

UNITED STATES FOOD & DRUG ADMINISTRATION

Financial Disclosure by Clinical Investigators

OMB Control Number 0910-0396

Terms of Clearance: None.

SUPPORTING STATEMENT – Part A: Justification

1. Circumstances Making the Collection of Information Necessary

FDA regulations in 21 CFR Part 54 require the sponsor of any drug, including a biological product, or device marketing application (applicant) and 21 CFR 1114 tobacco products, to submit certain information concerning the compensation to, and financial interests of, any clinical investigator conducting certain clinical studies. This requirement applies 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 the demonstration of safety. The regulations require applicants to certify to the absence of certain financial interests of clinical investigators and/or disclose those financial interests, as required, when covered clinical studies are submitted to FDA in support of product marketing. The regulations are intended to ensure that financial interests and arrangements of clinical investigators that could affect reliability of data submitted to FDA in support of product marketing are identified and disclosed by the sponsor of any drug, biological product, or device marketing application. 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.

We therefore request extension of OMB approval for the information collection associated with financial disclosure of clinical investigator requirements found in the applicable regulations, as discussed in this supporting statement, and found in the referenced collection instruments, forms FDA 3454 and 3455.

2. Purpose and Use of the Information Collection

Using forms FDA 3454 and 3455, the information collected from sponsors of product marketing applications is submitted to FDA as part of the marketing applications. For each clinical investigator who took part in a covered clinical study, the sponsor will either certify that the investigator has no financial interest or arrangement identified in § 54.4(a)(3), or will disclose identified interests and arrangements held by the clinical investigator and describe steps taken to minimize potential bias of such interests and arrangements on the clinical study results. Clinical investigators will provide sponsors with sufficient accurate information to enable the sponsor to submit certification and disclosure statements. Certification of a

clinical investigator helps to assure FDA reviewers of the integrity of a clinical study. Disclosure of an identified interest or arrangement and steps taken to minimize potential bias is used by reviewers to evaluate whether the integrity of the study may be relied on. When identified interests or arrangements are disclosed, FDA responds in one of the following ways: If the clinical study in which the investigator participated was well designed and managed, FDA may accept the data without further question. If a clinical investigator's financial interests and arrangements raise serious questions about the integrity of the data and the study design does not include sufficient bias-minimizing steps to offset these questions, FDA initiates audits of the data by reviewers, requests further analyses of the data from the sponsor, requests that the sponsor conduct additional studies to confirm the potentially biased study, or refuses to treat data from the study as pivotal or primary data upon which an agency action can be taken. Under currently applicable product review regulations, reviewers can and do request further analyses of data from a sponsor as appropriate, or request that a sponsor conduct additional studies to confirm the results of a questionable study.

3. Use of Improved Information Technology and Burden Reduction

Sponsors may maintain and make available records, electronically, in accordance with the requirements in § 54.6. FDA will also accept electronic submissions, such as are required under § 54.5(a) to the extent allowed by the agency's capability for automated data processing of marketing applications. For tobacco related submissions, sponsors and applicants have the option to submit information required under 21 CFR part 54 electronically via NextGen Portal. See <https://www.fda.gov/tobacco-products/manufacturing/submit-documents-ctp-portal-next-generation>. With regard to submission of Forms FDA 3454 and 3455 as part of application files submitted for review in CDER, most sponsors (INDs) and applicants (NDAs, BLAs, ANDAs) are required to submit these forms electronically, whether through the Electronic Submissions Gateway (ESG) in the appropriate structure and format (eCTD – electronic Common Technical Document) or through some other avenue, such as the CDER NextGen Portal.

4. Efforts to Identify Duplication and Use of Similar Information

There is potential for the FDA and PHS regulations to overlap in a very small number of instances involving PHS-funded clinical research on FDA-regulated products. FDA concludes that the agency's reporting requirements meet different needs and the information submitted in the PHS and NSF formats does not overlap and is not adequate for product review purposes.

Because there is currently no other FDA mechanism for collecting the information that is required under the FDA regulation, there is no internal duplication.

5. Impact on Small Businesses or Other Small Entities

FDA concludes that these requirements do not have a significant impact on a substantial number of small businesses. Not only are the majority of firms that submit marketing

applications to FDA of a size to be considered small businesses by the Small Business Administration, but also the firms most apt to be affected by the disclosure provisions of the regulation are small entities of two types: (1) firms whose owners are likely to have developed the tested product and who serve as clinical investigators and (2) small start-up firms that are not heavily capitalized and provide clinical investigators with equity interests as reimbursement. FDA has addressed the need to minimize burden in a number of ways. The regulation does not prohibit any financial interest, such as compensation to investigators in the form of equity in the sponsors firm, nor is the agency proposing to require divestiture by the investigator of any financial interest, because such provisions could impact significantly on small entities and hinder their ability to bring innovative products to market. The reporting and recordkeeping burdens are the minimum necessary to achieve the goals of the regulation.

Submission of the required information has been made as simple as possible for small entities. FDA has developed forms for certification and disclosure, and a sponsor may submit one form for all clinical investigators for whom certification is being made.

6. Consequences of Collecting the Information Less Frequently

The information collection schedule is consistent with statutory and regulatory requirements. The required information is submitted once as part of a product marketing application, The concept of less frequent collection is not applicable.

Without the information that is required by this regulation, FDA lacks the means to evaluate whether clinical data submitted in support of the safety and effectiveness of a regulated product are vulnerable to a recognized source of potential bias, and to assure that the public health is not threatened with the consequences of biased data.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There is one special circumstance relating to the guidelines of 5 CFR 1320.5: The records required to be kept under § 54.6 would be retained by sponsors for 2 years after the date of approval of the application. As such, records will be generated at the outset of a clinical trial; it is conceivable that they would be kept by sponsors for more than 3 years. Two years after the date of approval of the application is the normal period of time for retention of all other information related to an application.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), FDA published a 60-day notice for public comment in the FEDERAL REGISTER of November 29, 2024 (89 FR 94735). FDA received one comment not related to the PRA.

9. Explanation of Any Payment or Gift to Respondents

There will not be any payment or gift to respondents.

10. Assurance of Confidentiality Provided to Respondents

The Privacy Act of 1974

This ICR collects personally identifiable information (PII). Form 3454 (Certification: Financial Interests and Arrangements of Clinical Investigators) collects name and signature. Form 3455 (Disclosure: Financial Interests and Arrangements of Clinical Investigators) collects name, signature, and an attachment with detailed information about financial interests and arrangements. PII is collected in the context of the subject individuals' professional capacity and the FDA-related work they perform for their employer (e.g., point of contact at a regulated entity).

FDA has made no guarantee of confidentiality to sponsors or clinical investigators, but will keep disclosed information private to the fullest extent allowed by law. Information provided to, or obtained by, FDA is subject to release under the Freedom of Information Act (5 U.S.C. 552) and the implementing regulations contained in 21 CFR Parts 20 and 21.

FDA further determined that although PII is collected the collection is not subject to the Privacy Act of 1974 and the particular notice and other requirements of the Act do not apply. Specifically, FDA does not use name or any other personal identifier to routinely retrieve records from the information collected via submitted Forms 3454 and 3455 or otherwise in relation to this collection.

FDA also minimized the PII to be collected to protect the privacy of the individuals. To ensure against the solicitation or submission of unnecessary PII, FDA designed the forms to provide fields soliciting only information required to meet the intended purpose behind the forms.

The Freedom of Information Act

Under the Freedom of Information Act (FOIA) (5 U.S.C. 552), the public has broad access to government documents. However, FOIA provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1-9)).

11. Justification for Sensitive Questions

The information collection does not include questions that are of a sensitive nature, such as, sexual behavior and attitudes, religious beliefs, and other matters that are commonly considered private.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

Respondents to this collection are sponsors or applicants of marketing applications that contain clinical data from studies covered by the regulations. These sponsors or applicants represent pharmaceutical, biologic, tobacco, and medical device firms. Respondents are also clinical investigators who provide financial information to the sponsors of marketing applications. Applicants already submit in a marketing application a complete list of clinical investigators for each covered study (BLAs, 21 CFR part 601, are covered under OMB control number 0910-0338; PMAs, 21 CFR part 814, are covered under OMB control number 0910-0231; 510(k)s, 21 CFR part 807 subpart E, are covered under OMB control number 0910-0120; De Novo requests, 21 CFR part 860, subpart D, are covered under OMB control number 0910-0844; NDAs and ANDAs, 21 CFR part 314, are covered under OMB control number 0910-0001; PMTA's, 21 CFR 1114, are covered under OMB control number 0910-0879).

Table 1 shows information that is the basis of the estimated number of respondents in Tables 2 through 4:

Table 1.--Estimated Number of Applications, Clinical Trials, and Investigators Subject to the Regulation by Type of Application¹

Application Type	Total Number of Applications	Number of Applications Affected	Number of Trials	Number of Investigators
Drugs:				
New drug application (NDA), new molecular entity (NME)	35	35	3 to 10	3 to 100
NDA non-NME	94	44	3 to 10	3 to 100
NDA efficacy supplement	171	100	1 to 3	10 to 30
Abbreviated new drug application (ANDA)	685	1	1.1	2
ANDA supplement	10,366	1	1	2
CBER² Biologics:				
Biologics license application (BLA)	26	26	3 to 10	3 to 100
BLA efficacy supplement	326	26	1 to 3	10 to 30
CDER³ Biologics:				
BLAs	19	19	3 to 10	3 to 100
BLA efficacy supplements	64	50	1 to 3	10 to 30
Medical Devices:				
Premarket approval (PMA)	43	50	1 to 3	10 to 20
PMA supplement	28	30	1 to 3	3 to 10
Reclassification devices	0	0	0	0
510(k)	3,401	254	1	3 to 10
De Novo requests	84	76	1 to 3	10 to 20
CTP⁴				
PMTA	4,000	1,000	1 to 3	3 to 20
Investigational Tobacco Products (ITP)	100	25	1	1 to 3

¹ Source: Agency estimates

² Center for Biologics Evaluation and Research (CBER)

³ Center for Drug Evaluation and Research (CDER)

⁴ Center for Tobacco Products (CTP)

Reporting Burden:

For clinical 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 estimates that almost all applicants submit a certification statement under § 54.4(a)(1) and (a)(2). Preparation of the statement using Form FDA 3454 should require no more than 1 hour per study. The number of respondents is based on the estimated number of affected applications (see table 1 above).

When certification is not possible and disclosure is made using form FDA 3455, the applicant must describe, under § 54.4(a)(3), the financial arrangements or interests and the steps that were taken to minimize the potential for bias in the affected study. As the applicant would 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 5 hours to prepare this narrative. Based on our experience with this collection, FDA estimates that approximately 10 percent of the respondents with affected applications will submit disclosure statements.

Table 2.--Estimated Annual Reporting Burden

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Certification--54.4(a)(1) and (a)(2)--Form FDA 3454	712	1	712	1	712
Disclosure--54.4(a)(3)--Form FDA 3455	71	1	71	5	355
Total					1,067

Recordkeeping Burden:

The sponsors of covered studies are 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 2 years after the date of approval of the applications. This time is consistent with the current recordkeeping requirements for other information related to marketing applications for human drugs, biologics, and medical devices. Under § 54.6, sponsors of covered studies must maintain many records regarding clinical investigators, including protocol agreements and investigator resumes or curriculum vitae. FDA estimates that it takes an average of 15 minutes for each recordkeeper to add this record to the clinical investigators file.

Table 3.--Estimated Annual Recordkeeping Burden

21 CFR Section	No of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours ¹
Recordkeeping--54.6	712	1	712	0.25	178

¹ Numbers have been rounded.

Third-Party Disclosure Burden:

Under §54.4(b), clinical 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; we used the median, 10 minutes, for the average burden per disclosure. The number of respondents is the sum of the number of affected applications multiplied by the mean of the estimated number of investigators for each application type (rounded) in table 1 above.

Table 4.--Estimated Annual Third-Party Disclosure Burden

21 CFR Section	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours ¹
54.4(b)--Clinical Investigators	13,646	1	13,646	0.17	2,320

¹ Numbers have been rounded.

*12b. Annualized Cost Burden Estimate**

Reporting (certification and disclosure): FDA estimates that virtually all of the sponsors submitting marketing applications that contain clinical data (approximately 712) will be able to certify for one or more investigators, and the names of all investigators for whom the sponsor is certifying may be attached to one certification form. The agency estimates that preparation of the certification form will take at most 1 hour, of which 80% is clerical time (\$21.29/hr.) and 20% management time (\$64.36/hr.). We then doubled to account for benefits and overhead, providing a weighted wage rate of \$59.81/hr. The agency bases this estimate on sampling of time taken in preparation of other portions of marketing applications. The total estimated time spent by sponsors of marketing applications on certification in a given year is estimated to be 712 hours.

The agency estimates that preparation of the disclosure form, which includes identifying the interest or arrangement held by the investigator and describing steps taken to minimize bias of study results, will take 5 hours, of which 90% is management time (\$64.36/hr.) and 10% clerical time (\$21.29/hr.). We then doubled to account for benefits and overhead, providing a weighted wage rate of \$120.11/hr. The total estimated time spent by sponsors of marketing applications on disclosure in a given year is estimated to be 355 hours.

Recordkeeping: As stated, recordkeeping requires minimal time because a sponsor can incorporate financial disclosure information into the sponsors existing system for maintaining investigator information. It is estimated that an average of 15 minutes is needed for inclusion

of this information in an application record. In calculating the cost of recordkeeping, the same weighted wage rate is used as for certification: \$59.81/hr.

Third-party disclosure: Clinical investigators report to sponsors, in whose studies they participate, sufficient, accurate information to enable the sponsor to complete certification and disclosure forms. Most clinical investigators will have no disclosable information to report to the sponsor, and for these investigators reporting will amount to checking a box or writing the equivalent of disclosable financial arrangements. Even if an investigator holds disclosable interests or arrangements, most of this information will already be known by the sponsor, i.e., a financial arrangement between the sponsor and the clinical investigator whereby the value of the compensation to the investigator could be influenced by the outcome of the study; any significant payments of other sorts to the clinical investigator by the sponsor; any proprietary interest in the tested product held by the clinical investigator; and, if the sponsor is not a publicly held corporation, any significant equity interest in the sponsor that is held by the investigator. The investigator will need only provide the sponsor with information concerning a significant equity interest in the sponsor, providing the sponsor is publicly held. Because the investigator will have such information readily available for tax purposes, FDA estimates that only minimal time will be spent by the investigator in providing this information to the sponsor. FDA believes the average time spent by a clinical investigator in providing a sponsor with the required financial information will be 10 minutes (0.17 hours). Approximately 13,646 clinical investigators participate in covered clinical studies in a given year. Thus, a total of 2,320 burden hours is estimated for reporting by clinical investigators to sponsors in a given year. Cost of this burden is calculated using the mean hourly wage (\$63.50) for “Healthcare Diagnosing or Treating Practitioners,” doubled to account for benefits and overhead, \$127.00.

Annualized Cost Burden Estimate			
	Hours	Hourly Wage Rate	Cost (rounded)
Sponsors’ costs:			
Certification	712	\$59.81	\$ 42,585
Disclosure	355	\$120.11	\$ 42,639
Recordkeeping	179	\$59.81	\$ 10,706
Sponsors’ total costs:			\$ 95,930
Clinical Investigators’ costs:			
Third-party disclosure	2,320	\$127.00	\$ 294,640
Total costs to sponsors and investigators:			\$ 390,570

* Wage rate calculations are based on: Bureau of Labor and Statistics May 2023 data (http://www.bls.gov/oes/current/naics4_561100.htm#00-0000) for “Office Clerks, General” (occupation code 43-9061); “Managers, All Others” (occupation code 11-9199); and “Healthcare Diagnosing or Treating Practitioners” (occupation code 29-1000).

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no additional information collection costs to respondents and recordkeepers beyond those estimated in the previous item. This is because the information will be collected and submitted as part of preparation of a marketing application, and sponsors already have in place processes and equipment for collecting and maintaining information

from clinical investigators who study FDA-regulated products. Investigators who participate in clinical studies of regulated products provide sponsors of the studies with a variety of information and are thus accustomed to this activity.

14. Annualized Cost to the Federal Government

Because FDA already has in place equipment and processes for handling information contained in product marketing applications, the information collected under this regulation will generate new costs to the agency in only two areas:

- (1) Additional review of applications to assure that the required information has been submitted and all clinical investigators participating in covered studies are accounted for. Agency staff estimates that this review could take from 15 to 20 minutes for an application in which all clinical investigators are certified to upwards of 5 hours for an application that includes disclosure for an investigator. For planning purposes, an average of 2 hours is estimated for this review. The initial review and assessment of applications would be conducted by a Consumer Safety Officer.
- (2) Agency data audit of a covered clinical study. If a clinical investigators financial interests and arrangements raise serious questions about the integrity of the data, and the study design does not include sufficient bias-minimizing steps to offset these questions, one course of action FDA can take is to request a data audit by agency bioresearch monitoring staff. FDA estimates that 10 percent of sponsors of marketing applications will submit disclosures for clinical investigators in a given year. The agency estimates that only a very few would contain financial interests and arrangements that raise questions about the integrity of the data that are sufficiently serious, and study design sufficiently questionable, to trigger a data audit. For planning purposes, the agency has set this figure at one-half of one percent of submitted applications, or 5 applications. A data audit may cover a wide range of time, based on the size and complexity of a study and the number of investigators participating, but 40 hours is a realistic average time for such an audit.

The hourly rate is based an internal, fully loaded cost model for FY 2023.

Estimated Annual Costs to FDA

	Hours per Review	Average Hourly Rate	No. of Applications	Cost
Additional review	2	\$168.71	715	\$ 241,255
Data audit	40	\$168.71	5	\$ 33,742
Total				\$ 274,997

15. Explanation for Program Changes or Adjustments

Our estimated burden for the information collection reflects an overall increase of 87 hours and a corresponding increase of 557 responses/records. We attribute this adjustment to an increase in the number of affected applications and the number of investigators. The estimated number of respondents has decreased from 715 to 712 for Certification, from 72 to

71 for Disclosure, and from 715 to 712 for Recordkeeping due to a decrease in the estimated number of affected applications. The estimated number of respondents for third-party disclosure has increased from 13,082 to 13,646 due to adjustments in the number of affected applications and the number of investigators. No program changes were made.

16. Plans for Tabulation and Publication and Project Time Schedule

Information collected will not be tabulated or published.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

Display of OMB expiration date is appropriate

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.