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Client Alert

FDA & Life Sciences Group, Healthcare Practice Group, and Government Affairs Group

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HHS Issues Final Rule Amending Regulations Regarding Investigator Financial Conflicts of Interest Related to Research Funded by PHS

Major Changes Regarding Investigator Disclosures, Obligations of Institutions, and Public Access to Information

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The Department of Health and Human Services (HHS) issued a Final Rule on August 25 that amends the 1995 regulations "Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought" (42 C.F.R. Part 50, Subpart F) and "Responsible Prospective Contractors" (45 C.F.R. Part 94).[i] These regulations address financial interests of investigators that relate to research funded by the Public Health Service (PHS). Despite complaints from research institutions regarding the increased administrative burdens created by the proposed amendments, HHS adopted most of the amendments as proposed in the Notice of Proposed Rulemaking.[2] The Final Rule includes major changes to the definition of an investigator's significant financial interests, including the monetary threshold, the scope of investigator disclosures to their institution, the responsibilities of institutions, and public disclosure of investigator financial conflicts of interest. Although HHS invited comment on addition regulatory provisions to address institutional conflicts of interest, the agency concluded that additional study was needed prior to formulation of such provisions. The Final Rule takes effect on September 24, 2011 and institutions must be in compliance by August 24, 2012.

For the first time, investigators must disclose all significant financial interests (SFI) related to their instititutional responsibilities, and the institution, not the investigator, must make the determination whether the SFI relates to the PHS-funded research. Consistent with the current regulations, institutions will then determine if the SFI constitutes a financial conflict of interest (FCOI). The Final Rule also imposes new obligations on institutions regarding investigator training, management of FCOI, and reporting to the PHS awarding component. Institutions must also ensure that information regarding certain FCOI of senior/key research personnel is accessible to the public.

This client alert highlights the most significant changes in the regulations. It also addresses the potential indirect effects on pharmaceutical and medical device manufacturers who engage PHS-funded investigators in financial relationships.

Changes in Financial Disclosures for Investigators.

- **Scope and Monetary Thresholds.** Currently, an investigator must disclose to the institution only those financial interests (and those of the investigator's spouse and dependent children) that the investigator deems to be affected by the PHS-funded research. Under the Final Rule, investigators must disclose all "significant financial interests" (SFI) that relate to their "institutional responsibilities." The definition of "institutional responsibilities" is broad and includes virtually all professional activities in which an investigator might engage, including professional practice (*e.g.*, practice of medicine), research, consulting, teaching, and service on institutional committees and panels. HHS clarified that the institution, not the investigator, defines the investigator's institutional responsibilities in the institution's policy on FCOI. Similar to the current regulations, investigators must disclose intellectual property rights and interests (e.g., patents and copyrights). Under the Final Rule, the monetary threshold at which a SFI exists and must be disclosed has been lowered from $10,000 to $5,000. With regard to a publicly held entity, investigators must disclose any remuneration (salary and payment for services) received in the 12 months preceding disclosure as well as any equity interest as of the date of disclosure that when aggregated exceeds $5,000. With regard to a non-publicly held entity, investigators must disclose the value of any remuneration received in the 12 months preceding disclosure that when aggregated exceeds $5,000. Similar to the current regulations, investigators must disclose any equity interest in a non-publicly held entity. In addition, investigators must disclose the occurrence of any reimbursed or sponsored travel (*i.e.*, travel which is paid for on behalf of the investigator) related to their "institutional responsibilities," and the institution will then determine if further information, including disclosure of monetary value, is needed to determine whether the travel constitutes a FCOI. Investigators must make disclosures of financial interests no later than the time of application for PHS-funded research, at least annually while participating in the research, and within 30 days of discovering or acquiring a new SFI.

- **Exemptions from Disclosure.** The term SFI does not include salary, royalties, or other remuneration paid by the institution to the investigator if the investigator is currently employed by the institution or otherwise appointed to the institution. Thus, remuneration such as royalties assigned by institutions where the investigator was previously employed is not exempt. Remuneration for participation in educational activities, seminars, panels, and advisory committees is not exempt from the definition of SFI unless the engagement is sponsored by a government agency, an institution of higher learning as defined at 20 U.S.C. § 1001(a), or an academic teaching hospital, medical center, or research institution that is affiliated with an institution of higher learning. This represents a broadening of the exemption for educational activities, as the proposed rule did not exempt income paid by an academic teaching hospital or a medical center. Further, in contrast with the proposed rule, the current and amended regulations are not applicable to Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) Phase I applications.

Changes in Accountability of Institutions that Receive PHS Funds. The amended regulations continue the current requirement that institutions must maintain a written, enforced policy on FCOI related to PHS-funded research. Consistent with current regulations, prior to expenditure of any PHS funds and periodically as investigators submit new disclosures of SFI, institutions must determine if the SFI constitutes a FCOI based on the determination that the financial interest "could directly and significantly affect the design, conduct, or reporting of PHS-funded research." However, institutions will have extensive new obligations, the most significant of which are highlighted here:

- **Training of Investigators.** Institutions will have new responsibilities to ensure that investigators complete training related to the amended regulations and the institution's FCOI policy prior to each investigator's participation in the PHS-funded research and at least every four years. In addition, training must occur "immediately" if an investigator is new to the institution, an investigator is determined to be not in compliance with the institution's FCOI policy or the management plan, or the institution revises its FCOI policy or procedures.
- **Management of FCOI.** Prior to expenditure of funds and during the funding period, institutions must develop a written management plan that specifies the actions that have been, and shall be taken, to manage any FCOI that has been identified. The Final Rule cites several conditions or limitations that might be imposed, including disclosure of FCOI directly to participants in human subjects research. In addition, institutions have responsibilities, which must be carried out within 60 days of the event, for reviewing SFI and implementing interim measures if the financial interest is deemed to be a FCOI under the following circumstances: a new investigator joins the research project, an existing investigator makes a new disclosure, or the institution identifies a SFI that was either not disclosed or reviewed in a timely manner. The Final Rule also imposes additional requirements regarding financial disclosures and management of FCOI of subrecipient investigators at other institutions who participate in the research.
- **Reporting of FCOI to the PHS Awarding Component.** Previously, an institution's FCOI reporting obligation was to provide the name of the investigator with FCOI and an assurance that the FCOI was managed, reduced, or eliminated. Under the Final Rule, institutions must report additional information about FCOI including the name of the entity with which the investigator has a FCOI, its nature and its value in dollar increments, how the financial interest relates to the research, the basis for the decision that it is a FCOI, and key elements of the management plan.
- **Compliance and Remedies.** In the event of noncompliance with the institution's policy or the FCOI management plan, including untimely investigator disclosure or institutional review of a SFI that is determined to be a FCOI, the institution must within 120 days conduct a retrospective review of the investigator's activities and research to determine whether any portion of the research was biased in design, conduct or reporting of the data. If bias is identified by an institution following a retrospective review of noncompliance, the institution must promptly submit a "mitigation report" that includes key elements documented in the retrospective review, the impact of the bias on the research, and the plan of action to eliminate or mitigate the effect of the bias. In addition, the PHS Awarding Component and/or HHS may inquire at any time into an individual investigator's disclosure of financial interests and the institution's response, regardless of whether or not the disclosure was determined to be a FCOI by the institution.

    - If the PHS Awarding Component determines that a particular FCOI will bias the objectivity of the PHS-funded research or that the institution has not managed or reported the FCOI in accordance with the Final Rule, HHS may provide directions to the institution on how to maintain objectivity in the research project. In addition, the PHS Awarding component may determine that the issuance of a "Stop Work Order" or other enforcement action is necessary until the matter is resolved.
    - In any case in which HHS determines that PHS-funded clinical research whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment is associated with a FCOI that was not managed or reported by the institution as required by the Final Rule, the institution shall order the investigator to disclose the FCOI in each public presentation of the research and as an addendum to previously published presentations.

- Although the Final Rule does not provide for any specific fines or monetary penalties, the preamble clarifies that HHS may initiate enforcement actions available under other federal regulations, as appropriate under the circumstances, such as government-wide suspension or debarment of the investigator under 2 C.F.R. Part 376. The preamble also clarifies that HHS may initiate enforcement under 45 C.F.R. 74.62 whereby if a recipient materially fails to comply with the terms and conditions of an award, HHS may take one or more or the following actions, as appropriate under the circumstances: temporarily withhold payments, disallow use of funds related to the award, wholly or partly suspend or terminate the current award, withhold further awards for the project, and "take any other remedies that may be legally available."

Ensuring Public Accessibility to Financial Conflicts of Interest. Institutions have the new obligation to ensure public accessibility, via a publicly accessible web site or written response to a requestor within five business days of a request, of information regarding FCOIs held by the project director/principal investigator and all other persons identified as "key personnel" in the research contract proposal and contract. This information must be accessible prior to the institution's expenditure of any funds, and must be updated at least annually, and within sixty days of the identification of new FCOI. The information must include, at a minimum, the name and role of the investigator in the research project, the nature of the SFI that is a FCOI, and the approximate dollar value based on monetary ranges cited in the Final Rule. In a press release, the National Institutes of Health emphasized that the Final Rule tightens the financial conflict of interest rules and will add transparency.[3] However, Senator Charles Grassley, who previously conducted investigations into alleged inadequacies regarding NIH investigator financial disclosures, issued a press release[4] stating that the Final Rule is "disappointing on transparency" and predicting that institutions will "opt for the written request, knowing that requiring a request in writing is a barrier." In the proposed rule, posting information regarding FCOIs on a publicly available website was mandatory.

Impact on Institutions and Investigators, as well as Pharmaceutical and Medical Device Manufacturers.

- The Final Rule will greatly increase the scope and number of financial disclosures that must be made by investigators to their institutions. Investigators will no longer be permitted to make the judgment that a SFI is related to the research as that determination will be made by their institutions. In addition, due to the new requirement for public accessibility to FCOI, principal investigators and other key research personnel can anticipate that detailed information about their personal financial interests that are deemed to be FCOI, as well as those of their spouse and dependent children, will be publicly accessible. Institutions will have extensive additional administrative burdens, including new responsibilities regarding the training of investigators, the development of management plans to mitigate individual FCOI, and reporting.
- The new regulations have the potential to indirectly affect pharmaceutical and medical device manufacturers who have financial relationships with individuals who are PHS-funded investigators. Due to the broader scope of financial relationships that constitute SFI, including the new lower monetary threshold for disclosure, and the fact that the investigator will not be determining if the financial interest is related to the PHS-funded research, manufacturers should anticipate that virtually all of their financial relationships with PHS-funded investigators will be disclosed and subject to review by the investigators' institutions. In addition, if such financial interests are deemed by the institution to be FCOI with the potential to bias the research, the nature and approximate monetary value of the financial interests will be publicly accessible. If the PHS-funded research involves human subjects research, institutions may determine that the

management plan for the FCOI also includes direct disclosure to human subjects. Thus, in addition to the disclosures of financial relationships with physicians and their medical centers now required by certain states and the "sunshine" provisions of the Patient Protection and Affordable Care Act, manufacturers should plan for an additional venue of disclosure of financial relationships with physicians that will be subject to public and Congressional scrutiny.

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If you have questions regarding the Final Rule or if you need assistance in understanding its implications for your institution, please contact us.

[i] 76 Fed. Reg. 53256. August 25, 2011. Accessible at, http://www.gpo.gov/fdsys/pkg/FR-2011-08-25/pdf/2011-21633.pdf
[2] 75 Fed. Reg. 28688. May 21, 2010.
[3] Accessible at, http://www.nih.gov/news/health/aug2011/od-23.htm
[4] Accessible at, http://grassley.senate.gov/news/Article.cfm?customel_dataPageID_1502=36565