INSTRUCTIONS FOR COMPLETING ANNUAL REPORT OF INTERLOCKING POSITIONS

GENERAL INFORMATION:

Purpose of Report

The data collected by this report will be used by the Federal Energy Regulatory Commission's staff for the review and oversight of interlocking positions between public utilities and certain other entities as described below.

Who Must Submit

This report must be completed by all persons holding interlocking positions between public utilities and certain other entities (described in the specific instructions) during any portion of the calendar year.

When to Submit

Submit this report on or before April 30 of each year for the preceding calendar year. (For example, the report for the year 1999 would be filed on or before April 30, 2000.)

What and Where to Submit

Submit an original and one (1) copy of this report to: Federal Energy Regulatory Commission, Office of the Secretary, Attention FERC 561, 888 First Street NE, Washington, DC 20426

Sanctions

This report is mandatory and is prescribed by Section 305(c)(1) of the Federal Power Act and 18 CFR 46.4. Failure to report may result in certain penalties and other sanctions as provided by law.

Where to Send Comments on Public Reporting Burden

The public reporting burden for this collection of information is estimated to average 0.25 hours per response, including the time for reviewing the instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to: Federal Energy Regulatory Commission, Attn: Federal Energy Regulatory Commission Information Clearance Officer, 888 First Street NE, Washington, DC 20426.

You shall not be penalized for failure to respond to this collection of information unless the collection of information displays a valid OMB control number.

GENERAL INSTRUCTIONS

1. Prepare this report in conformity with the requirements prescribed in 18 CFR 46.4.

2. Leave blank any columns that are not applicable.

SPECIFIC INSTRUCTIONS

Item and Instruction

Respondent Information

1 and 2 Enter your full name and your business address.

3 Enter the calendar year for which this report is filed.

4 and 5 If you are authorized by this Commission to hold the position of officer or director in accordance with Part 45 of the Commission's regulations: enter in space 4 the complete FERC docket number of such authorization; enter in space 5 the latest date of such authorization. Otherwise, leave these spaces blank.

6 Enter the public utility or public utility holding company to which you want next year's Form 561 sent.

Public Utility Data

Col (1) and Col (2) Enter in column (1) the name of each public utility in which you hold an executive position. In column (2) enter the appropriate code for each such position, according to the list below:

Code and Name

Dir Director
CEO Chief Executive Officer
PRES President
VP Vice President
SEC Secretary
TREA Treasurer
GM General Manager
COMP Comptroller
PURA Chief Purchasing Agent
OEP Other Executive Position

Interlocking Entity Data

Col (3) and Col (4) Enter in Column (3) the name of each entity in which you hold an interlocking position. Enter the appropriate code for each executive position you hold in the entity named in Column (3), using the list below:

Code and Name

DIR Director
CEO Chief Executive Officer
PRES President
VP Vice President
SEC Secretary
TREA Treasurer
GM General Manager
COMP Comptroller
PURA Chief Purchasing Agent
PART Partner
APPT Appointee
REP Representative
OEP Other Executive Position

Col (5) Enter in Column (5) the appropriate code type for each entity listed in Column (3), using the list below:

Code and Name

FIN Investment bank; bank holding company; foreign bank or subsidiary thereof doing business in the United States; other organization primarily engaged in the business of providing financial services or credit; mutual savings bank; or savings and loan association
FINI Insurance company
SECU Entity authorized by law to underwrite or participate in the marketing of securities of a public utility
ELEQ Entity which produces/supplies electric equipment for the use of any public utility
FUEL Entity which produces/supplies coal, natural gas, nuclear fuel, or other fuel for the use of any public utility
20CL Entity specified in 18 CFR 46.3 (one of the 20 largest purchasers of electric energy from a utility)
CNEN Entity which is controlled by any one of the above named entities
305B Entity referred to in Section 305(b) of the Federal Power Act (not otherwise identified above)

Col (6) For each entity that supplies electric equipment (ELEQ) named in Column (3) enter the aggregate amount of revenues from producing or supplying electrical equipment to any public utility named in column (1) in the subject calendar year, rounded to the nearest $100,000. Otherwise, leave this column blank.

Signature The original of this report must be dated and signed. The copy must bear the date that appeared on the original. The signature on the copy may be stamped or typed on the copy.

[FR Doc. 98–34131 Filed 12–30–98; 8:45 am]

BILLING CODE 6717–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 54

[Docket No. 93N–0445]

RIN 0910–AB77

Financial Disclosure by Clinical Investigators

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; action on petition for reconsideration.

SUMMARY: The Food and Drug Administration (FDA) is revising the requirements regarding financial disclosure by clinical investigators in order to add material to the codified language that was inadvertently omitted and to clarify the compliance dates to, in some cases, restrict the retroactive application of certain requirements of the rule. FDA is making these changes in order to respond to concerns raised by the Pharmaceutical Research Manufacturers Association (hereinafter referred to as ''PhRMA''). By making these changes, FDA will be reducing the administrative burden for manufacturers and other affected parties while, at the same time, ensuring that the agency obtains the information that is most relevant to its review of clinical data submitted in marketing applications.

DATES:

Effective Date: This regulation becomes effective February 2, 1999.

Comment Date: Submit written comments on the information collection provisions in the rule published on

February 2, 1998 (63 FR 5233), by February 1, 1999.

Compliance Date: Compliance with collection of information on any equity interest in a publicly traded corporation that exceeds $50,000 as defined in § 54.2(b) (21 CFR 54.2(b)) as published at 63 FR 5250 (February 2, 1998) is required for covered clinical trials that are ongoing as of February 2, 1999.

Compliance with collection of information on significant payments of other sorts as defined in § 54.2(f), as published at 63 FR 5250 (February 2, 1998) is required for those payments made on or after February 2, 1999.

ADDRESSES: Submit written comments on the information collection provisions of this final rule to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: Mary C. Gross, Office of External Affairs (HF–60), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–3440, FAX 301–594–0113.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of February 2, 1998 (63 FR 5233), FDA published a final rule entitled ''Financial Disclosure by Clinical Investigators'' (hereinafter referred to as ''the February 2, 1998, final rule''). The February 2, 1998, final rule required the sponsor (hereinafter referred to as ''the applicant'') of a marketing application for any drug product, including any biological product, or any device to submit certain information concerning the compensation to, and financial interests of, clinical investigators conducting certain clinical studies. This requirement applied to any covered clinical study of a drug or device submitted in a marketing application that the applicant or FDA relies on to establish that the product is effective, including studies that show equivalence to an effective product, or that make a significant contribution to evidence of safety. The February 2, 1998, final rule required applicants to certify to the absence of certain financial interests of clinical investigators and/or disclose those financial interests, when covered clinical studies were submitted to FDA in support of a marketing application. The purpose of the February 2, 1998, final rule is to help ensure that financial interests and compensation arrangements of clinical investigators that could affect the reliability of data submitted to FDA in support of product marketing are identified and disclosed by the applicant. If the applicant does not include certification or disclosure, or both if required, or does not certify that it was not possible to obtain the information, the agency may refuse to file the application.

In the February 2, 1998, final rule, all reporting requirements applied to any marketing application submitted on or after February 2, 1999. This final rule will change the reporting requirements by greatly reducing the need to gather required information retrospectively for studies already completed. Specifically, information on the equity interests of investigators in a publicly traded corporation, as described in § 54.2(b), must be collected only for those covered clinical studies that are ongoing as of February 2, 1999. In addition, manufacturers will only be required to report any significant payments of other sorts as described in § 54.2(f) made on or after February 2, 1999.

FDA is also revising the definition of ''covered clinical studies'' in § 54.2(e). With regard to studies that make a significant contribution to the demonstration of safety, the agency has concluded that only those studies in which a single investigator makes a significant contribution to the demonstration of safety will be included in the definition of covered clinical study. This change would generally exclude phase 1 tolerance studies or pharmacokinetic studies (unless they are critical to an efficacy determination), large open safety studies conducted at multiple sites, treatment protocols and parallel track protocols from the definition of covered clinical study and, therefore, eliminate the need to collect and report information on the financial interests of investigators in those trials. Finally, in order to obtain information only about investigators who had significant roles in covered clinical studies, FDA is amending the definition of ''clinical investigator'' in § 54.2(d) to clarify that it is intended to include only listed or identified investigators or subinvestigators who are directly involved in the treatment or evaluation of research subjects. These changes are being made in part in response to a petition for reconsideration submitted to the agency by PhRMA on August 3, 1998. The Health Industry Manufacturers Association submitted a comment to the rule supporting the petition on August 17, 1998.

II. Petition for Reconsideration

FDA received a petition for reconsideration on August 3, 1998, from PhRMA requesting that some provisions of the final rule be reconsidered and changed. The petition argued that these provisions imposed substantial logistical and information collection burdens on sponsors and applicants without providing any significant benefit to the public. As discussed in section V of this document, PhRMA had also submitted a comment under the Paperwork Reduction Act of 1995 (the PRA) on the information collection provisions of the rule. The comment made essentially the same arguments as the petition, although it was slightly broader. Aspects of the PhRMA comment not included in the petition are addressed in section V of this document.

In the petition, PhRMA asked that the agency reconsider requiring applicants to retrospectively collect information; that is, PhRMA asked that the final rule be applied only to studies commenced after the February 2, 1999, effective date of the rule. The petition also sought to modify the final rule in several respects. Specifically, PhRMA requested that the rule not apply to large multicenter studies, subinvestigators who do not have primary responsibility for a clinical trial, and that it not apply to payments of less than $1,000 to individuals and less than $2,500 to sponsors' associated institutions when sponsors are collecting information about ''significant payments of other sorts'' as defined in § 54.2(f). PhRMA also asked FDA to respond to the petition by September 28, 1998, or stay the effective date of the final rule pending reconsideration, with 12 months of lead time for implementation when the stay is lifted.

Under § 10.33(b) and (g) (21 CFR 10.33(b) and (g)), a petition for reconsideration must be submitted within 30 days after the date of the decision involved. However, § 10.33(b) also provides that, for good cause, the Commissioner of Food and Drugs may consider an untimely petition for reconsideration. Although PhRMA's petition was submitted well after the deadline, FDA finds that good cause exists because of the strength of certain arguments in the petition concerning the desirability of modifications to some aspects of the February 2, 1998, rule.

III. Response to Petition

FDA has carefully evaluated the petition for reconsideration and reviewed the administrative record of the February 2, 1998, final rule to determine whether the standard in § 10.33(d) for granting a petition for reconsideration has been met. As explained in the following paragraphs, the agency concludes that the standard has been met with respect to some of the actions requested in the petition for

reconsideration. Specifically, the agency concludes that: (1) The petitioner's position is not frivolous and is being pursued in good faith; (2) with respect to certain provisions of the February 2, 1998, final rule, the agency did not adequately consider certain information or views in the administrative record; (3) the petition has demonstrated sound public policy grounds supporting reconsideration of those provisions; and (4) reconsideration of those provisions is not outweighed by public health or other public interests. Therefore, the agency is revising parts of the final rule based on arguments in the petition for reconsideration. By making these revisions, the agency will also reduce the information collection burden associated with implementation of this final rule.

A. Retrospective Collection of Information

FDA received some comments on the proposed rule that asked FDA to apply the rule prospectively, to avoid penalizing applicants and clinical investigators whose clinical investigations were concluded or already in progress. FDA responded in the February 2, 1998, final rule that it was important to know about the financial arrangements and payments that were considered to be problematic in a timely manner and that implementation should not be long deferred. The agency also stated that in order to give applicants time to comply with the final rule and to avoid delayed submissions, applicants would not be required to comply with the final rule until 1 year after the publication date of the final rule. The agency recognized that there may be times where, despite the applicant's diligent efforts to collect this information, the applicant may be unable to obtain it. FDA amended the final rule to permit an applicant who can show conclusively why this information could not be obtained to certify that the applicant acted diligently to obtain the information, but was unable to do so and to include the reason why such information could not be obtained.

Based on arguments presented in the petition for reconsideration, FDA is revising this final rule with regard to collection of information on equity interests in a publicly traded company when such interests exceed $50,000 in value as defined in § 54.2(b). Sponsors will be required to collect information regarding such interests only in those covered clinical studies that are ongoing as of February 2, 1999. FDA is also revising the final rule with regard to collection of information concerning significant payments of other sorts, defined under § 54.2(f), so that submission of this information is required only for payments made on or after February 2, 1999.

Collection of information described under § 54.2(a), ''compensation affected by the outcome of clinical studies'', and § 54.2 (c), ''proprietary interests in the tested product'', will be required for investigators participating in covered clinical studies, whether they are ongoing or already completed, if the studies are used to support applications that are submitted on or after February 2, 1999. In addition, sponsors will be required under § 54.2(b) to collect information on any ownership interest whose value cannot be readily determined through reference to public prices (generally interests in a nonpublicly traded corporation) for investigators participating in all covered clinical studies, whether they are ongoing or already completed, if they are used to support applications that are submitted on or after February 2, 1999. FDA is not changing these requirements because the agency believes that the information required under § 54.2(a), (b), (with regard to any ownership interest whose value cannot be readily determined through reference to public prices) and (c) is the most critical to the agency and therefore, its collection should not be deferred. By modifying the compliance dates of § 54.2(b) (equity interests that exceed $50,000 in a publicly traded corporation) and (f) (significant payments of other sorts), FDA has eliminated the potential administrative burden to sponsors of reconstructing records after the fact, thereby reducing the information collection burden on regulated industry without compromising the integrity of the final rule.

B. Clinical Investigator Definition

In the September 22, 1994 (59 FR 48708) proposed rule, FDA defined clinical investigator to mean any investigator who is directly involved in the treatment or evaluation of research subjects, or who could otherwise influence the outcome of the research. Spouses and dependent children were also included under the definition of clinical investigator. The proposed rule asked for comment on whether the definition of clinical investigator should include business partners of the investigator who might share in profits from the investigator's arrangements or financial interests. Most comments objected to including business partners under the definition of clinical investigator. Several comments on the proposed rule found the definition to be too broad and stated that, as proposed, the definition would involve all study personnel and pose an enormous administrative burden. One comment recommended limiting the scope of the definition to the principal investigator only.

In the February 2, 1998, final rule, FDA agreed with comments that stated that including business partners under this definition was unnecessary and potentially burdensome. FDA also agreed with those comments that supported narrowing the definition. The February 2, 1998, final rule defined clinical investigator to mean any listed or identified investigator who is directly involved in the treatment or evaluation of research subjects. The definition also included the investigator's spouse and dependent children. It was not intended to include hospital or office staff who may provide occasional care to subjects.

In the petition for reconsideration, PhRMA argued that the final rule should not apply to subinvestigators because it would be too burdensome to collect and report financial information concerning subinvestigators. In addition, the petition asserted that subinvestigators often play a limited role in the conduct of a trial and do not have a significant effect on the trial's outcome and therefore should be excluded.

After careful consideration of this request, the agency disagrees with the reasoning in the petition about subinvestigators and declines to adopt the request that they all be excluded from the final rule. FDA believes that it is appropriate to clarify the definition of clinical investigator, however, in light of this request. The agency wishes to make clear that individuals included in the definition of clinical investigator are only those who actually and directly participate in the conduct of the trial and not those who may occasionally provide treatment to subjects.

The agency believes that most of the individuals participating in the conduct of a clinical trial could be described as subinvestigators. If the position recommended in the petition were adopted, the agency would likely receive financial information for no more than a handful of individuals for each trial, regardless of how many individuals were actually directly involved in the treatment or evaluation of research subjects. FDA believes that subinvestigators generally perform a significant amount of the work involved in the conduct of a trial and can therefore influence its results. It would not be prudent to exclude all subinvestigators because to do so would mean that much of the most meaningful

and relevant information would not be reported which, in turn, would greatly weaken the agency's ability to assess the reliability of clinical trial data. For this reason, FDA will not eliminate subinvestigators from the definition of ''clinical investigator.''

The agency believes that it has addressed the issue raised in the petition of the burden involved in reporting information concerning subinvestigators in several ways. First, as will be discussed more fully as follows, by narrowing the definition of covered clinical study to exclude large open safety studies conducted at multiple sites, treatment protocols, and parallel track protocols, the agency has eliminated the need for collecting and reporting information from the large number of individuals, many of whom are subinvestigators, who typically participate in those types of studies. Second, the change being made to eliminate the need for retrospective reporting of equity interests in publicly traded companies will also make the information on subinvestigators easier to collect. With these steps, FDA has considerably reduced the administrative burden associated with this final rule while maintaining the agency's ability to obtain the information it needs to assess the reliability of clinical trial data.

C. Covered Clinical Study Definition

In the September 1994 proposed rule, ''clinical study'' was defined as any study involving human subjects, including a study to establish bioavailability or bioequivalence, submitted in a marketing application subject to this part, that either the sponsor identifies as one that the sponsor relies on to establish that the product meets the regulatory requirements for marketing, or FDA identifies as one that it intends to rely on to support its decision to permit the marketing of the product. Under the proposal, studies submitted as publications or in brief summary form would generally not be considered ''covered clinical studies'' unless FDA informed the sponsor otherwise. The agency further proposed that a sponsor could consult with FDA as to which clinical studies constituted ''covered clinical studies'' for purposes of complying with financial disclosure requirements. Several comments recommended that FDA limit the scope of the rule with respect to covered studies. One comment said that the rule appeared to include large-scale open label studies, such as studies involving some cardiovascular therapies, compassionate use studies and parallel track studies, all of which might be submitted in support of a new drug application (NDA). The comment noted that investigators in such studies could number in the thousands and said that it would be an unwarranted burden to require an applicant to obtain financial information from each clinical investigator.

FDA responded in the preamble to February 2, 1998, final rule that in general, large open studies, treatment protocols, and other such studies with large numbers of investigators would not be covered studies. The preamble further states that because these studies generally have large numbers of investigators, no single investigator has a major responsibility for the data. The agency said in the preamble that although it is not impossible that a financial interest could be important in these studies, it is relatively unlikely, and the agency has concluded that the effort needed to obtain financial information for these investigators should not be undertaken. It has been brought to the agency's attention that the codified language of the regulation at § 54.2(e) did not fully reflect those preamble statements. The petitioners have asked FDA to reconsider whether the final rule should apply to these types of large, multicenter studies. FDA acknowledges that some material was inadvertently omitted from the codified language in the February 2, 1998, final rule and accordingly is adding language to the definition of ''covered clinical study'' to reflect the agency's original intention. The definition of ''covered clinical study'' has been amended to indicate that generally it does not include phase I tolerance studies or pharmacokinetic studies, most clinical pharmacology studies (unless they are critical to an efficacy determination), large open safety studies conducted at multiple sites, treatment protocols, and parallel track protocols.

D. Tracking Small Gifts in Calculating $25,000 Threshold for ''Significant Payments of Other Sorts''

The petitioners have asked that FDA amend the definition of significant payments of other sorts'' in § 54.2(f) so that sponsors are not required to collect or report information concerning individual payments less than $1,000 to physicians or less than $2,500 to institutions so that such payments are not counted in determining whether the $25,000 reporting threshold has been reached. The petitioners argued that the administrative burden of tracking such payments is unjustified. FDA declines to amend the final rule in this way. Payments under $1,000 or $2,500 respectively, if numerous or when added to a fairly large grant or to the value of equipment provided to the investigator, could bring the total amount of significant payments of other sorts to $25,000 or more. The agency believes that the aggregate amount of such payments is important, not the size of individual payments. In addition, FDA is reluctant to create a mechanism that could be used to circumvent the reporting requirement entirely by making many small payments to an investigator or institution. The agency has changed the compliance date regarding these payments, however, so that sponsors will begin to collect and report information regarding ''significant payments of other sorts'' only on such payments made on or after February 2, 1999. The agency believes this modification reasonably addresses sponsors' concerns about the burdensomeness of the requirement.

E. Request for Response by September 28, 1998 or Request to Stay the Rule

FDA does not believe there is a need to stay the rule indefinitely because by making the changes described previously, the agency has both clarified the requirements of the rule and significantly decreased the administrative burden associated with collecting this information. The agency finds that the petitioners have not demonstrated a need to delay the effective date for this rule and therefore declines to grant this request.

IV. Analysis of Impact

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act (Pub. L. 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; and distributive impacts and equity). The agency believes that the final rule is consistent with the regulatory philosophy and principles identified in the Executive Order and concludes that it is not a significant regulatory action as defined. The Regulatory Flexibility Act requires agencies to prepare a regulatory flexibility analysis for each rule, unless the agency certifies that the rule would not have a significant economic impact on a substantial number of small entities. As explained in the February 2, 1998, final rule, the agency believes that this final rule will

not have a significant economic impact on a substantial number of small entities. Nevertheless, the rule may impose significant costs on a few small businesses. Because FDA cannot adequately quantify all of this impact, it prepared a regulatory flexibility analysis as part of its economic assessment. Title II of the Unfunded Mandates Reform Act (in section 202) requires that agencies prepare a written assessment of anticipated costs and benefits before proposing any rule that may result in an expenditure in any 1 year by State, local, and tribal governments, in the aggregate or by the private sector of $100 million (adjusted annually for inflation). Because the rule will not result in expenditures of this amount, FDA is not required to prepare a cost-benefit analysis under this Act.

FDA is publishing these revisions in response to a petition for reconsideration of some of the rules' requirements on the grounds that they imposed a substantial burden on sponsors. The agency has amended the requirements in the final rule so that the information collection requirements for reporting equity interests in publicly held corporations that exceed $50,000 in value will apply to studies ongoing as of February 2, 1999, and the requirements regarding significant payments of other sorts will apply to payments made on or after February 2, 1999 (see section III.A and III.D of this document, respectively).

These changes will substantially reduce the affected industry's near term regulatory burden. Nevertheless, the agency has not reduced its earlier cost estimate, because its original impact analysis did not fully reflect the cost of collecting retrospective information on equity interests in publicly held corporations or of making significant payments of other sorts. The agency now believes that its original figure of less than $450,000 annually may have understated the reporting costs of the rule as published on February 2, 1998, but reasonably reflects that reporting costs of the final rule as amended. The revised definitions for ''clinical investigator'' and ''covered clinical study'' do not result in any change to the cost analysis because they continue to reflect the agency's earlier intent.

V. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the PRA of 1995 (44 U.S.C. 3501–3520). A description of these provisions is given as follows with an estimate of the annual reporting and recordkeeping burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

Title: Financial Disclosure by Clinical Investigators (21 CFR part 54)

Description: In the February 2, 1998, final rule, FDA issued regulations requiring the sponsor of any drug (including a biological product) or device marketing application to submit information concerning the compensation to, and financial interests of, any clinical investigator directly involved in the treatment or evaluation of subjects enrolled in certain clinical studies. This final rule revises the requirements of the February 2, 1998, final rule to reduce the information collection burden imposed on sponsors of drug and medical device products. The revisions are described in section III of this document.

As modified by this revised final rule, the requirement to disclose information about compensation to, and financial interests of, clinical investigators will apply to any study of a drug or device in humans submitted in a marketing application or reclassification petition that the applicant or FDA relies on to establish that the product is effective and to any study in which a single investigator makes a significant contribution to the demonstration of safety. The regulations require applicants to certify to the absence of certain financial interests of clinical investigators or disclose those financial interests as required, when covered clinical studies are submitted to FDA in support of product marketing. The purpose of the regulations is to ensure that financial interests and arrangements of clinical investigators that could affect the reliability of the data submitted to FDA in support of product marketing are identified and disclosed. The regulations will become effective on February 2, 1999.

FDA will evaluate the information provided about each covered clinical study in an application to determine the impact of any disclosed financial interests on the reliability of the study. If FDA determines that the financial interests of any clinical investigator raise serious questions about the integrity of the data, FDA may take any action it deems necessary to resolve those questions, including initiating agency audits of the questioned data; requesting that the applicant submit further analyses of data that evaluate the effect of the clinical investigator's data on overall study outcome; requesting that the applicant conduct additional independent studies to confirm the results of the questioned study; or refusing to consider the data from the questioned study in deciding whether to approve the application.

Description of Respondents: Respondents are sponsors of marketing applications containing clinical data from studies covered by the regulation. These sponsors represent pharmaceutical, biologic, and medical device firms. Many of these firms are small entities, especially those which manufacture medical devices and biotechnology products. Respondents are also clinical investigators who provide financial information to the sponsors of marketing applications.

The applicant will incur reporting costs in order to comply with the final rule. Applicants will be required to submit, for example, a complete list of clinical investigators for each covered study, a list that is already submitted in a marketing application. For investigators not employed by the applicant and/or the sponsor of the covered study, the applicant must either certify to the absence of certain financial arrangements with clinical investigators or disclose those arrangements to FDA.

FDA expects that almost all applicants will submit a certification statement under 21 CFR 54.4(a)(1) and (a)(2). Preparation of the statement using the following Form FDA 3454 will represent little effort and should require no more than 1 hour per study.

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. XXXX-XXXX
Expiration Date: XX/XX/XX

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☐ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
FIRM / ORGANIZATION	
SIGNATURE	DATE

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

Please **DO NOT RETURN** this form to this address.

FORM FDA 3454 (10/98)

EF
Created by Electronic Document Services/USDHHS: (301) 443-2454

BILLING CODE 4160–01–C

TABLE 1.—ESTIMATED NUMBER OF APPLICATIONS, CLINICAL TRIALS, AND INVESTIGATORS SUBJECT TO THE PROPOSED RULE BY TYPE OF APPLICATION[1]

Application Type	Total Number of Applications	Number of Applications Affected	Number of Trials	Number of Investigations
Drugs				
New drug application (NDA), new molecular entity (NME)	35	35	3 to 10	3 to 100
NDA nonNME	100	100	1 to 3	10 to 30
NDA efficacy supplement	100	100	1 to 3	10 to 30
Abbreviated new drug application (ANDA)	400	240	1.1	2
ANDA supplement	2,500	120	1	2
Rx switch	20	10	2	4
Biologics				
Product license application (PLA)	25	25	3 to 10	3 to 100
PLA efficacy supplement	10	10	1 to 3	3 to 100
Medical Devices				
Premarket approval (PMA)	50	50	1	10 to 20
PMA supplement	40	10	1	3 to 10
Reclassification devices	8	4	1	3 to 10
510(k)	6,000	300	1	20

[1] Source: Agency estimates.

When certification is not possible and disclosure is made using the following Form FDA 3455, the applicant must describe the financial arrangements or interests and the steps that were taken to minimize the potential for bias in the affected study. As the applicant will be fully aware of those arrangements and the steps taken to address them, describing them will be straightforward. The agency estimates that it will take about 4 hours to prepare this narrative.

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. XXXX-XXXX
Expiration Date: XX/XX/XX

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning _____ (*Name of clinical investigator*), who participated as a clinical investigator in the submitted study _____ (*Name of clinical study*), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☐ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
FIRM / ORGANIZATION	
SIGNATURE	DATE

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

<--Please **DO NOT RETURN** this form to this address.

FORM FDA 3455 (10/98)

EF

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Until the agency begins to collect information on the financial arrangements between investigators and applicants, it cannot know the actual number of disclosable arrangements. Therefore, it is not possible to predict the total cost to industry of preparing these explanatory statements with any certainty because the financial arrangements described in this rule are uncommon. FDA estimates that from 1 to 10 percent of the applications would need disclosure statements, and has used the extremely conservative estimate of 10 percent in Table 2 of this document.

Investigators must provide sponsors of the covered studies with sufficient accurate information to make the required disclosure or certification. Because much of the information required can be obtained from the applicant's own records, the costs incurred by the clinical investigator will be minimal. Clinical investigators are required to do one of two things: (1) Provide a statement that they, their spouse, and their dependent children did not have a significant equity interest as defined in § 54.2(b) in the sponsor of the covered study, or (2) disclose any such interest. Clinical investigators are accustomed to supplying such information in even greater detail when applying for research grants. Most people know the financial holdings of their immediate family, and records of such interests are generally accessible because they are needed for preparing tax records. FDA estimates that the time required for this task may range from 5 to 15 minutes.

TABLE 2.—ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Hours per Response	Total Hours
54.4(a)(1) and (a)(2)	1,000	1	1	1	1,000
54.4(a)(3)	100	1	1	4	400
54.4 (Clinical Investigators)	46,000	1	1	.10	4,600
Total					6,000

[1] There are capital costs or operating and maintenance costs associated with this collection of information.

The sponsors of covered studies will be required to maintain complete records of compensation agreements with any compensation paid to nonemployee clinical investigators, including information showing any financial interests held by the clinical investigator, for a period of 2 years after the date of approval of the application. This time is consistent with the current recordkeeping requirements for other information related to marketing applications for human drugs, biologics, and medical devices. FDA judged the incremental costs associated with this new activity to be negligible because firms already maintain records of compensation as standard business practice, and the required records pertaining to the financial interests of the investigators will typically consist of only one additional piece of paper per investigator. Currently, sponsors of covered studies must maintain many records with regard to clinical investigators, including protocol agreements and investigator resumes or curriculum vitae, and the inclusion of information required by this rulemaking would add little to this recordkeeping burden. FDA estimates that on average 15 minutes will be required for each recordkeeper to add this record to clinical investigators' files.

TABLE 3.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

21 CFR Section	No. of Recordkeepers	No. of Responses per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
54.6	1,000	1	1,000	.25	250

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

In the February 2, 1998, final rule (63 FR 5233 at 5249), FDA requested comments on the information collection provisions of the final rule. The agency received three comments in response to this request. As discussed previously, one of the comments was very similar to the petition for reconsideration to which this revised final rule responds. The issues raised by that comment that have already been discussed in earlier sections of this document will not be addressed again here.

One comment suggested that FDA use different criteria for disclosure of equity interests depending on the amount of sponsor capital. FDA disagrees. The $50,000 threshold was chosen to represent a dollar amount that could be important to an investigator. During the rulemaking, many comments were received on the issue of the appropriate threshold. Some suggested that FDA's rule should be made consistent with the Public Health Service final rule and the National Science Foundation statement of policy on Objectivity in Research published on July 11, 1995 (a considerably more stringent requirement than the disclosure requirement in FDA's final rule); others suggested different dollar thresholds, such as $10,000, or particular percentages of company equity. One comment suggested that investigators be banned from owning an equity interest in a sponsor that exceeded $25,000 a year. FDA's original proposal of a percent equity threshold was deleted from the final rule because the agency recognized that for many corporations this would represent an unrealistically large interest (e.g., 5 percent of a $10 million company is $500,000). Based on discussions with FDA's Science Board and comments received on FDA's proposed rule, FDA continues to believe that a $50,000 disclosure threshold strikes the appropriate balance between the agency's need to be aware of, and to help minimize, the potential for bias in clinical data.

This comment also stated that FDA underestimated the amount of time necessary to collect, analyze, and store the information needed to comply with the February 2, 1998, final rule. FDA agrees that the time estimates in that document may have been too low because FDA was not able to accurately predict the burden associated with collecting information from past covered clinical trials. FDA continues to believe that the majority of applicants will certify to the absence of covered financial interests and that sponsors will incorporate the collection of this information into the routine administration of their studies. FDA agrees that additional time would have been needed to gather information from investigators in past studies prior to the revisions made by this final rule. As FDA is revising the rule to eliminate most retrospective reporting, however, the burden will be significantly less than it would have been under the February 2, 1998, final rule. The agency has reevaluated its burden estimate and concludes that, although the estimate in the February 2, 1998, final rule (63 FR 5233 at 5249) underestimated the burden of retrospective reporting at that time, it now accurately reflects the lessened burden of the financial disclosure regulations as revised by this final rule. Therefore, the agency is not modifying its burden estimate.

Finally, this comment requests guidance from FDA on what the comment characterizes as ambiguities in the final rule. FDA has provided clarification through revisions made to this final rule. FDA declines to issue a guidance document before the rule becomes effective; however, FDA will assess the need for guidance after the agency and those subject to the rule have gained some experience with it's implementation.

A second comment suggested that FDA modify section 9 of Form FDA 1572, ''Statement of Investigator,'' to add a commitment that the investigator will comply with the financial disclosure regulations and to state whether the investigator holds a significant equity interest in the sponsor. The comment stated that this change to Form FDA 1572 would eliminate the need for investigators to complete additional documentation.

FDA does not agree with the comments' recommendation that Form FDA 1572 be changed. Clinical investigators are already required to comply with the financial disclosure regulations and, as part of this obligation, must provide financial information to the sponsor under 21 CFR 312.53(c)(4) and 312.64(d) of the final rule. The agency has developed FDA Forms 3454 and 3455 in an effort to facilitate the collection of this information. FDA also notes that the proposed change would not eliminate the need for the investigator to provide the details of any significant equity interests as required by the final rule. Therefore, the recommended change would make Form FDA 1572 more burdensome without reducing the burden under the final rule.

A third comment submitted by two clinical investigators from a government agency asked that a division within a Federal Government agency be exempted from reporting financial interests to FDA because it does not submit marketing applications to FDA for products tested under its investigational new drug application (IND's) and because, according to the comment, its phase III studies are designed, monitored, and assessed in such a way that the studies are not subject to the same potential bias found in smaller, investigator-initiated or company-sponsored studies. A government researcher conducting a clinical study under an IND held by a government agency does not have to report financial interests or arrangements to FDA, as it is the submission of a marketing application that triggers the disclosure requirement. If, however, the study were used to support an application, the applicant would be required to report any covered financial interests of the clinical investigators. FDA declines to make a change in response to this comment.

The information collection provisions of the February 2, 1998, final rule, as modified by this final rule, have been submitted to OMB for review. Individuals and organizations may submit comments on the information collection provisions by February 1, 1999. Comments should be directed to the Office of Information and Regulatory Affairs, OMB (address above).

Prior to the effective date of the final rule, FDA will publish a notice in the **Federal Register** announcing OMB's decision to approve, modify, or disapprove the information collection provisions. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

List of Subjects in 21 CFR Part 54

Biologics, Drugs, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 54 is amended as follows:

PART 54—FINANCIAL DISCLOSURE BY CLINICAL INVESTIGATORS

1. The authority citation for 21 CFR part 54 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 360, 360c–360j, 371, 372, 373, 374, 375, 376, 379; 42 U.S.C. 262.

2. Section 54.2 is amended by revising paragraphs (d) and (e) to read as follows:

§ 54.2 Definitions.

* * * * *

(d) *Clinical investigator* means only a listed or identified investigator or subinvestigator who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the investigator.

(e) *Covered clinical study* means any study of a drug or device in humans submitted in a marketing application or reclassification petition subject to this part that the applicant or FDA relies on to establish that the product is effective (including studies that show equivalence to an effective product) or any study in which a single investigator makes a significant contribution to the demonstration of safety. This would, in general, not include phase l tolerance studies or pharmacokinetic studies, most clinical pharmacology studies (unless they are critical to an efficacy determination), large open safety studies conducted at multiple sites, treatment protocols, and parallel track protocols. An applicant may consult with FDA as to which clinical studies constitute ''covered clinical studies'' for purposes of complying with financial disclosure requirements.

* * * * *

Dated: November 24, 1998.

Michael A. Friedman,

Lead Deputy Commissioner for the Food and Drug Administration.

Donna E. Shalala,

Secretary of Health and Human Services.

[FR Doc. 98–34546 Filed 12–30–98; 8:45 am]

BILLING CODE 4160–01–F

INTERNATIONAL DEVELOPMENT COOPERATION AGENCY

U.S. Agency for International Development

22 CFR Part 228

RIN 0412–AA40

Rules on Source, Origin and Nationality for Commodities and Services Financed by USAID: Special Source Rules Requiring Procurement from the United States

AGENCY: United States Agency for International Development (USAID), IDCA.

ACTION: Final rule.

SUMMARY: USAID is amending its regulation on source, origin and nationality for commodities and services financed by USAID by dropping the requirement that vehicles must be manufactured by, and bear the nameplates of, Chrysler, Ford or General Motors in order to be considered U.S.-manufactured vehicles eligible for USAID financing. The rule served little practical purpose since these are the only vehicles manufactured in the U.S. that are generally available for export from the United States. Foreign corporations manufacturing vehicles in the U.S. are doing so for U.S. consumption. Removing the requirement simplifies the rules and has no significant impact.

DATES: Effective March 1, 1999.

FOR FURTHER INFORMATION CONTACT: Kathleen O'Hara, Office of Procurement, Policy Division (M/OP/P) USAID, Washington, DC 20523–7801. Telephone: (202) 712–4759, facsimile: (202) 216–3395, e-mail address: koharausaid.gov.

SUPPLEMENTARY INFORMATION: This change is being published as a final rule since the regulation is being amended to reflect a change the Agency has made in its internal policy documents. However, we welcome any comments from the public. This rule will not have an impact on a substantial number of small entities within the meaning of the Regulatory Flexibility Act, 5 U.S.C. 601, *et seq.* and is not a major rule under 5 U.S.C. 804. This regulatory action was not subject to Office of Management and Budget review under Executive Order 12866, dated September 30, 1993.

List of Subjects in 22 CFR Part 228

Administrative practice and procedure, Commodity procurement, Grant programs—foreign relations.

Accordingly 22 CFR part 228 is amended as follows:

PART 228—[AMENDED]

1. The authority citation continues to read as follows:

Authority: Sec. 621, Pub. L. 87–195, 75 Stat. 445 (22 U.S.C. 2381), as amended; E.O. 12163, Sept. 29, 1979, 44 FR 56673; 3 CFR 1979 Comp., p. 435.

§ 228.13 [Amended]

2. Sec. 228.13 is amended by removing the last two sentences in the paragraph (b).

Dated: November 17, 1998

Marcus L. Stevenson,

Procurement Executive.

[FR Doc. 98–34718 Filed 12–30–98; 8:45 am]

BILLING CODE 6116–01–M