PhRMA

July 25, 2011

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Draft Guidance for Clinical Investigators, Industry, and FDA Staff: Financial Disclosure by Clinical Investigators; Docket No. FDA–1999–D–0792; 76 Fed. Reg. 30,175 (May 24, 2011)

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America ("PhRMA") is pleased to submit these comments in response to the Food and Drug Administration's ("FDA's") draft *Guidance for Clinical Investigators, Industry and FDA Staff: Financial Disclosure by Clinical Investigators* ("Draft Guidance"). PhRMA is a voluntary, non-profit association that represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. In 2010, the biopharmaceutical industry invested more than $67 billion to develop new medicines.[1]

PhRMA supports FDA's decision to update and revise its existing guidance document on financial disclosure by clinical investigators, which was issued on March 20, 2001,[2] to address issues raised by the Office of the Inspector General and to answer questions received from biopharmaceutical companies and other stakeholders since issuance of the existing guidance document. PhRMA believes that additional guidance regarding the Agency's interpretation of its financial disclosure regulations set forth at 21 C.F.R. Part 54 will assist clinical trial sponsors and investigators in complying with those important requirements. Of course, it is also essential that such requirements do not become so burdensome as to serve as a disincentive for participation in often life-saving clinical research.

Prior to finalizing the Draft Guidance, FDA should ensure that its financial disclosure policies do not create a chilling effect on innovative research by releasing the private financial information of clinical investigators. PhRMA is particularly concerned that new policies aimed at increasing the amount of personal financial information that is disclosed to the public could have the perverse effects of (a) dissuading clinical investigators from participating in innovative research and (b) creating public confusion. FDA's existing policies regarding public disclosure of financial information strike an appropriate balance between the public interest in transparency and the investigator's legitimate privacy interests and recognize that the public's interest in

[1] Pharmaceutical Research and Manufacturers of America, PHARMACEUTICAL INDUSTRY PROFILE 11 (2011), *available at* http://www.phrma.org/sites/default/files/159/phrma_profile_2011_final.pdf (hereinafter PHARMACEUTICAL INDUSTRY PROFILE).

[2] *Guidance for Industry: Financial Disclosure by Clinical Investigators* (March 20, 2001).

disclosure will outweigh an investigator's privacy interests "only rarely."[3] This careful balancing ensures that transparency concerns do not serve to harm the public health by creating disincentives for innovative research.

If FDA nevertheless decides to revise its existing disclosure policies, however, it should do so transparently and only through notice-and-comment rulemaking. Moreover, in order to avoid confusion that could be caused by the release of multiple and potentially inconsistent financial information, FDA should ensure that any financial information about clinical investigators sought by FDA from sponsors is requested in a manner that is consistent with any overlapping disclosure requirements under the Sunshine Act provisions of the Patient Protection and Affordable Care Act ("PPACA").[4]

1. FDA Should Maintain Its Current Policies With Respect to Public Disclosure of Clinical Investigators' Personal Financial Information

In the Draft Guidance, FDA requests comment on whether and how the Agency should change its existing policies regarding the public disclosure of an investigator's personal financial information. According to the Draft Guidance, FDA is contemplating this change because of recent interest by various entities in the public disclosure of industry financial arrangements with physicians. FDA states that it is seeking to address this increased interest in public disclosure by achieving a "proper balance between transparency and the right to privacy of clinical investigators with respect to their financial arrangements . . . ."[5]

PhRMA does not believe FDA's existing disclosure policies regarding investigator financial arrangements should be modified, because clinical investigators have come to expect that, unless their financial interests otherwise are public (*e.g.,* patent interests), such information will be protected from public disclosure under FDA's existing and long-standing policies. In the preamble to its final financial disclosure regulations, FDA acknowledged that some types of financial information, such as equity interests, are surrounded by a "reasonable expectation of privacy" and thus "would be protected from public disclosure unless circumstances clearly outweigh the identified privacy interest."[6] Although FDA refused to adopt a blanket rule, preferring instead to proceed on a case-by-case basis, the Agency nevertheless acknowledged that public disclosure would be appropriate only in a "small subset" of cases.[7] Because FDA should not disincentivize the involvement of clinical investigators in research, PhRMA believes that FDA should retain its current financial disclosure standards.

PhRMA is concerned that if FDA modifies its current policies to increase the public disclosure of the personal financial information of clinical investigators, FDA will discourage

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[3] Draft Guidance at 24.

[4] *Patient Protection and Affordable Care Act*, Pub. L. No. 111-148, §6002 (2010) (codified at 42 U.S.C. §1320-7h).

[5] Draft Guidance at 24.

[6] 63 Fed. Reg. 5233, 5237-38 (Feb. 2, 1998).

[7] *Id.*

highly qualified investigators from participating in innovative medical research. Clinical investigators who have a legitimate interest in maintaining the privacy of their personal financial information may view FDA's revised disclosure policies as an unwarranted intrusion into their private affairs. This, in turn, may dissuade many qualified investigators from participating in clinical investigations subject to FDA's new disclosure policies. PhRMA believes that this would have a negative impact on the public health that outweighs any public interest in the disclosure of personal financial information. Consequently, PhRMA believes FDA should maintain its existing disclosure policies without change and reiterate that, under those policies, public disclosure typically would be appropriate in only a small subset of cases.

If FDA nevertheless decides to revise its existing disclosure policies, it should do so only through notice-and-comment rulemaking.

Moreover, the Agency should ensure that any financial information about clinical investigators sought by FDA from sponsors is requested in a manner that is consistent with any overlapping disclosure requirements under the Sunshine Act provisions of PPACA.[8] Pending the issuance of proposed regulations by the Centers for Medicare and Medicaid Services ("CMS"), an open issue remains regarding the scope of *investigator level* payments that might be disclosed under section 6002 of PPACA ("the Sunshine Act provisions"). Under the Sunshine Act provisions, manufacturers are required to report research payments to covered recipients (*i.e.*, "Teaching Hospitals" and "Physicians"). Until the CMS regulations are finalized, there will be uncertainty about whether and how manufacturers will be required to report details about payments that may be received by physician investigators when manufacturers make payments to a teaching hospital or to another entity to conduct a clinical trial. Press reports have indicated that various stakeholders, including physician groups, teaching hospitals, clinical research organizations, and others, may take varied positions on the degree to which manufacturers should be required to obtain detailed financial information from research partners to comply with the Sunshine Act reporting requirements.

Depending upon what level of disclosure is ultimately required by the CMS regulations, it is quite possible that both FDA and CMS will separately require public disclosure of similar, or even duplicative, information for the same covered recipients, including clinical investigators who are U.S. physicians. Different data collection and public disclosure requirements under the FDA Guidance and the final regulations implementing the Sunshine Act provisions will be likely to create public confusion, negatively impact clinical research into innovative new treatments for patients, and frustrate the overall policy goal of promoting transparency. In addition, different reporting requirements for any of the same requested data from both FDA and CMS will create additional data collection burdens on both research sponsors and clinical investigators.

Further, the FDA reporting requirements of 21 C.F.R. Part 54 apply only to "covered clinical studies" (21 C.F.R. §54.2(e)), whereas the reporting requirements under the Sunshine Act provisions are potentially much broader, encompassing all research spending by

[8] 42 U.S.C. §1320a-7h.

manufacturers to "covered recipients," subject to the narrow exceptions of 42 U.S.C. §1320a-7h(e)(10)(B). In light of the potentially different public disclosure requirements of FDA and CMS involving investigators, research spending involving a non-covered clinical study (under 21 C.F.R. Part 54) may still be reportable by CMS and create an unwarranted perception that an investigator did not accurately complete his/her FDA disclosure Form 3455 pursuant to 21 C.F.R. Part 54.

In addition to potential public perception issues, any confusion in the administration of any dual disclosure requirements by two separate agencies (or by manufacturers in validating the data against two different regulatory mechanisms) could also result in marketing authorization delays under 21 C.F.R. §54.4(c), as the FDA could refuse to consider the relevant data submission pending clarification of the investigator financial disclosure. Given the strong public policy of bringing innovative products to the market in a timely fashion, as well as the significant amount of investment to accomplish this objective, the risk of delay from dual administration of potentially similar public disclosure requirements should not be underestimated.

Accordingly, PhRMA does not support modifying FDA's current policies regarding the public disclosure of financial information, which recognize that the investigator's interest in privacy and that this privacy interest should be breached in the public interest only rarely. If FDA nevertheless decides to modify its current disclosure policies, it should do so only through notice-and-comment rulemaking and in a manner and on a time schedule that ensures consistency with any overlapping disclosure requirements under the Sunshine Act provisions, including any final rules issued by CMS.

2. FDA Should Clarify That Hospital Staff Are Not Considered to be "Clinical Investigators" for Purposes of Financial Disclosure

On page 13 of the Draft Guidance, in response to Question D.1, FDA states that hospital staff, including nurses, residents, fellows and office staff are not meant to be covered by the definition of "clinical investigator" if they provide ancillary or intermittent care but "do not make direct and significant contribution to the data." This suggests that hospital staff may be considered "clinical investigators" for purposes of financial disclosure if they do make a "direct and significant contribution to the data."

PhRMA believes that FDA's proposed interpretation is inconsistent with the regulatory definition of "clinical investigator," which is limited to "a listed or identified investigator or subinvestigator who is directly involved in the treatment or evaluation of research subjects."[9] Hospital staff who are not listed or identified as investigators or subinvestigators on a study should not be considered "clinical investigators" for purposes of financial disclosure regardless of whether they make a direct and significant contribution to the data in a study. FDA should revise the Draft Guidance to ensure it is consistent with the final regulations.

[9] 21 C.F.R. §54.2(d).

3. FDA Should Clarify The Studies for Which Financial Disclosure Is Required

On page 19, in the proposed answer to Question G1, FDA states that it would be prudent for sponsors to collect financial information "for most studies in the event that the study will ultimately require certification and disclosure statements." Although PhRMA agrees that sponsors should apply the financial disclosure requirements prudently, the recommendation to require financial disclosure for "most studies" is overbroad and could be extremely burdensome for sponsors to implement. PhRMA thus recommends that FDA reiterate in its response to Question G1 that certain studies, including most phase 1 tolerance studies and pharmacokinetic studies, most clinical pharmacology studies, and large open safety studies conducted at multiple sites, are not considered to be "covered clinical studies" and thus that sponsors of such studies would not be required or expected to collect financial information for such studies.[10] PhRMA believes this clarification would be helpful to ensure that the Draft Guidance is in alignment with FDA's financial disclosure regulations.

4. Due Diligence

In the draft guidance's discussion of due diligence to locate investigators to obtain financial disclosure information (Q&A B.6), FDA recommends that sponsors and/or applicants:

> try to locate the clinical investigator through at least two telephone calls and make written memoranda of their calls and any telephone conversations. In addition, they should follow-up in writing and send no fewer than two certified letters in an effort to locate missing investigators. If an investigator is no longer at the institution where the study was conducted, the applicant should make a reasonable attempt to locate the investigator, such as by requesting contact information from the institution where the study was conducted or the institution with which the investigator was affiliated, contacting professional associations the investigator may have been affiliated with, and/or conducting internet searches.

PhRMA agrees that sponsors should exercise due diligence to obtain financial disclosure information, and that FDA's recommendation may be appropriate in some cases. We do suggest, however, that the guidance acknowledge that appropriate due diligence (defined in the guidance as the "measure of activity expected from a reasonable and prudent person under a particular circumstance") may vary, and that sponsors may exercise judgment regarding the effort spent searching for investigators whose impact on the study is minimal. For example, a subinvestigator who was involved in the study for a limited period of time, or an investigator whose contribution of data was limited to a small number of study participants in a large study such that, even assuming a disclosable interest might exist, the risk of bias to the overall study by that investigator's data contribution is negligible, may not require the same level of due diligence as investigators with significant data contributions to the study.

[10] See 21 C.F.R. §54.2(e).

5. **Mutual Funds**

In the Draft Guidance's discussion of disclosure of equity interests in mutual funds (Q&A C.3), the draft guidance states that "if . . . the fund invested a substantial proportion of its capital in a sponsor of the covered clinical study, equity interests held in such publicly traded mutual funds would be reportable." This appears to require investigators to closely monitor the holdings of mutual funds in which they invest (but do not *control*) for investments in a sponsor, and to report if such holdings form a "substantial proportion" of the fund's capital. It is not realistic to expect investigators to track the investment decisions of mutual funds in this manner, and no guidance is given as to what would constitute a "substantial" investment by the fund. FDA should clarify that the guidance is limited to funds in which the investigator *controls* investment decisions.

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PhRMA appreciates the opportunity to provide comments on the Draft Guidance. We would be happy to discuss our concerns with the agency in more detail. If you have any questions, please do not hesitate to contact me.

Respectfully submitted,

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