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Client Alert

FDA & Life Sciences Practice Group

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FDA Issues Final Guidance on Financial Disclosure by Clinical Investigators

On March 1, 2013, the U.S. Food and Drug Administration (FDA or "the Agency") published a final guidance entitled, "Guidance for Clinical Investigators, Industry, and FDA Staff: Financial Disclosure by Clinical Investigators" ("Final Guidance") (available here).[1] The Final Guidance addresses compliance with the regulations governing financial disclosure by clinical investigators contained in 21 C.F.R. part 54. The guidance summarizes these regulations and then addresses specific issues in an updated question-and-answer format. The Final Guidance incorporates comments received on the 2011 draft guidance with the same title ("Draft Guidance"), and recommendations made in a 2009 report by the U.S. Department of Health and Human Services Office of Inspector General (HHS OIG).[2]

Under 21 C.F.R. part 54, applicants that submit a marketing application for a drug, device, or biological product are required to submit specific information regarding the compensation to, and financial interests and arrangements of, any clinical investigator conducting studies covered by the regulations. Applicants must disclose such interests that could affect the reliability of data submitted to FDA and identify steps taken to minimize the potential for bias, or they must certify the absence of these interests.

Notable Developments in the Final Guidance

- Clarifies key terms and concepts, including: "applicant," "clinical investigator," "covered clinical study," "dependent child," "material support," "responsible corporate official or representative," "sponsor of the covered clinical study," and the "$25,000 threshold amount for reporting;"
- Describes a more flexible approach based on "reasonable judgment" for the "due diligence" exercised in the collection of financial information; and
- Provides additional details on FDA's analysis of financial disclosure information and the Agency's plan to disclose information about the number of clinical investigators with financial interests.

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1. **Clarification of Key Terms and Concepts**

- **"Applicant":** The Final Guidance clarifies that, for the purposes of financial disclosure, "applicant" includes a "submitter," and the term "application" includes a "510(k) submission." Final Guidance at 3.

- **"Clinical Investigator":** The Final Guidance clarifies that even clinical investigators that did not participate for the entire duration of the study are included in the definition of "clinical investigator". For such individuals, financial disclosure information should be collected for the period of time he or she participated in the study and for one year following the end of his or her participation. Final Guidance at 2-3.

- **"Covered Clinical Study":** The Final Guidance provides specific examples of the types of clinical studies that constitute "covered clinical studies" for the purposes of 21 C.F.R. part 54: clinical studies submitted in support of new drug applications (NDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), abbreviated new drug applications (ANDAs) under section 505(j) of the FDCA, premarket notification submissions under FDCA section 510(k), reclassification petitions under FDCA section 513, premarket approval applications (PMAs) under FDCA section 515, biologics licensing applications (BLAs) submitted under section 351 of the Public Health Services Act, as well as studies submitted in support of amendments or supplements to any such applications. FDA also clarifies that covered clinical studies would generally not include expanded access under FDCA section 561. Final Guidance at 3.

- **"Dependent Child":** According to the Final Guidance, for the purposes of clinical financial disclosure under 21 C.F.R. Part 54, a "dependent child" includes "the investigator's child (whether by blood or adoption), stepchild or foster child who is unmarried, and for whom the investigator provides more than one-half of the child's support." This would include "a child who, at any time during the course of the study and for one year following completion of the study, is under the age of 19, under the age of 24 if a full-time student, or who is permanently and totally disabled. Such a child would generally have the same principal residence as the investigator." Final Guidance at 16.

- **"Employee":** If the clinical investigator's spouse or dependent child is an employee of the sponsor, the applicant should identify the clinical investigator as an employee. Final Guidance at 6.

- **"Material Support":** Parties that provide "material support" are considered sponsors of the covered clinical study. FDA clarifies in the Final Guidance that "material support" includes "providing direct funding or other monetary support such as through a grant, or providing services or materials." Final Guidance at 21. By contrast, parties that receive reimbursement for the services and/or materials provided are generally not considered to be sponsors. The Final Guidance states that "a CRO paid by a sponsor to perform services would not be considered a sponsor of the covered clinical study. Materials could include the product under study as well as other products and/or equipment that are needed for the conduct of the study, such as ancillary medication and equipment used in testing required by the protocol." Final Guidance at 21.

- **"Other Responsible Corporate Official or Representative":** In the Final Guidance, FDA recommends that the "other responsible corporate official or representative" be a senior official who has the authority to ensure the information is collected and reported accurately. Final Guidance at 9. FDA suggests that, depending on corporate structure, such an individual could be the person in charge of regulatory or clinical affairs. *Id.*

- **"Sponsor of the Covered Clinical Study":** In the Final Guidance, FDA provides an example to supplement its definition of "sponsor of the clinical study," specifically with regard to studies involving more than one sponsor for whom financial information will need to be collected. FDA explains that "if one party designed and conducted the covered clinical study, a second party provided funding, and a third party provided the test product, there would be three sponsors of the covered clinical study. However, if the third party in this example was reimbursed for the test product, it would not be considered a sponsor of the covered clinical study and the study would be considered to have two sponsors." FDA clarifies that the dollar amounts that trigger disclosure are per sponsor. Final Guidance at 3.

- **"$25,000 Threshold Amount for Reporting":** The Final Guidance clarifies that the $25,000 threshold amount for reporting "significant payments of other sorts" (SPOOS) is based on the cumulative amount of SPOOS received by the clinical investigator over the course of the study and for one year following completion of the study, and not on the amount received annually. A grant of at least $25,000 to the clinical investigator's institution that does not name the investigator, but which is worded so that only he/she could fulfill it would be a SPOOS. Final Guidance at 4, 12-13, 14.

2. Due Diligence Expected under 21 C.F.R. Part 54

Under 21 C.F.R. § 54.4, an applicant must exercise "due diligence to obtain the information required in this section." If an applicant is unable to obtain the information, "the applicant shall certify that despite the applicant's due diligence in attempting to obtain the information, the applicant was unable to obtain the information and shall include the reason." In the Draft Guidance, FDA specified the efforts that applicants should make to obtain information that was not available from a sponsor to make a complete certification or disclosure: at least two telephone calls, documentation of these calls in written memoranda, and no fewer than two certified letters.

The Final Guidance, however, recognizes a more flexible approach to this due diligence and recommends that sponsors and applicants "should exercise reasonable judgment regarding the appropriate amount of effort to expend when attempting to contact investigators, which may include consideration of the role of the investigator in the study and the importance of the investigator's data contribution." Final Guidance at 9. As in the Draft Guidance, the Final Guidance provides suggestions regarding how to document such efforts, emphasizing that the method used to contact investigators should allow verification of receipt (*e.g.*, certified mail or courier service). Final Guidance at 9. Furthermore, consistent with the Draft Guidance, an applicant must exercise due diligence whether a covered study was conducted domestically or internationally.

The Final Guidance emphasizes that the policies and procedures of the clinical investigator's institution for disclosure, review, and management of financial conflicts of interests of their employees (including spouse and dependent children)

are not a substitute for compliance with 21 C.F.R. part 54. FDA explains that although the investigator's institution "may take steps to manage a clinical investigator's financial interests and arrangements," FDA "must make its own evaluation." Applicants should include in their disclosure statements to FDA any pertinent steps taken by the institution to minimize bias. Final Guidance at 8.

3. FDA Review of Financial Information and Potential Disclosure

In the Final Guidance, FDA expands its description of how the Agency analyzes clinical investigator financial disclosure information and determines whether to refuse to file an application. The Final Guidance acknowledges that "some financial interests and arrangements are of greater concern than others when assessing the reliability of the data." Final Guidance at 27. FDA reviewers should consider the steps taken by the sponsor to minimize bias and consider elements of the study design, among other factors, to "make a judgment as to whether the financial interests or arrangements disclosed may have affected the interpretation of study results or otherwise require further action." Final Guidance at 27. FDA reviewers also should attempt to contact applicants to obtain missing information, but the Final Guidance encourages applicants to "take reasonable steps" to ensure the completeness of applications. Final Guidance at 26.

In a nod to the increased interest in financial arrangements between clinical investigators and manufacturers, "FDA intends to provide information about the number of clinical investigators with disclosable financial interests or arrangements in the new product reviews FDA posts for an approval decision." The Final Guidance states that this information would not identify clinical investigators by name, but would likely identify the number of clinical investigators in a study and the number of investigators with disclosable financial interests or arrangements. Final Guidance at 29.

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King & Spalding would be happy to assist in preparing comments regarding FDA's Final Guidance. Please contact us if you would like further information or assistance.

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[1] FDA's Office of Commissioner prepared the Final Guidance, with input from the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Devices and Radiological Health (CDRH). Final Guidance at Footnote 1.

[2] Specifically, OIG recommended that FDA: (1) ensure that sponsors submit complete financial information for all clinical investigators; (2) ensure that reviewers consistently review financial information and take action in response to disclosed financial interests; and (3) require that sponsors submit financial information for clinical investigators as part of the pretrial application process. *See* Office of Inspector General, U.S. Department of Health and Human Services, OEI-05-07-00730, *The Food and Drug Administration's Oversight of Clinical Investigators' Financial Information, available at* https://oig.hhs.gov/oei/reports/oei-05-07-00730.pdf (published in 2009).