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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

[1] ''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.

[2] ''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.

[3]

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)[8] 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.''[9] A 2009 report from the HHS Office of Inspector General (OIG) stated ''Vulnerabilities exist at grantee institutions regarding conflicts.''[10]

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
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[8] 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.

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

[10] 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.

[16] Protecting Patients, Preserving Integrity, Advancing Health: Accelerating the Implementation of COI Policies in Human Subjects Research, A

[20] 75 FR 28705 (May 21, 2010).

[21] 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

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 Pro/Thddvio

[27] *http://grants.nih.gov/grants/policy/coifaq.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.

[28] 42 CFR 50.604(a) and 45 CFR 94.4(a).

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,[30] ire02 0 0 5O both nrtify a whether the subrecipient uthaate the I etitution pro InveDT20su

[30] 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.

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 pan sub441 -1,5g.111 AMCd andAAU1), hirch could includa defining theSFIt that could prnclude an Investigator frombeping d

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suggested that the iske of dvnancing conflicded research should bewemigted against the iske of not dvnancing the researc. GiveIn thewsder

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,[31] 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 cnd deT*(ouagraphf0a)(3spebyI, an Institu)Tj0 -1itutiona tro1tro1t must

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[31] 75 FR 28697 (May 21, 2010).

[32] 75 FR 28707 (May 21, 2010).

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

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[35] 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

[36] 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.

[37] 60 FR 35813 (July 11, 1995).

[38] 74 FR 21612 (May 8, 2009).

[39] All applicant Institution numbers are based on the number of Institutions that applied for NIH funding in FY 2008.

[40] All applicant Institution numbers are based on the number of Institutions that applied for NIH funding in FY 2008.

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 yours. 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.[41] 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[42]	Estimated annual cost[43]
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[44]	1	$2,835	$8,505,000.
(b)	Institutions: 2,000[45]	Institutions: 1	Institutions: $210 ..	Institutions: $420,000.
	Investigators: 38,000[46]	Investigators 0.25[47].	Investigators: $17.5[48].	Investigators: $665,000.
			Total: $227.5.	Total: $1,085,000.
(c)(1)	500[49]	1	$35.00	$17,500.
(c)(2)	Included in the cost estimate in 50.605/94.5(b)(3).	NA	NA.	
(d)	3,000[50]	1	$35	$105,000.
(e)(1)	38,000[51]	1	$140	$5,320,000.

[41] 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 [42]	Estimated annual cost [43]
(e)(2)	38,000 [52]			

[62] 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.
[63] Assumes 950 FCOI reports annually × 2 hours to prepare the report/complete an NIH-provided Web form.
[64] Assumes it takes less time to update a report than to create a new one—1 hour per update.
[65] 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).
[66] 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.
[67] 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.
[68] 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),

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 [69]
(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 [81]	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 [82] The burden is included in 50.605/94.5 (b)(2) below.	NA	NA	NA.
(a)(3)	500 [83]	1	3	1,500.
(a)(3)(i)	50 [84]	1	80	4,000.
(a)(3)(ii)	50 [85]	1	80	4,000.
(a)(3)(iii)	50	1	1	50.
(a)(4)	950 [86]	1	12	11,400.

[93] 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.

[94] 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.

[95] 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.

(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,

project; extent of harm done, including any qualitative and quantitative data to support any actual or future harm; analysis of whether the research project

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

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

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 pearsignificant financial interest cVflicts of a

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:

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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.

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