS grant(s) involves such an Investigator."

This revision is intended to reference the range of options for the PHS Awarding Component to consider, depending on the specific circumstances at issue. For example, PHS may decide to initiate government-wide suspension or debarment of the Investigator under 2 CFR part 376; or to use enforcement measures under 45 CFR 74.62, *e.g.*, perhaps to make the approval of a transfer contingent upon the former Institution's disclosure of the corrective action—including the specific sanctions against the Investigator—to the new Institution; and/or to use special award conditions under 45 CFR 74.14, *e.g.*, perhaps to make the new Institution agree to take the same or similar action against that Investigator or explain to the PHS Awarding Component in writing why such action was not taken and what alternative measures will be used to ensure compliance.

One respondent suggested that the regulations include a description of a process to resolve differences of opinion between the PHS Awarding Component and the Institution regarding evaluation and management of FCOIs. We declined that change, as we believe it would be unnecessary and overly prescriptive to impose a particular process as a regulatory requirement; we will continue to work collaboratively with Institutions to resolve any such differences on a case by case basis,

taking into consideration the specific circumstances of each disagreement. We note, however, that the Institution may have an opportunity for a hearing, appeal, or other administrative process or proceeding to which it is entitled under any applicable statute or regulation, in the event that the PHS Awarding Component takes enforcement action against the Institution.

As we proposed in NPRM, we also have revised paragraph (b) to clarify 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, and response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of an FCOI. Consistent with the 1995 regulations, an Institution must submit, or permit on site review of, all records pertinent to compliance with the regulations. One respondent suggested that the regulations restrict the period during which HHS may inquire to a defined number of years after the end of the award period. We have not made this change because the effects of compromising objectivity in PHS-funded research may continue for some time after the award period. Another suggested that the regulations state that HHS may request information not deemed relevant to a finding of FCOI only for the purpose of investigating an allegation of noncompliance with these rules. Although we agree that an allegation of noncompliance is one circumstance that could trigger this provision, we disagree that it would be appropriate to limit HHS' oversight authority to this specific event.<sup>36</sup>

In paragraph (b), we also have retained the statement in the 1995 regulations that, to the extent permitted by law, HHS will maintain the confidentiality of all records of financial interests. In response to a question from a respondent, we note that this includes the information required under 42 CFR 50.605(b) and 45 CFR 94.5(b).

As we proposed in the NPRM, we have revised paragraph (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,

<sup>36</sup> Among other examples of HHS' oversight authority, we note that with regard to grants or cooperative agreements from HHS to Institution of higher education, hospitals, other non-profit organizations, and commercial organizations, HHS awarding agencies have the right of timely and unrestricted access to any books, documents, papers, or other records of recipients that are pertinent to its awards, to make audits, examinations, excerpts, transcripts and copies of such documents. See 45 CFR 74.53(4)(e).

medical device, or treatment has been designed, conducted, or reported by an Investigator with an 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. One respondent suggested that this requirement may not achieve the desired aim, as Investigators could refrain from publicly presenting their results and publishers could refuse to publish the addendum or could publish it in an inconspicuous manner. We have implemented the proposed language from the NPRM because we believe the disclosure requirements as modified further the objective of the regulations to promote objectivity in research. Institutions are in the position to identify other actions that may be appropriate in such instances, depending on the specific case. We also note that the provision regarding public presentations has been in place since the 1995 regulations and that the revision merely expands the potential venues in which the FCOI must be disclosed, which is intended to strengthen transparency and accountability.

#### *Other HHS Regulations That Apply (42 CFR 50.607)*

As we proposed in the NPRM, we have revised the list of other HHS regulations that apply, to update changes that have been made in the CFR location or title of the references in this section since 1995. In the NPRM, we asked for comment on whether the regulations should be further revised to delete this section. Only one respondent suggested deleting this section; we have retained it as a useful point of reference.

#### **IV. Institutional Conflict of Interest**

Institutional conflict of interest is a subject that is not specifically addressed in the 1995 regulations for reasons stated in the 1995 final rule.<sup>37</sup> Because this is a topic of increasing interest to HHS as well as in the research community, we invited 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.<sup>38</sup>

Consistent with the public comments that we received on this topic, we continue to 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 1995 regulations address Investigator FCOI. Because we believe it is important to revise the 1995 regulations in a timely manner, specific revisions that we proposed in the NPRM were limited to the subject of Investigator FCOI.

In the NPRM, we asked for public comments 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. We received a wide range of responses to this question, with some respondents stating that the regulations should include a basic provision requiring Institutions to have a policy on institutional conflict of interest without specifying the nature or scope of such a policy, and others suggesting that it would be premature to include such a provision in the regulations. Respondents in both groups urged HHS to engage the biomedical research community in discussions on the definition of institutional conflict of interest and how it should be addressed. One respondent suggested that the regulations should include a definition of institutional conflict of interest and specific provisions for policies addressing the issue.

We have considered all the comments and believe that requiring Institutions to have a policy on institutional conflict of interest without providing additional guidance as to the nature and scope of that policy would lead to confusion and inconsistencies across Institutions. We also believe that substantial additional information and deliberations are needed to formulate such guidance. Therefore, we have limited the final rule to Investigator conflict of interest. HHS will continue to consider the issue of institutional conflict of interest together with the biomedical research community, including the question of whether it is appropriate to propose specific regulations to address this subject.

#### **V. Regulatory Impact Analyses (RIA)**

The following is provided as public information.

##### *Analysis of Impacts*

We have examined the impacts of the amendments to 42 CFR part 50 subpart F and 45 CFR part 94 under Executive

Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4). Executive Orders 13563 and 12866 direct agencies to assess all costs and benefits of available regulatory alternatives and, if regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, distributive impacts, and equity). Executive Order 13563 emphasizes the importance of quantifying both costs and benefits, of reducing costs, of harmonizing rules, and of promoting flexibility. This rule has been designated a “significant regulatory action” although not economically significant, under section 3(f) of Executive Order 12866. Accordingly, the rule has been reviewed by the Office of Management and Budget.

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 2,800 such organizations<sup>39</sup> apply to NIH for research funding annually, of which approximately 1,300 Institutions<sup>40</sup> are awarded funds. These regulations do not cover SBIR/STTR Program Phase I applications or awards. Therefore, the provisions of the regulations apply to the approximately 800 applicants to the SBIR/STTR Phase II program annually, of which approximately 300 Institutions receive funding. There is no change to the 1995 regulations that pertain specifically to applicant organizations. Rather, all changes to the regulations apply only to the approximately 300 small business concerns that receive Phase II SBIR/STTR PHS funding. The cost of implementing the amended regulations is an allowable cost that may be eligible for reimbursement as a Facilities and Administrative cost on PHS-supported grants, cooperative agreements and contracts. This could offset the cost burdens of implementation. Therefore, we do not believe that the changes to the regulations will have a significant economic impact on a substantial number of small entities. Our analysis is

<sup>39</sup> All applicant Institution numbers are based on the number of Institutions that applied for NIH funding in FY 2008.

<sup>40</sup> All applicant Institution numbers are based on the number of Institutions that applied for NIH funding in FY 2008.

<sup>37</sup> 60 FR 35813 (July 11, 1995).

<sup>38</sup> 74 FR 21612 (May 8, 2009).

further supported by the small number of FCOI reports submitted by small business concerns; for example, ten reports by small business concerns were submitted to NIH in FY 2009 and eleven in FY 2010. We also considered the impact of the requirement for Investigator training on small entities and have lowered the frequency of training required from every two years as proposed in the NPRM to every four years. We believe this expanded timeframe will decrease the burden on Institutions, including small businesses. In addition, for the 1995 regulations, NIH developed training materials that Institutions 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 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 \$143.5 million.<sup>41</sup> The agency does not expect that the amendments to the regulations will result in any 1-year expenditure that would meet or exceed this amount.

**Benefits**

The amendments to the regulations will 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. Specifically, the revisions will provide Institutions with additional information on Investigator financial interests so they can make a more informed evaluation of whether the disclosed SFI constitutes an FCOI with PHS-funded research. Also, the revisions will provide HHS with additional information on an identified FCOI to enable improved oversight. Finally, the revised regulations will provide interested stakeholders such as Congress and the public with information about Investigator financial interests that were identified as an FCOI with research funded by PHS, enabling increased transparency and accountability, with the goal of preserving and strengthening public trust in the output of the Federal investment in biomedical research.

**Costs**

Approximately 3000 Institutions that apply for PHS funding annually are subject to the regulations. As there are no changes to the regulations in the requirements for Institutions that are applying for PHS-funding, the amendments will affect the approximately 2000 organizations (including small businesses but excluding those that receive funding through the SBIR/STTR Phase I program) that are awarded PHS funding annually and, through the implementation of the regulations by the Institutions, to the estimated 38,000 Investigators (using the definition of Investigator in the regulations) participating in PHS-funded research that have SFIs. Many of the revisions expand requirements that already existed in the regulations. For instance,

the number of Investigators who would be required to disclose their SFI is unchanged under the revised regulations as the definition of Investigator is not changed substantially. That said, however, Investigators would be required to disclose a larger number of financial interests due to the revisions to the SFI definition (e.g., changing the de minimis from \$10,000 to \$5,000, and including income from a subset of non-profit Institutions). Also, Institutions are already required to report any identified FCOI to the PHS Awarding Component under the 1995 regulations. The revised regulations will require these reports to contain additional information. Several new requirements are included in the revised regulations, including the requirement for making information available upon request and the requirement for a retrospective review in those rare cases in which an Institution identifies noncompliance with the regulations. We discuss the rationale for each of these requirements in the preamble. In sum, the estimated burden for current implementation of the 1995 regulations is approximately 80% of the burden estimated for implementing the revised regulations.

The cost of implementing the amended regulations is an allowable cost that may be eligible for reimbursement as a Facilities and Administrative cost on PHS supported grants, cooperative agreements and contracts. This could offset some portion of the cost burdens of implementation for the affected Institutions and through their implementation of the regulations, to the Investigators. Nonetheless, we are including a description of the estimated costs of the amendments to the regulations for general information.

Section of 42 CFR part 50 subpart F or 45 CFR part 94	Number of respondents	Frequency of response (annual)	Estimated cost per response <sup>42</sup>	Estimated annual cost <sup>43</sup>
50.602 or 94.2 .....	Total: approximately 3,000 applicant Institutions and 2,000 awardee Institutions (based on FY 2008 numbers) and an estimated 38,000 Investigators.	NA .....	NA.	
50.604 or 94.4				
(a) .....	3,000 <sup>44</sup> .....	1 .....	\$2,835 .....	\$8,505,000.
(b) .....	Institutions: 2,000 <sup>45</sup> .....	Institutions: 1 .....	Institutions: \$210 ..	Institutions: \$420,000.
	Investigators: 38,000 <sup>46</sup> .....	Investigators .....	Investigators: ..	Investigators: \$665,000.
		0.25 <sup>47</sup> .	\$17.5 <sup>48</sup> .	Total: \$1,085,000.
			Total: \$227.5.	
(c)(1) .....	500 <sup>49</sup> .....	1 .....	\$35.00 .....	\$17,500.
(c)(2) .....	Included in the cost estimate in 50.605/94.5(b)(3).	NA .....	NA.	
(d) .....	3,000 <sup>50</sup> .....	1 .....	\$35 .....	\$105,000.
(e)(1) .....	38,000 <sup>51</sup> .....	1 .....	\$140 .....	\$5,320,000.

<sup>41</sup> Bureau of Labor Statistics inflation calculator.

Section of 42 CFR part 50 subpart F or 45 CFR part 94	Number of respondents	Frequency of response (annual)	Estimated cost per response <sup>42</sup>	Estimated annual cost <sup>43</sup>
(e)(2) .....	38,000 <sup>52</sup> .....	1 .....	\$35.00 .....	\$1,330,000.
(e)(3) .....	950 <sup>53</sup> .....	1 .....	\$17.50 .....	\$8,313.
(f) .....	2,000 awardee Institutions .....	1 .....	\$35.00 .....	\$70,000.
(g) .....	Included in the cost estimate in 50.605/94.5(a)(1).	NA .....	NA.	
(h) .....	Included in the cost estimate in 50.605/94.5(b)(3).	NA .....	NA.	
(i) .....	2,000 awardee Institutions .....	1 .....	\$140 .....	\$280,000.
(j) .....	Included in the cost estimate in 50.604/94.4(a).	NA .....	NA.	
(k) .....	Included in the cost estimate in 50.604/94.4(a).	NA .....	NA.	
50.605 or 94.5				
(a)(1) .....	2,000 awardee Institutions <sup>54</sup> .....	1 .....	\$70 for review and \$2,800 for developing management plan.	\$2,660,000 for review of all disclosures plus \$2,660,000 for developing management plans of those identified as FCOI.
(a)(2) .....	950 <sup>55</sup> .....	NA .....	Total: \$2,870 .....	Total: \$5,320,000.
(a)(3) .....	The cost is included in 50.605/94.5(b)(2) below.		NA .....	NA.
(a)(3)(i) .....	500 <sup>56</sup> .....	1 .....	\$105 .....	\$52,500.
(a)(3)(ii) .....	50 <sup>57</sup> .....	1 .....	\$2,800 .....	\$140,000.
(a)(3)(iii) .....	50 <sup>58</sup> .....	1 .....	\$2,800 .....	\$140,000.
(a)(4) .....	50 .....	1 .....	\$35 .....	\$1,750.
(a)(5) .....	950 <sup>59</sup> .....	1 .....	\$420 .....	\$399,000.
(b)(1) .....	2,000 <sup>60</sup> .....	1 .....	\$175 .....	\$350,000.
(b)(2) .....	Cost included in 50.605(b)(3)/94.5(b)(3) below.	NA .....	NA .....	NA.
(b)(2) .....	50 FCOI reports as in a(3)(ii) above <sup>61</sup> 5 mitigation reports <sup>62</sup> .....	1 for reporting FCOI and 1 for mitigation reports in the case bias was determined during the retrospective review.	\$70 for FCOI report and \$70 for mitigation report.	\$70 × 50 = \$3,500 for FCOI report and \$70 × 5 = \$350 for mitigation report. Total = \$3,850.
(b)(3) .....	950 <sup>63</sup> .....	1 .....	\$70 .....	\$66,500.
(b)(4) .....	950 <sup>64</sup> .....	1 .....	\$35.00 .....	\$33,250.
50.606 or 94.6				
(a) <sup>65</sup> .....	20 <sup>66</sup> .....	1 .....	\$350 .....	\$7,000.
(c) .....	50 <sup>67</sup> .....	3 <sup>68</sup> .....	\$31.50 .....	\$1,575.

Total annual cost: \$23,236,238.

<sup>42</sup> Average burden hours × \$35/hour based on recent NIH cost analyses.

<sup>43</sup> Number of respondents × estimated cost per response.

<sup>44</sup> Assumes 3,000 applicant Institutions and 80 hours per Institution for formulating and maintaining the policy. Also assumes that most Institutions already maintain a public Web site. Therefore, posting the policy to the Web site or providing it upon request is an incremental cost—estimated at 1 hour annually.

<sup>45</sup> Assumes that 2,000 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 = 5 hours.

<sup>46</sup> Assumes 38,000 Investigators undergo 2 hours of training every four 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.

<sup>47</sup> Once every 4 years.

<sup>48</sup> \$70 every 4 years.

<sup>49</sup> An estimated maximum 25% of Institutions may have subrecipients in any one year—assuming 1 hour per Institution to incorporate the requirement of the regulations into an already existing written agreement. Includes burden on subrecipients.

<sup>50</sup> Assuming that 3,000 Institutions solicit disclosures on an annual basis by sending a notification to all Investigators.

<sup>51</sup> The financial disclosure burden estimate is based upon an Investigator figure of 38,000 with an average response time of 4 hours.

<sup>52</sup> Assuming that updating a disclosure takes less time/effort than creating a new one—1 hour.

<sup>53</sup> Assuming that only a small number of the 38,000 Investigators will have a new SFI in any year.

<sup>54</sup> Although an estimated 950 reports of Conflict of Interest are expected annually, the 2,000 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 76,000 hours is based upon estimates that it will take on the average 2 hours for an institutional official(s) to review each of 38,000 financial disclosures associated with PHS funded awards. The burden for developing a management plan for identified FCOI is estimated at 80 hours × 950 cases = 76,000 hours.

<sup>55</sup> Based on 50.604/94.4(e)(3) above.

<sup>56</sup> Assuming that this is a rare occurrence, based on prior experience.

<sup>57</sup> Assuming only a fraction of the newly identified SFIs will constitute FCOI.

<sup>58</sup> Assuming only a fraction of the newly identified SFIs will constitute FCOI.

<sup>59</sup> Based on previous assumption of 950 FCOI reports annually—estimated 12 hours annually, which may consist of 1 hour monthly or any other division the Institution deems appropriate.

<sup>60</sup> Since the information could be provided as a simple document or spreadsheet, providing the required information to multiple requestors or adding it to an existing Web site is an incremental cost. Updating annually does have an additional cost.

<sup>61</sup> 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.

<sup>62</sup> After retrospective review—the cost of which is accounted for in a(3)(ii) above—we estimate that bias will be found in only a fraction of cases.

<sup>63</sup> Assumes 950 FCOI reports annually × 2 hours to prepare the report/complete an NIH-provided Web form.

<sup>64</sup> Assumes it takes less time to update a report than to create a new one—1 hour per update.

<sup>65</sup> This estimate includes inquiries by the PHS Awarding Component as described in 50.606.(b) and 94.6(b) and in accordance with 50.604(k) and 94.4(k).

<sup>66</sup> 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 Fed. Reg. 132 (July 11, 1995) pps. 35810–35819. This burden estimate, and others was increased in 2002 "due to increased numbers of Institutions and Investigators." Although there has been an increase in the number of cases of noncompliance in the past few years, the number has not approached this estimate so we believe it is still reasonable.

<sup>67</sup> 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 estimated cost.

<sup>68</sup> Assuming an average of 3 publications annually.

Alternatives

The key alternative to the amendment of these regulations would be to continue to operate under the 1995 regulations. In the intervening years since the regulations were promulgated, Investigator collaborations have become more complex and public scrutiny has increased significantly creating an environment that would benefit from regulation with more effective means for management and oversight. If we continue to operate under the 1995 regulations, we would then lose the opportunity to implement enhanced Institutional management of Investigator FCOIs related to PHS-funded research, increased oversight by the PHS Awarding Component, and enhanced transparency. In addition, Congress has expressly directed and supported the ongoing regulation of FCOI (42 U.S.C. 216, 289b–1, 299c–4; Sec. 219, Tit. II, Div. D, Pub. L. 111–117, 123 Stat. 3034), and we agree that strengthening such regulation is necessary to enhance

public trust and ensure the responsible stewardship of Federal funds.

*Paperwork Reduction Act*

This final 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.

42 CFR 50.604(i), and 45 CFR 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 revised 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 approval, we will publish the OMB control number in the **Federal Register**.

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

Section of 42 CFR part 50 subpart F or 45 CFR part 94	Number of respondents	Frequency of response (annual)	Average burden hours	Annual burden hours <sup>69</sup>
50.602 or 94.2	Total: approximately 3,000 applicant Institutions and 2,000 awardee Institutions (based on FY2008 numbers) and an estimated 38,000 Investigators.	NA	NA.	
50.604 or 94.4				
(a)	3,000 <sup>70</sup>	1	81 <sup>71</sup>	243,000.
(b)	Institutions: 2,000 <sup>72</sup> Investigators: 38,000 <sup>73</sup>	Institutions: 1 Investigators 0.25 <sup>74</sup>	Institutions: 6 Investigators: 0.5 <sup>75</sup>	Institutions: 12,000. Investigators: 19,000. Total: 31,000.
(c)(1)	500 <sup>76</sup>	1	1	500.
(c)(2)	Included in the burden estimate in 50.605/94.5 (b)(3).	NA	NA	NA.
(d)	3,000 <sup>77</sup>	1	1	3,000.
(e)(1)	38,000 <sup>78</sup>	1	4	152,000.
(e)(2)	38,000 <sup>79</sup>	1	1	38,000.
(e)(3)	950 <sup>80</sup>	1	0.5	475.
(f)	2,000 awardee Institutions	1	1	2,000.
(g)	Included in the burden estimate in 50.605/94.5 (a)(1).	NA	NA	NA.
(h)	Included in the burden estimate in 50.605/94.5 (b)(3).	NA	NA	NA.
(i)	2,000 awardee Institutions	1	4	8,000.
(j)	Included in the burden estimate in 50.604/94.4 (a).	NA	NA	NA.

Section of 42 CFR part 50 subpart F or 45 CFR part 94	Number of respondents	Frequency of response (annual)	Average burden hours	Annual burden hours <sup>69</sup>
(k) .....	Included in the burden estimate in 50.604/94.4 (a).	NA .....	NA .....	NA.
50.605 or 94.5				
(a)(1) .....	2,000 awardee Institutions <sup>81</sup> .....	1 .....	2 hours per disclosure to review plus 80 hours per identified FCOI to develop management plan.	76,000 for reviewing disclosures from 38,000 Investigators plus 76,000 for developing management plans for 950 identified FCOIs = 152,000.
(a)(2) .....	950 <sup>82</sup> .....	NA .....	NA .....	NA.
	The burden is included in 50.605/94.5 (b)(2) below.			
(a)(3) .....	500 <sup>83</sup> .....	1 .....	3 .....	1,500.
(a)(3)(i) .....	50 <sup>84</sup> .....	1 .....	80 .....	4,000.
(a)(3)(ii) .....	50 <sup>85</sup> .....	1 .....	80 .....	4,000.
(a)(3)(iii) .....	50 .....	1 .....	1 .....	50.
(a)(4) .....	950 <sup>86</sup> .....	1 .....	12 .....	11,400.
(a)(5) .....	2,000 <sup>87</sup> .....	1 .....	5 .....	10,000.
(b)(1) .....	Included in 50.605(b)(3)/94.5 (b)(3) below.	NA .....	NA .....	NA.
(b)(2) .....	50 FCOI reports as in a(3)(ii) above <sup>88</sup> 5 mitigation reports <sup>89</sup> .....	1 for reporting FCOI and 1 for mitigation reports in the case bias was determined during the retrospective review.	2 for FCOI report and 2 for mitigation report.	50×2 = 100 for FCOI report and 5×2=10 for mitigation report. Total =110.
(b)(3) .....	950 <sup>90</sup> .....	1 .....	2 .....	1,900.
(b)(4) .....	950 <sup>91</sup> .....	1 .....	1 .....	950.
50.606 or 94.6				
(a) <sup>92</sup> .....	20 <sup>93</sup> .....	1 .....	10 .....	200.
(c) .....	50 <sup>94</sup> .....	3 <sup>95</sup> .....	0.3 .....	45.

Total burden hours: 664,130.

<sup>69</sup> Number of respondents × average burden hours × frequency of response.

<sup>70</sup> Assumes 3,000 applicant Institutions and 80 hours per Institution for formulating and maintaining the policy. Also assumes that most Institutions already maintain a public Web site. Therefore, posting the policy to the Web site or providing it upon request is an incremental burden—estimated at 1 hour annually.

<sup>71</sup> 80 h for policy formulation and maintenance; 1h for posting the policy or providing it upon request.

<sup>72</sup> Assumes that 2,000 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 = 5 hours.

<sup>73</sup> Assumes 38,000 Investigators undergo 2 hours of training every four 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.

<sup>74</sup> Once every 4 years.

<sup>75</sup> 2 hours every 4 years.

<sup>76</sup> An estimated maximum 25% of Institutions may have subrecipients in any one year—assuming 1 hour per Institution to incorporate the requirement of the regulations into an already existing written agreement. Includes burden on subrecipients.

<sup>77</sup> Assuming that 3,000 Institutions solicit disclosures on an annual basis by sending a notification to all Investigators.

<sup>78</sup> The financial disclosure burden estimate is based upon an Investigator figure of 38,000 with an average response time of 4 hours.

<sup>79</sup> Assuming that updating a disclosure takes less time/effort than creating a new one—1 hour.

<sup>80</sup> Assuming that only a small number of the 38,000 Investigators will have a new SFI in any year.

<sup>81</sup> Although an estimated 950 reports of Conflict of Interest are expected annually, the 2,000 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 76,000 hours is based upon estimates that it will take on the average 2 hours for an institutional official(s) to review each of 38,000 financial disclosures associated with PHS funded awards. The burden for developing a management plan for identified FCOI is estimated at 80 hours × 950 cases = 76,000 hours.

<sup>82</sup> Based on 50.604/94.4 (e)(3) above.

<sup>83</sup> Assuming that this is a rare occurrence based on prior experience.

<sup>84</sup> Assuming only a fraction of the newly identified SFIs will constitute FCOI.

<sup>85</sup> Assuming only a fraction of the newly identified SFIs will constitute FCOI.

<sup>86</sup> Based on previous assumption of 950 FCOI reports annually—estimated 12 hours annually, which may consist of 1 hour monthly or any other division the Institution deems appropriate.

<sup>87</sup> Since the information could be provided as a simple document or spreadsheet, providing the required information to multiple requestors or adding it to an existing Web site is an incremental burden. Updating annually does have an additional burden.

<sup>88</sup> 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.

<sup>89</sup> After retrospective review—the burden of which is accounted for in a(3)(ii) above—we estimate that bias will be found in only a fraction of cases.

<sup>90</sup> Assumes 950 FCOI reports annually × 2 hours to prepare the report/complete an NIH-provided Web form.

<sup>91</sup> Assumes it takes less time to update a report than to create a new one—1 hour per update.

<sup>92</sup> This estimate includes inquiries by the PHS Awarding Component as described in 50.606.(b) and 94.6.(b) and in accordance with 50.604(k) and 94.4(k).

<sup>93</sup> 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." Although there has been an increase in the number of cases of noncompliance in the past few years, the number has not approached this estimate so we believe it is still reasonable.

<sup>94</sup> 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 estimated burden.

<sup>95</sup> Assuming an average of 3 publications annually.

### 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.

### Catalogue of Federal Domestic Assistance

The Catalogue of Federal Domestic Assistance numbered programs applicable to this revised 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
- 93.213—Research and Training in Complementary and Alternative Medicine
- 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
- 93.281—Mental Health Research Career/Scientist Development Awards
- 93.282—Mental Health National Research Service Awards for Research Training
- 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 in 42 CFR Part 50 and 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, HHS is amending 42 CFR chapter I, subchapter D, part 50, and 45 CFR subtitle A, subchapter A, part 94 as follows:

### TITLE 42—PUBLIC HEALTH

#### 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 Public Health Service (PHS) grants or cooperative agreements will be 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 who is planning to participate in, or is participating in, such research; provided, however, that this subpart does not apply to SBIR Program Phase I applications. 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.

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

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

*Financial interest* means anything of monetary value, whether or not the value is readily ascertainable.

*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, and as defined by the Institution in its policy on financial conflicts of interest, which may include for example: 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 project director or principal Investigator 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, which may include, for example, collaborators or consultants.

*Manage* means taking action to address a financial conflict of interest, which can include reducing or eliminating the financial conflict of interest, to ensure, to the extent possible, that the design, conduct, and reporting of research will be free from bias.

*PD/PI* means a project director or principal Investigator of a PHS-funded research project; the PD/PI is included in the definitions of senior/key personnel and Investigator under this subpart.

*PHS* means the Public Health Service 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 (NIH).

*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, study or experiment 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 (*e.g.*, a published article, book or book chapter) and product development (*e.g.*, a diagnostic test or drug). 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 or cooperative agreement, 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.

*Senior/key personnel* means the PD/PI and any other person identified as senior/key personnel by the Institution in the grant application, progress report, or any other report submitted to the PHS by the Institution under this subpart.

*Significant financial interest* means:

(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); 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 when 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 and interests (*e.g.*, patents, copyrights), upon receipt of income related to such rights and interests.

(2) Investigators also must disclose the occurrence of any reimbursed or sponsored travel (*i.e.*, that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), related to their institutional responsibilities; provided, however, that this disclosure requirement does not apply to travel

that is reimbursed or sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education. The Institution's FCOI policy will specify the details of this disclosure, which will include, at a minimum, the purpose of the trip, the identity of the sponsor/organizer, the destination, and the duration. In accordance with the Institution's FCOI policy, the institutional official(s) will determine if further information is needed, including a determination or disclosure of monetary value, in order to determine whether the travel constitutes an FCOI with the PHS-funded research.

(3) 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, including intellectual property rights assigned to the Institution and agreements to share in royalties related to such rights; any ownership interest in the Institution held by the Investigator, if the Institution is a commercial or for-profit organization; income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles; income from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education; or income from service on advisory committees or review panels for a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

*Small Business Innovation Research* (SBIR) Program means the extramural research program for small businesses that is established by the Awarding Components of the Public Health Service and certain other Federal agencies under Public Law 97-219, the Small Business Innovation Development Act, as amended. For purposes of this subpart, the term SBIR Program also includes the Small Business Technology Transfer (STTR) Program, which was established by Public Law 102-564.

**§ 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 the Institution does not have any current presence on a publicly accessible Web site (and only in those cases), the Institution shall make its written policy available to any requestor within five business days of a request. If, however, the Institution acquires a presence on a publicly accessible Web site during the time of the PHS award, the requirement to post the information on that Web site will apply within 30 calendar days. 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 and within the timeframe prescribed by this subpart.

(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 the same prior to engaging in research related to any PHS-funded grant and at least every four years, and immediately when any of the following circumstances apply:

(1) The Institution revises its financial conflict of interest policies or procedures in any manner that affects the requirements of Investigators;

(2) An Investigator is new to an Institution; or

(3) An Institution finds that an Investigator is not in compliance with the Institution's financial conflict of interest policy or management plan.

(c) If the Institution carries out the PHS-funded research through a subrecipient (*e.g.*, subcontractors or consortium members), the Institution (awardee Institution) must take reasonable steps to ensure that any subrecipient Investigator complies with this subpart by:

(1) Incorporating as part of a written agreement with the subrecipient terms that establish whether the financial conflicts of interest policy of the awardee Institution or that of the

subrecipient will apply to the subrecipient's Investigators.

(i) If the subrecipient's Investigators must comply with the subrecipient's financial conflicts of interest policy, the subrecipient shall certify as part of the agreement referenced above 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 for disclosing significant financial interests that are directly related to the subrecipient's work for the awardee Institution;

(ii) Additionally, if the subrecipient's Investigators must comply with the subrecipient's financial conflicts of interest policy, the agreement referenced above 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 as required by this subpart;

(iii) Alternatively, if the subrecipient's Investigators must comply with the awardee Institution's financial conflicts of interest policy, the agreement referenced above 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) Providing FCOI reports to the PHS Awarding Component regarding all financial conflicts of interest of all subrecipient Investigators consistent with this subpart, *i.e.*, prior to the expenditure of funds and within 60 days of any subsequently identified FCOI.

(d) Designate an institutional official(s) to solicit and review disclosures of significant financial interests from each Investigator who is planning to participate in, or is participating 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) no later than the time of application for PHS-funded research.

(2) Require each Investigator who is participating in the PHS-funded

research to submit an updated disclosure of significant financial interests at least annually, in accordance with the specific time period prescribed by the Institution, 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 (*e.g.*, any financial conflict of interest identified on a PHS-funded project that was transferred from another Institution), 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 each Investigator who is participating in the PHS-funded research to submit an updated disclosure of significant financial interests within thirty days of discovering or acquiring (*e.g.*, through purchase, marriage, or inheritance) a new significant financial interest.

(f) Provide guidelines consistent with this subpart for the designated institutional official(s) 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 official(s), reasonably determines that the significant financial interest: could be affected by the PHS-funded research; or is in an entity whose financial interest could be affected by the research. The Institution may involve the Investigator in the designated official(s)'s determination of whether a significant financial interest is related to the PHS-funded research. A financial conflict of interest exists when the Institution, through its designated official(s), 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 retrospective review and a mitigation report 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, and response to, such disclosures (whether or not a disclosure resulted in the Institution's determination of a financial conflict of interest) and all actions under the Institution's policy or retrospective review, if applicable, for at least three years from the date the final expenditures report is submitted to the PHS or, where applicable, from other dates specified in 45 CFR 74.53(b) and 92.42 (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 Awarding Component 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, and 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 official(s) 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 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 financial conflicts.

(2) Whenever, in the course of an ongoing PHS-funded research project, an Investigator who is new to 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 official(s) of the Institution shall, within sixty days: review the disclosure of the significant financial interest; 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 official(s) 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)(A) In addition, whenever a financial conflict of interest is not identified or managed in a timely manner including failure by the Investigator to disclose a significant financial interest that is determined by the Institution to constitute a financial conflict of interest; failure by the Institution to review or manage such a financial conflict of interest; or failure by the Investigator to comply with a financial conflict of interest management plan, the Institution shall, within 120 days of the Institution's determination of noncompliance, complete a retrospective review of the Investigator's activities and the PHS-funded research project to determine whether any PHS-funded research, or portion thereof, conducted during the time period of the noncompliance, was biased in the design, conduct, or reporting of such research.

(B) The Institution is required to document the retrospective review; such documentation shall include, but not necessarily be limited to, all of the following key elements:

- (1) Project number;
- (2) Project title;
- (3) PD/PI or contact PD/PI if a multiple PD/PI model is used;
- (4) Name of the Investigator with the FCOI;
- (5) Name of the entity with which the Investigator has a financial conflict of interest;
- (6) Reason(s) for the retrospective review;
- (7) Detailed methodology used for the retrospective review (*e.g.*, methodology of the review process, composition of the review panel, documents reviewed);
- (8) Findings of the review; and
- (9) Conclusions of the review.

(iii) Based on the results of the retrospective review, if appropriate, the Institution shall update the previously submitted FCOI report, specifying the actions that will be taken to manage the financial conflict of interest going forward. If bias is found, the Institution is required to notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component. The mitigation report must include, at a minimum, the key elements documented in the retrospective review above and a description of the impact of the bias on the research project and the Institution's plan of action or actions taken to eliminate or mitigate the effect of the bias (*e.g.*, impact on the research

project; extent of harm done, including any qualitative and quantitative data to support any actual or future harm; analysis of whether the research project is salvageable). Thereafter, the Institution will submit FCOI reports annually, as specified elsewhere in this subpart. Depending on the nature of the financial conflict of 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 financial conflict of interest or the Investigator's noncompliance is determined and the completion of the Institution's retrospective 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 ensure public accessibility, via a publicly accessible Web site or written response to any requestor within five business days of a request, of 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 senior/key personnel as defined by this subpart;

(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 or written response to any requestor within five business days of a request, shall include, at a minimum, the following: the Investigator's name; the Investigator's title and role with respect to the research project; the name of the entity in which the significant financial interest is held; the nature of the significant financial interest; and the approximate dollar value of the significant 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.

(iii) If the Institution uses a publicly accessible Web site for the purposes of this subsection, the information that the Institution posts 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 of the senior/key personnel for the PHS-funded research project that was not previously disclosed, or upon the disclosure of a significant financial interest of senior/key personnel new to 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. The Web site shall note that the information provided is current as of the date listed and is subject to updates, on at least an annual basis and within 60 days of the Institution's identification of a new financial conflict of interest. If the Institution responds to written requests for the purposes of this subsection, the Institution will note in its written response that the information provided is current as of the date of the correspondence and is subject to updates, on at least an annual basis and within 60 days of the Institution's identification of a new financial conflict of interest, which should be requested subsequently by the requestor.

(iv) Information concerning the significant financial interests of an individual subject to paragraph (a)(5) of this section shall remain available, for responses to written requests or for posting via the Institution's publicly accessible Web site for at least three 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 in its policy on 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 an FCOI report regarding any Investigator's 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. In cases in which the Institution identifies a financial conflict

of interest and eliminates it prior to the expenditure of PHS-awarded funds, the Institution shall not submit an FCOI report to the PHS Awarding Component.

(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 an Investigator who is new to the research project), the Institution shall provide to the PHS Awarding Component, within sixty days, an FCOI report regarding the financial conflict of interest and ensure that the Institution has implemented a management plan in accordance with this subpart. Pursuant to paragraph (a)(3)(ii) of this section, 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 or managed by the Institution (e.g., was not timely reviewed or reported by a subrecipient), the Institution also is required to complete a retrospective review 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. Additionally, pursuant to paragraph (a)(3)(iii) of this section, if bias is found, the Institution is required to notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component.

(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 necessarily limited to the following:

(i) Project 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) Name of the entity with which the Investigator has a financial conflict of interest;

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

(vi) 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;

(vii) 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; and

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

(A) Role and principal duties of the conflicted Investigator in the research project;

(B) Conditions of the management plan;

(C) How the management plan is designed to safeguard objectivity in the research project;

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

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

(F) 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 to the PHS Awarding Component an annual FCOI report that addresses the status of the financial conflict of interest and any changes to the management plan 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 in its policy on 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 PHS-funded research project. PHS may, for example, require Institutions employing such an Investigator to enforce any applicable corrective actions prior to a PHS award or when the transfer of a PHS grant(s) involves such an Investigator.

(b) The PHS Awarding Component and/or HHS may inquire at any time before, during, or after award into any Investigator disclosure of financial interests and the Institution's review (including any retrospective review) of, and response to, such disclosure, regardless of whether 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 and 92.12, or suspension of funding or other enforcement action under 45 CFR 74.62 and 92.43, 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 will be free from bias resulting from Investigator financial conflicts of interest.

#### § 94.2 Applicability.

This part is applicable to each Institution that submits a proposal, or that receives, Public Health Service (PHS) research funding by means of a contract and, through the implementation of this part by the Institution, to each Investigator who is planning to participate in, or is participating in such research; provided, however, that this part does not apply to SBIR Program Phase I applications.

#### § 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.

*Financial conflict of interest (FCOI)* means a significant financial interest that could directly and significantly

affect the design, conduct, or reporting of PHS-funded research.

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

*Financial interest* means anything of monetary value, whether or not the value is readily ascertainable.

*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 submits a proposal, or that receives, PHS research funding.

*Institutional responsibilities* means an Investigator's professional responsibilities on behalf of the Institution, and as defined by the Institution in its policy on financial conflicts of interest, which may include for example: 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 project director or principal Investigator 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, which may include, for example, collaborators or consultants.

*Key personnel* includes the PD/PI and any other personnel considered to be essential to work performance in accordance with HHSAR subpart 352.242-70 and identified as key personnel in the contract proposal and contract.

*Manage* means taking action to address a financial conflict of interest, which can include reducing or eliminating the financial conflict of interest, to ensure, to the extent possible, that the design, conduct, and reporting of research will be free from bias.

*PD/PI* means a project director or principal Investigator of a PHS-funded research project; the PD/PI is included in the definitions of key personnel and Investigator under this part.

*PHS* means the Public Health Service 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 (NIH).

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

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

*Research* means a systematic investigation, study or experiment 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 (*e.g.*, a published article, book or book chapter) and product development (*e.g.*, a diagnostic test or drug). As used in this part, the term includes any such activity for which research funding is available from a PHS Awarding Component through a contract, whether authorized under the PHS Act or other statutory authority.

*Significant financial interest* means:

(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); 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 when 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 and interests (*e.g.*, patents, copyrights), upon receipt of income related to such rights and interests.

(2) Investigators also must disclose the occurrence of any reimbursed or sponsored travel (*i.e.*, that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), related to their Institutional responsibilities; provided,

however, that this disclosure requirement does not apply to travel that is reimbursed or sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education. The Institution's FCOI policy will specify the details of this disclosure, which will include, at a minimum, the purpose of the trip, the identity of the sponsor/organizer, the destination, and the duration. In accordance with the Institution's FCOI policy, the Institutional official(s) will determine if further information is needed, including a determination or disclosure of monetary value, in order to determine whether the travel constitutes an FCOI with the PHS-funded research.

(3) 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, including intellectual property rights assigned to the Institution and agreements to share in royalties related to such rights; any ownership interest in the Institution held by the Investigator, if the Institution is a commercial or for-profit organization; income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles; income from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education; or income from service on advisory committees or review panels for a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

*Small Business Innovation Research* (SBIR) Program means the extramural research program for small businesses that is established by the Awarding Components of the Public Health Service and certain other Federal agencies under Public Law 97-219, the Small Business Innovation Development Act, as amended. For purposes of this part, the term SBIR Program also includes the Small Business Technology

Transfer (STTR) Program, which was established by Public Law 102-564.

**§ 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 the Institution does not have any current presence on a publicly accessible Web site (and only in those cases), the Institution shall make its written policy available to any requestor within five business days of a request. If, however, the Institution acquires a presence on a publicly accessible Web site during the time of the PHS award, the requirement to post the information on that Web site will apply within 30 calendar days. 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 and within the timeframe prescribed by this part.

(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 the same prior to engaging in research related to any PHS-funded contract and at least every four years, and immediately when any of the following circumstances apply:

(1) The Institution revises its financial conflict of interest policies or procedures in any manner that affects the requirements of Investigators;

(2) An Investigator is new to an Institution; or

(3) An Institution finds that an Investigator is not in compliance with the Institution's financial conflict of interest policy or management plan.

(c) If the Institution carries out the PHS-funded research through a subrecipient (e.g., subcontractors, or consortium members), the Institution (awardee Institution) must take reasonable steps to ensure that any subrecipient Investigator complies with this part by

(1) Incorporating as part of a written agreement with the subrecipient terms that establish whether the financial

conflicts of interest policy of the awardee Institution or that of the subrecipient will apply to the subrecipient's Investigators.

(i) If the subrecipient's Investigators must comply with the subrecipient's financial conflicts of interest policy, the subrecipient shall certify as part of the agreement referenced above 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 for disclosing significant financial interests that are directly related to the subrecipient's work for the awardee Institution;

(ii) Additionally, if the subrecipient's Investigators must comply with the subrecipient's financial conflicts of interest policy, the agreement referenced above 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 as required by this part;

(iii) Alternatively, if the subrecipient's Investigators must comply with the awardee Institution's financial conflicts of interest policy, the agreement referenced above 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) Providing FCOI reports to the PHS Awarding Component regarding all financial conflicts of interest of all subrecipient Investigators consistent with this part, *i.e.*, prior to the expenditure of funds and within 60 days of any subsequently identified FCOI.

(d) Designate an institutional official(s) to solicit and review disclosures of significant financial interests from each Investigator who is planning to participate in, or is participating 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) no later than date of submission of the

Institution's proposal for PHS-funded research.

(2) Require each Investigator who is participating in the PHS-funded research to submit an updated disclosure of significant financial interests at least annually, in accordance with the specific time period prescribed by the Institution, 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 (e.g., any financial conflict of interest identified on a PHS-funded project that was transferred from another Institution), 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 each Investigator who is participating in the PHS-funded research to submit an updated disclosure of significant financial interests within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new significant financial interest.

(f) Provide guidelines consistent with this part for the designated institutional official(s) 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 official(s), reasonably determines that the significant financial interest: Could be affected by the PHS-funded research; or is in an entity whose financial interest could be affected by the research. The Institution may involve the Investigator in the designated official(s)'s determination of whether a significant financial interest is related to the PHS-funded research. A financial conflict of interest exists when the Institution, through its designated official(s), 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 retrospective

review and mitigation report 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, and response to, such disclosures (whether or not a disclosure resulted in the Institution's determination of a financial conflict of interest), and all actions under the Institution's policy or retrospective review, if applicable, 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 Awarding Component 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, and 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 official(s) 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, 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 financial conflicts.

(2) Whenever, in the course of an ongoing PHS-funded research project, an Investigator who is new to 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 official(s) of the Institution shall, within sixty days: review the disclosure of the significant financial interest; 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 official(s) 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) (A) In addition, whenever a financial conflict of interest is not identified or managed in a timely manner including failure by the Investigator to disclose a significant financial interest that is determined by the Institution to constitute a financial conflict of interest; failure by the Institution to review or manage such a financial conflict of interest; or failure by the Investigator to comply with a financial conflict of interest management plan, the Institution shall, within 120 days of the Institution's determination of noncompliance, complete a retrospective review of the Investigator's activities and the PHS-funded research project to determine whether any PHS-funded research, or portion thereof, conducted during the time period of the noncompliance, was biased in the design, conduct, or reporting of such research.

(B) The Institution is required to document the retrospective review; such documentation shall include, but not necessarily be limited to, all of the following key elements:

- (1) Project number;
- (2) Project title;
- (3) PD/PI or contact PD/PI if a multiple PD/PI model is used;
- (4) Name of the Investigator with the FCOI;
- (5) Name of the entity with which the Investigator has a financial conflict of interest;
- (6) Reason(s) for the retrospective review;
- (7) Detailed methodology used for the retrospective review (e.g., methodology of the review process, composition of the review panel, documents reviewed);
- (8) Findings of the review; and
- (9) Conclusions of the review.

(iii) Based on the results of the retrospective review, if appropriate, the Institution shall update the previously submitted FCOI report, specifying the actions that will be taken to manage the financial conflict of interest going forward. If bias is found, the Institution is required to notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component. The mitigation report must include, at a minimum, the key elements documented in the retrospective review above and a description of the impact of the bias on the research project and the Institution's

plan of action or actions taken to eliminate or mitigate the effect of the bias (e.g., impact on the research project; extent of harm done, including any qualitative and quantitative data to support any actual or future harm; analysis of whether the research project is salvageable). Thereafter, the Institution will submit FCOI reports annually, as specified elsewhere in this part. Depending on the nature of the financial conflict of 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 financial conflict of interest or the Investigator's noncompliance is determined and the completion of the Institution's retrospective 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 ensure public accessibility, via a publicly accessible Web site or written response to any requestor within five business days of a request, of 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 key personnel as defined in this part;

(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 or written response to any requestor within five business days of a request, shall include, at a minimum, the following: The Investigator's name; the Investigator's title and role with respect to the research project; the name of the entity in which the significant financial interest is held; the nature of the significant financial interest; and the approximate dollar value of the significant 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.

(iii) If the Institution uses a publicly accessible Web site for the purposes of this subsection, the information that the Institution posts 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 of the senior/key personnel for the PHS-funded research project that was not previously disclosed, or upon the disclosure of a significant financial interest of senior/key personnel new to 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. The Web site shall note that the information provided is current as of the date listed and is subject to updates, on at least an annual basis and within 60 days of the Institution's identification of a new financial conflict of interest. If the Institution responds to written requests for the purposes of this subsection, the Institution will note in its written response that the information provided is current as of the date of the correspondence and is subject to updates, on at least an annual basis and within 60 days of the Institution's identification of a new financial conflict of interest, which should be requested subsequently by the requestor.

(iv) Information concerning the significant financial interests of an individual subject to paragraph (a)(5) of this section shall remain available, for responses to written requests or for posting via the Institution's publicly accessible Web site for at least three 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 in its policy on 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 an FCOI report regarding any Investigator's 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. In cases in which the Institution identifies a financial conflict of interest and eliminates it prior to the expenditure of PHS-awarded funds, the Institution shall not submit an FCOI report to the PHS Awarding Component.

(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 an Investigator who is new to the research project), the Institution shall provide to the PHS Awarding Component, within sixty days, an FCOI report regarding the financial conflict of interest and ensure that the Institution has implemented a management plan in accordance with this part. Pursuant to paragraph (a)(3)(ii) of this section, 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 or managed by the Institution (e.g., was not timely reviewed or reported by a subrecipient), the Institution also is required to complete a retrospective review 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. Additionally, pursuant to paragraph (a)(3)(iii) of this section, if bias is found, the Institution is required to notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component.

(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 necessarily 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) Name of the entity with which the Investigator has a financial conflict of interest;

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

(vi) 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;

(vii) 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; and

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

(A) Role and principal duties of the conflicted Investigator in the research project;

(B) Conditions of the management plan;

(C) How the management plan is designed to safeguard objectivity in the research project;

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

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

(F) 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 to the PHS Awarding Component an annual FCOI report that addresses the status of the financial conflict of interest and any changes to the management plan 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 in its policy on 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 PHS-funded research project.

(b) The PHS Awarding Component and/or HHS may inquire at any time (before, during, or after award) into any Investigator disclosure of financial interests and the Institution's review of, and response to, such disclosure, regardless of 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: February 24, 2011.

**Francis S. Collins,**

*Director, National Institutes of Health.*

Approved: March 2, 2011.

**Kathleen Sebelius,**

*Secretary.*

[FR Doc. 2011-21633 Filed 8-23-11; 8:45 am]

**BILLING CODE 4140-01-P**