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FDA and HHS Rules on Disclosure of Conflicts of Interest in Research

The issue of potential conflicts of interests by those engaged in research is not new. However, within the last twelve months, two Federal agencies have published guidance with respect to disclosures of conflicts of interest by those engaged in clinical research. The following sets forth a summary of the current Food and Drug Administration ("FDA") requirements with respect to financial conflicts of interest and where noted, incorporates provisions of a draft guidance that was issued by the FDA in 2011. The summary also includes the U.S. Department of Health and Human Services ("HHS") requirements with respect to financial conflicts of interest held by researchers including new provisions which go into effect on August 24, 2012. The summary should be used only as a guide and is not intended to replace the need for you to review the FDA or HHS regulations in their entirety and/or to seek legal counsel with respect to your set of facts as these rules are subject to agency interpretation.

Topic	FDA Regulations	HHS Regulations
The Rule:	21 CFR 54 and *Draft Guidance for Clinical Investigators, Industry, and FDA Staff Financial Disclosure by Clinical Investigators * The FDA issued guidance in 2001 and subsequently issued the cited draft guidance in 2011 (the "Draft Guidance"). The comment period has closed for the Draft Guidance and we await a final guidance. This summary chart includes provisions of the Draft Guidance where noted.	42 CFR Part 50, Subpart F (grants and cooperative Agreements)* *HHS issued the above cited regulation in August of 2011 (the "HHS Rule") which requires implementation by August 24, 2012, or immediately upon an organization's revision of its conflict of interest policy to comply with the HHS Rule and the organization making its policy publically available.
Applicable to:	Clinical studies submitted in a marketing application that the applicant or FDA relies on to establish that the product is effective and any study where a single investigator "makes a significant contribution to" the demonstration of safety.	Federally funded research (receiving funding from the U.S. Public Health Service ("PHS")).
Financial interest is reported to:	FDA	HHS
Financial interest is reported by:	The applicant submitting a marketing application or an amendment or supplement to a marketing application of any drug, biological product, or device to the FDA.* *Although the applicant submitting the marketing application is the one that reports to the FDA, the Draft Guidance indicates that in the case of IND/IDE sponsors, sponsors should collect the financial disclosure information of clinical investigators for most clinical studies in the event they are used in a marketing application.	The Institution (as defined in the HHS Rule) or individual that applies for or receives research funding from PHS awarding components, including the National Institutes of Health ("NIH"), for grants, cooperative agreements, and research contracts.

Questions or Assistance?

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Joan W. Feldman
(860) 251-5104
jfeldman@goodwin.com

David M. Mack
(860) 251-5058
dmack@goodwin.com

John H. Lawrence, Jr.
(860) 251-5139
jlawrence@goodwin.com

Vincenzo Carannante
(860) 251-5096
vcarannante@goodwin.com

Lina Estrada McKinney
(860) 251-5660
lmckinney@goodwin.com

William J. Roberts
(860) 251-5051
wroberts@goodwin.com

Maurice A. Headley
(860) 251-5048
mheadley@goodwin.com

Alex J. Hwang
(860) 251-5334
ahwang@goodwin.com

www.shipmangoodwin.com

What needs to be disclosed:	The financial interests of any listed or identified investigator or sub-investigator who is directly involved in the treatment or evaluation of research subjects in the study (includes the spouse and each dependent child of such investigator or sub-investigator).	All significant financial interests of an "Investigator" (and those of the Investigator's spouse and dependent children) that are: • related to an NIH-funded research project (or related to an investigator's Institutional Responsibilities (as defined in the HHS Rule)) and • could directly and significantly affect the design, conduct, or reporting of NIH- funded research. An Investigator is defined as the Project Director/Principal Investigator, as well as any other person regardless of title or position, who is responsible for the design, conduct or reporting of research funded by the PHS.
What is a reportable financial conflict of interest:	• Compensation made to the investigator by any sponsor of the covered clinical study where the value of compensation to the investigator could be affected by the outcome of the study. • Any proprietary interest in the tested product (patent, trademark, copyright, licensing agreement). • During the study and 1 year after completion with respect to a clinical investigator (includes spouse and dependent children aggregate): (i) any equity interest in any sponsor of the covered clinical study, ownership interest, stock options, other financial interest whose value cannot be readily ascertained through reference to public prices (generally, interests in a non-publicly traded company), or (ii) any equity interest in a publicly traded company that exceeds $50,000; or (iii) significant payment of other sorts-payments made by the sponsor of a study to the investigator/researcher to support activities of the investigator that have a monetary value of more than $25,000, exclusive of the costs of conducting the clinical study or other clinical studies (e.g. a grant to fund	Reportable Significant Financial Interest are: • With regard to any publicly traded entity, a financial interest where the value of the remuneration received from the entity in the 12 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. Remuneration includes salary and any payment for services not otherwise indentified as salary (e.g. consulting fees, honoraria, paid authorship). Equity interests includes any stock, stock option, or other common ownership interest, as determined through reference to public prices or other reasonable measures of fair market value. • With regard to any non-publicly traded entity, a financial interest where the value of any remuneration received from the entity in the 12 months preceding the disclosure, when aggregated, exceeds $5,000 or when the Investigator (or the Investigator's

	ongoing research, compensation in the form of equipment or retainers for ongoing consultation or honoraria).	spouse or dependent children) holds an equity interest (e.g. stock, stock option, or the ownership interest). • IP rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests. • With some exceptions, Investigators also must disclose the occurrence of any reimbursement 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.
Exclusions from disclosure requirements:	• Generally, reasonable payments made to investigators to cover reimbursable expenses such as transportation, lodgings and meals would not need to be tracked, with several exceptions. • Equity interest on mutual funds and 401(k)s if investigator has no control over buying/selling stock is, in most cases, not reportable. • Payments by a sponsor for the cost of conducting the clinical study of the product under consideration. • Payments made to the Institution that are not made on behalf of the investigator and are not specifically targeted towards the investigator. • Payments that meet the same criteria and are made to other researchers at the Institution, who are not part of the covered study.	• Salary, royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed or otherwise appointed by the Institution. • Intellectual property rights assigned to the Institution and agreements to share in royalties related to such rights. • Any ownership interests 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 retirements 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, an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education.

		• Income from service on advisory committees or review panels for a federal, state, or local government agency, or an institution of higher education, an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education.
How information is reported:	Requires applicant to submit for each clinical investigator a Form FDA 3454 attesting to absence of financial interests/arrangements or a form FDA 3455 disclosing financial interests.	Institution submits Financial Conflict of Interest reports to the NIH through the Electronic Research Administration ("ERA").
Public Accessibility Requirement:	The FDA is currently developing its policy on transparency, which may affect what information, and in what manner, the FDA may publicly disclose clinical investigators' financial interests and arrangements. In the interval, the Draft Guidance indicates the FDA will carefully evaluate each circumstance on a case-by-case basis.	Requires an FCOI policy of an entity to be available via publically accessible web site if the entity has presence on a publicly accessible website or available to any requestor in writing within 5 business days of a request makes COIs of senior/key personnel accessible to public.
Management Plan Requirements:	Applicant must list any steps taken to minimize the potential for bias from any of the disclosed arrangements, interest, or payments in the disclosure statement to the FDA.	For all identified FCOIs, the Institution must develop and implement a management plan.
Mitigating Factors Considered:	• Whether multiple investigators are used; • Use of blinding objective endpoints; and • Measurement of endpoints by someone other than investigator. Draft guidance expands as follows: • The total number of investigators and subjects in the study, the number and percentage of subjects enrolled by the disclosing investigator, information obtained from on-site inspections, the design of the clinical study (double-blind, single-blind, placebo-controlled, active-controlled), the method of randomization, the nature of primary and secondary endpoints (objective, subjective), the method of endpoint assessment, method of evaluation, whether someone other than the disclosing investigator measured the endpoints, and the results of the investigator compared to the results of other investigators in the study.	Management plan for FCOIs, must include: • the role and principal duties of the conflicted Investigator in the research project; • conditions of the management plan; • how the management plan is designed to safeguard objectivity in the research project; • confirmation of the Investigator's agreement to the management plan; • how the management plan will be monitored to ensure Investigator compliance; and • other information as needed.

Retrospective Review:		Imposes retrospective review of a researcher's study if non compliance with the disclosure requirements has been found, to determine if bias existed in the research. Reporting to HHS is only required if bias is found.
Updating Requirements:	Prompt update if any relevant changes occur in the information provided during the investigation and 1 year following completion of the study.	Each Investigator who is participating in the PHS/NIH-funded research must submit to the Institution an updated disclosure of a new Significant Financial Interest or a Significant Financial Interest that was not timely disclosed.
Record Retention requirements:	2 years after date of approval of application.	Records maintained for at least 3 years from the date of submission of the final expenditures report or, where applicable, from other dates specified in 45 CFR 74.53(b) and 92.42(b) for different situations. Must maintain records of • all Investigator disclosures of financial interests • the Institution's review of, and response to, such disclosures (whether or not a disclosure resulted in the Institution's determination of FCOI) • all actions under the Institution's policy or retrospective review, if applicable.
Process for reporting FCOIs:	FDA forms are used to report. The sponsor of a covered clinical study is required to obtain certain clinical investigator information before allowing a clinical investigator to participate in covered clinical investigation. • Applicant (which may or may not be a sponsor) submits to the FDA a list of all clinical investigators who conducted a covered clinical study identifying those who are employees of the sponsor of a covered study and those who are not. • For those not employees of a sponsor, applicant must: (i) certify no financial interest/arrangement exists; (ii) disclose nature of interests and steps taken to minimize potential bias (if applicant can not certify that no financial interest	• Investigators of the Institution must disclose financial interests to the Institution and abide by entity's FCOI policy. • The Institution identifies a designated official(s) to review all financial disclosures by its investigators. • The Institution's designated official determines whether the significant financial interest is related to NIH funded research and whether a financial conflict of interest exists by making a reasonable determination that a Significant Financial Interest could be affected by the NIH-funded research or is an entity whose financial interest could be affected by the research.

	exists); (iii) if unable to collect all required information, certify that applicant was unable to obtain some or all of the financial information needed to disclose or certify for a clinical investigator, identify any disclosable financial interests of which it is aware, certify that it acted with due diligence to obtain the information listed and include an attachment identifying the reason why any missing information could not be obtained, in each case using appropriate forms. • The FDA makes the determination of whether a financial conflict of interest occurs in its review of the application.	• If a Financial Conflict of Interest exists, the Institution must submit an FCOI report to NIH within a 60-day period from date of disclosure by Investigator. • The Institution must manage the FCOI pursuant to its policies and procedures and a management plan that has certain key elements. • The Institution signifies compliance with HHS regulations by posting its Financial Conflict of Interest policy (or, if the Institution does not have current presence on a publicly accessible website, by making the policy publicly accessible by written request). • NIH professional and scientific staff will evaluate the information received to determine whether an Institution's actions are sufficient to manage the identified Financial Conflict of Interest given the program's knowledge about the NIH-funded project. • NIH will utilize the information to monitor the Institution's compliance with the regulation. NIH will follow-up when additional information is needed to complete NIH's review and/or address specific questions.
Penalties:	• The FDA may refuse to file any marketing application if it does not contain required information of certification. • If the FDA determines that the financial interests or arrangements of any clinical investigator raise a serious question about the integrity of the data, the FDA will take any action it deems necessary to ensure the reliability of the data (21 CFR § 545(c)) including: 1. Initiating agency audits of the data derived from the clinical investigator in question; 2. Requesting that the applicant submit further analyses of data,	Loss of funding.

	e.g., to evaluate the effect of the clinical investigator's data on the overall study outcome; 3. Requesting that the applicant conduct additional independent studies to confirm the results of the questioned study; and 4. Refusing to treat the covered clinical study as providing data that can be the basis for an agency action.	
Other:	The FDA regulations are silent as to whether an organization that has a more stringent FCOI policy is required to follow the more stringent policies. Applicants may need to include information regarding subinvestigators if they meet the definition of clinical investigator.	If an organization has more stringent FCOI policies it is required to follow its more stringent internal policies. In any case in which HHS determines that a NIH-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 conflicting interest that was not managed or reported by the Institution as required by the regulation, the Institution must require the Investigator(s) involved to disclose the Financial Conflict of Interest in each public presentation on the results of the research and to request an addendum to previously published presentations. The HHS Rule applies to subrecipients, subgrantees and collaborators (e.g., subcontractors or consortium members) who receive federal funds from an Institution who has been awarded the NIH funding for research.

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Joan W. Feldman
(860) 251-5104
jfeldman@goodwin.com

David M. Mack
(860) 251-5058
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John H. Lawrence, Jr.
(860) 251-5139
jlawrence@goodwin.com

Vincenzo Carannante
(860) 251-5096
vcarannante@goodwin.com

Lina Estrada McKinney
(860) 251-5660
lmckinney@goodwin.com

William J. Roberts
(860) 251-5051
wroberts@goodwin.com

Maurice A. Headley
(860) 251-5048
mheadley@goodwin.com

Alex J. Hwang
(860) 251-5334
ahwang@goodwin.com

One Constitution Plaza
Hartford, CT 06103-1919
860-251-5000

300 Atlantic Street
Stamford, CT 06901-3522
203-324-8100

1133 Connecticut Avenue NW
Washington, DC 20036-4305
202-469-7750

289 Greenwich Avenue
Greenwich, CT 06830-6595
203-869-5600

12 Porter Street
Lakeville, CT 06039-1809
860-435-2539

www.shipmangoodwin.com

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