Attachment 2: Historical Data Document: Historical information regarding the publication of the Final Rule 42 CFR 50 Subpart F and 45 CFR Part 94

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

The purpose of the 1995 regulations was to ensure that there is no reasonable expectation that the design, conduct, or reporting of PHS-funded research will be biased by any Investigator financial conflict of interest (FCOI).

Since the publication of the 1995 regulations, 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 significant financial interests (SFIs), enhancing regulatory compliance and effective institutional oversight and management of Investigators' FCOIs, as well as HHS' compliance oversight.

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

After considering all public comments, and consistent with the proposals articulated in the NPRM, HHS developed and published the final rule on August 25, 2011, which includes the following major changes to the 1995 regulations:

- Amending the definition of SFI to include a de minimis threshold of $5,000 for disclosure that generally applies to payments for services and/or equity interests as well as any equity interest in non-publicly traded entities.
- Excluding income from seminars, lectures, or teaching engagements sponsored by and service on advisory 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.
- 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 whether it constitutes an FCOI. Investigators must also disclose the occurrence of any reimbursed or sponsored travel related to their Institutional responsibilities for considerations by the Institutional official(s). The requirement to "disclose" information about Investigator sponsored travel or reimbursed travel (but not dollar amounts) does not apply to travel that is reimbursed or sponsored by a federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C.

1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education. Enhancing the information on an FCOI reported by the Institution to the PHS funding 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 under a PHS-supported research project, an Institution is required to ensure public accessibility, via a publicly accessible Web site or written response to any requestor within five business days of a request, of information concerning any significant financial interest disclosed to the Institution that meets the three criteria as described in the regulations.
- Clarifying that PHS could require Institutions employing previously sanctioned Investigators to enforce any applicable corrective actions prior to a PHS award or when the transfer of a PHS grant(s) involves such an Investigator.
- Clarifying that the PHS Awarding Component and/or HHS may inquire at any time before, during, or after award into any Investigator disclosure of financial interest and the Institution's review of, or response to, such disclosure, regardless of whether the disclosure resulted in the Institution's determination of a FCOI.
- Requiring training for Investigators prior to engaging in research related to any PHS-grant or contract, and at least every four years, and immediately when any of the following circumstances apply: (i) the Institution revises its financial conflict of interest policies or procedures in any manner that affects the requirements of Investigators; (ii) an Investigator is

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

- Requiring institutions to perform and document a retrospective review in cases of non-compliance with the regulation. Institutions will report to the PHS-Awarding Component only in cases where bias is found and will provide a mitigation report to address the impact of the bias on the research project and the actions the Institution has taken, or will take, to mitigate the bias.

The regulations require Investigators to disclose their SFIs[1], and those of the Investigator's spouse and dependent children, that reasonably appear to be related to the Investigator's institutional responsibilities. Institutions shall determine whether an Investigator's SFI is related to PHS-funded research by determining whether the SFI could be affected by the PHS-funded research or is in an entity whose financial interest could be affected by the research. A FCOI exists when the institution, through

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

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

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

(iii) Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

(2) Investigators also must disclose the occurrence of any reimbursed or sponsored travel (i.e., that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), related to their Institutional responsibilities; provided, however, that this disclosure requirement does not apply to travel that is reimbursed or sponsored by a federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education. The Institution's FCOI policy will specify the details of this disclosure, which will include, at a minimum, the purpose of the trip, the identity of the sponsor/organizer, the destination, and the duration. In accordance with the Institution's FCOI policy, the Institutional official(s) will determine if further information is needed, including a determination or disclosure of monetary value, in order to determine whether the travel constitutes an FCOI with the PHS-funded research.

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

its designated official(s), reasonably determines that a SFI could directly and significantly affect the design, conduct, or reporting of the PHS-funded research. The institutional official(s) solicit and review disclosures of SFIs from each Investigator who is planning to participate in, or is participating in, the PHS-funded research. Investigator who are planning to participate in the PHS-funded research must 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. Investigators participating in PHS-funded research must submit an updated disclosure of SFIs at least annually, in accordance with the specific time period prescribed by the Institution, during the period of award and within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new SFI. Institutions shall take such actions as necessary to manage FCOIs, including any financial conflicts of a subrecipient Investigator. Management of an identified FCOI requires development and implementation of a management plan and, if necessary, a retrospective review and mitigation report.

The Institution agrees to make information available, promptly upon request, to the HHS relating to any Investigator disclosure of financial interests and the Institution's review of, or response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of a FCOI. 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, or response to, such disclosure, regardless of whether the disclosure resulted in the Institution's determination of a FCOI. An Institution is required to submit, or permit on site review of, all records pertinent to compliance with the regulations. On the basis of its review of records or other information that may be available, the PHS Awarding Component may decide that a particular 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 conflict of interest in accordance with the regulations. The PHS Awarding Component may

determine that imposition of special award conditions under 45 CFR 75.207, or suspension of funding or other enforcement action under 45 CFR 75.371 (for grants and cooperative agreements) or issuance of a Stop Work Order by the Contracting Officer or other enforcement action (for contracts) is necessary until the matter is resolved.

The regulations meet the requirements originally set forth in the NIH Revitalization Act of 1993, P. L. 103-43, Section 164, Requirement of Regulations Regarding Protection Against Financial Conflicts of Interest in Certain Projects of Research. On January 15, 2007, the President signed H.R. 6164 as P.L. 109-482, the National Institutes of Health Reform Act of 2006, affirming the importance of NIH and its vital role in advancing biomedical research to improve the health of the Nation. Additional authority for the regulations derive from Section 216 of the PHS Act authorizing the Assistant Secretary for Health, with the approval of the Secretary, to promulgate regulations necessary for the administration of the Public Health Service. Additional authority also derives from 42 U.S.C. §289b-1, "Protection against financial conflicts of interests in certain projects of research" and 42 U.S.C. §299c-4, "Additional Provisions with respect to grants and contracts" which authorizes the Director by regulation to "define the specific circumstances that constitute financial interests …that will, or may be reasonably expected to create a bias in favor of obtaining results in the projects that are consistent with such interests." 42 U.S.C. §299c-4(a)(1). Further authority for the regulations and this information collection is found in 5 U.S.C. §301, the Secretary's general authority to issue regulations necessary for the administration of the Department.

As noted in the 1994 Notice of Proposed Rule Making (republished in the NIH GUIDE, Volume 23, Number 25, July 1, 1994), numerous statutes and programs demonstrate a continuing Federal interest in the promotion of interactions among Government, academia, and industry. For example, the Stevenson-Wydler Technology Innovation Act of 1980 (P.L. 96-480) encourages technology transfer, particularly through industrial-academic collaborations. The Patent and Trademark Act Amendments of 1980 (P.L.

96-517) allow universities and other award recipients to apply for patents developed with Federal funding (rather than awarding such rights to the Government), and expressly promote collaboration between commercial concerns and nonprofit organizations. The Economic Recovery Tax Act of 1981 (P.L. 97-34) is aimed at fostering research and development by small companies and associated university partners. The Federal Technology Transfer Act of 1986 (P.L. 99-502), which amended P.L. 96-480, and Executive Order 12592 provide similar patent and licensing authority to Federal laboratories and encourage them to participate in cooperative research and development agreements with the private sector and nonprofit organizations, including universities."

The regulations at 42 CFR Part 50, Subpart F, Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding Is Sought, and 45 CFR Part 94, Responsible Prospective Contractors, promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct, and reporting of research funded under PHS grants, cooperative agreements, and contracts will be free from bias resulting from Investigator FCOIs. The regulations define "Investigator" as 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. The regulations require that Institutions applying for, or receiving, PHS research funding by means of a grant, cooperative agreement, or contract maintain an up-to-date, written, enforced policy on FCOI that complies with the regulations, and make such policy available via a publicly accessible Web site[2]. Institutions must inform each Investigator of the Institution's policy on FCOI, the Investigator's responsibilities regarding disclosure of SFIs, and of the regulations. If an Institution maintains a policy on FCOI that includes standards that are more stringent than these regulations (e.g., that require a more extensive disclosure

[2] 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.

of financial interests), the Institution shall adhere to its policy and shall provide FCOI reports regarding identified FCOIs to the PHS Awarding Component in accordance with the Institution's own standards and within the timeframe prescribed by the regulations.

When an Institution seeks research funds for PHS grants, cooperative agreements, or contracts, the Institution certifies in the grant or cooperative agreement application or contract proposal that the Institution

(1) Has in effect at that Institution an up-to-date, written, and enforced administrative process that complies with this regulation to identify and manage FCOIs 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 regulatory's requirements including those pertaining to disclosure of SFIs;

(3) Shall manage FCOIs and provide initial and ongoing FCOI reports to the PHS Awarding Component consistent with these regulations;

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

(5) Shall fully comply with the requirements of the regulations. Moreover, Institutions are required to certify compliance with all aspects of the regulation, including that Investigators are informed of the institutional policy, their disclosure responsibilities, and of the regulations. The disclosure of certain SFI

information by Investigators to designated Institutional officials is necessary to provide a reasonable expectation that the design, conduct, and reporting of research funded under PHS grants, cooperative agreements, and contracts will be free from bias resulting from Investigator FCOIs. The SFI information disclosed by the Investigators to the designated Institutional officials remains under the control of the Institutions.