REPORTING INFORMATION REGARDING FALSIFICATION OF DATA
SUPPORTING STATEMENT

A. Justification

1. Circumstances Making the Collection of Information Necessary

FDA is proposing to amend its regulations to require sponsors to report information indicating that any person has, or may have, engaged in the falsification of data in the course of reporting study results, or in the course of proposing, designing, performing, recording, supervising, or reviewing studies that involve human subjects (e.g., clinical investigations) or animal subjects (e.g., nonclinical laboratory studies and clinical studies in animals) conducted by or on behalf of a sponsor or relied on by a sponsor. A sponsor would be required to report this information to the appropriate FDA center promptly, but no later than 45 calendar days after the sponsor becomes aware of the information. The proposed requirement for a sponsor to report information regarding falsification of data would be ongoing and cover the periods before and after study completion, including after the review, approval, or authorization of the affected product or labeling.

We are proposing to amend the appropriate regulations that govern the conduct of FDA-regulated research and the submission of information in support of applications and petitions for FDA product approvals and authorization of certain labeling claims. The requirement to report falsification or possible falsification of data would be added to FDA's regulations on the following:

- Good laboratory practice for nonclinical laboratory studies (21 CFR part 58),
- Color additive petitions in part 71 (21 CFR part 71),
- Petitions for nutrient content claims and petitions for health claims in part 101 (21 CFR part 101),
- Information in a premarket notification for a food contact substance in part 170 (21 CFR part 170),
- Food additive petitions (21 CFR part 171),
- Dietary supplement premarket notifications (21 CFR part 190),
- Investigational new drug applications (21 CFR part 312),
- New animal drugs for investigational use (21 CFR part 511),
- Animal food additive petitions (21 CFR part 571), and
- Investigational device exemptions (21 CFR part 812).

Falsification of data can, if not detected, undermine subject protection and the underlying basis for FDA actions. Each year, we discover falsification of data at study sites and in application submissions. Sometimes, falsification at a study site is not an isolated event and can lead to a finding of falsification of information at another site, or relating to other drugs being studied at the same site. It is critical that participants in the product development process assist FDA in detecting falsification of data.

We are proposing this rule for two principal reasons. First, it is important for the agency to have confidence in any data from studies conducted by, or on behalf of, a sponsor, or relied on by a sponsor for product approvals or authorization of labeling claims. This proposed rule is intended to help ensure the integrity of data submitted to FDA because reliance on falsified data could lead to clinical testing of unsafe products, approval of ineffective or unsafe products, or to the marketing of products with false or misleading claims. Second, it is important that the rights, safety, and welfare of subjects be protected. This proposed rule is intended to help protect research subjects by making it less likely that persons who falsify data will continue to conduct studies, come in contact with research subjects, or jeopardize the rights, safety, and welfare of such subjects through unsound scientific practices.

Although our own inspections sometimes uncover falsification of data, sponsors of studies are responsible for ensuring the integrity of study data and are in a better position to discover possible falsification of data through their monitoring, auditing, and reviewing of data. We understand that in the process of reviewing and monitoring studies, some sponsors have discovered falsification of data and have been reluctant, or uncertain as to whether it was necessary, to report the information to us. Therefore, we are proposing this rule to clarify sponsors' reporting requirements for studies conducted by, or on behalf of, a sponsor or on which a sponsor relies to support product approvals, new dietary ingredient notifications, or authorization of labeling claims, including nutrient content claims and health claims. This proposed rule makes it clear that sponsors would be required to promptly report information indicating that any person has, or may have, engaged in the falsification of data in the course of reporting study results, or in the course of proposing, designing, performing, recording, supervising, or reviewing studies conducted by, or on behalf of, a sponsor or relied on by a sponsor. This proposed rule, when finalized, would require sponsors to report information to the appropriate FDA center about possible falsification of data whenever (before, during, or after the completion of a study) a sponsor becomes aware of the information, but in no case later than 45 calendar days after the sponsor becomes aware of that information.

2. Purpose and Use of the Information Collection

The proposed rule would allow the agency to more rapidly identify persons who have falsified data and more effectively address problems. Such persons may include those who have falsified data submitted to FDA for product reviews, approvals, and authorizations of certain labeling claims, in addition to those who have falsified data in the course of conducting FDA regulated research. We intend to use the information collected from sponsors who notify us of possible falsification of data to identify patterns, potential signals, or other indications of misconduct, so that we can conduct further investigations. These investigations, in turn, may form the basis of administrative or enforcement actions, such as excluding clinical trials from consideration by FDA, placing a clinical trial on hold, or initiating disqualification of investigators or criminal proceedings. Taking effective action in response to falsification could lessen the magnitude and impact of the falsification in a current study, reduce the potential for delays or compromise to other studies and applications (including studies and applications from other sponsors for whom

such a person might also be working), and protect the rights, safety, and welfare of research subjects.

3. Use of Improved Information Technology and Burden Reduction

Under the proposal, a sponsor may provide information regarding falsification of data by any means, including telephone, mail, electronic mail, or facsimile.

4. Efforts to Identify Duplication and Use of Similar Information

The Public Health Service (PHS) regulations at 42 CFR part 93 and the National Science Foundation (NSF) regulations at 45 CFR part 689 address "research misconduct." The PHS research misconduct regulations generally apply to PHS-conducted or PHS-supported biomedical and behavioral research, research training, research-related activities, and applications and proposals for such PHS-supported research, research training, and related activities. The NSF regulations on research misconduct address research proposals submitted to NSF and funded by NSF. As a result, neither of these regulations encompasses sufficiently the scope of research subject to evaluation by FDA. FDA's proposed rule is intended to cover all studies that are subject to FDA evaluation, regardless of the source of funding.

5. Impact on Small Businesses or Other Small Entities

FDA must ensure that regulated products from all manufacturers (large and small) are safe and effective, a goal achieved through equal application of the law. It is not possible to provide an exemption or reduce requirements regarding reporting possible falsification of data for small businesses without seriously compromising public health objectives. In order to provide assistance to small business, FDA has a small business coordinator and small business field representatives who exclusively help small businesses whose products we regulate. These individuals are expressly available to deal with the special concerns of small firms. These officials provide information that clarifies how FDA laws and regulations apply to specific circumstances and suggest methods of meeting these requirements. These officials respond to inquiries, conduct or participate in workshops and conferences, and visit plants upon request to offer assistance. In addition, each Center within FDA has an appropriate small business contact person who can also help to set up workshops and conferences, provide informational materials or audiovisuals, and provide speakers for professional meetings.

Moreover, under the Regulatory Flexibility Act, FDA analyzes regulatory options that would minimize any significant impact on small entities resulting from rulemaking. In section VI of the proposed rule, Analysis of Impacts, FDA concluded that because most firms generally would not submit more than one report of potential data falsification per year at the estimated cost of $210 per report, FDA does not believe that the proposed rule would have a significant economic impact on a substantial number of small entities.

6. Consequences of Collecting the Information Less Frequently

The intent of this proposed requirement is for FDA to obtain information about possible falsification as soon as possible, with the full recognition that further investigation may be needed. Early reporting by sponsors could alert us to conditions that may affect data integrity and the rights, safety, and welfare of subjects. This reporting requirement would have the effect of providing us with an early alert to potentially serious lapses in subject protection or data integrity. If we were made aware of possible falsification of data sooner, we could undertake appropriate action, such as reviewing other studies conducted by the persons who have, or may have, falsified data to assess the reliability of the data and/or conducting site inspections. If we are not made aware of possible falsification when a sponsor becomes aware of it, this could allow an investigator who falsified data to continue to conduct studies, thereby jeopardizing the rights, safety, and welfare of the subjects involved in future research and the integrity of the data in other studies.

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

There is no inconsistency with the requirements of § 1320.5.

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

In 2000, FDA held a series of meetings with representatives from the pharmaceutical industry (including the Pharmaceutical Research and Manufacturers Association, the Biotechnology Industry Organization, and AdvaMed) to discuss the impact of falsification of data on drug product development. Industry expressed concerns about acting on incomplete information to terminate a clinical investigator and report to FDA under current regulations. Industry representatives generally supported the idea of requiring reporting to FDA of information concerning falsification, in part due to the belief that this might reduce the legal liability of sponsors in these circumstances. In addition, the proposed rule will offer an opportunity for public comment.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

Information provided to FDA by sponsors related to possible falsification of data might include information that is considered confidential and not releasable to the public. Confidentiality is maintained for trade secret or confidential, commercial, or financial information under 21 CFR 20.61 and investigatory records under 21 CFR 20.64. In addition, for human drugs, 21 CFR 312.130 describes which information submitted under an IND may be available for public disclosure.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Hour Burden and Costs

Burden Hours:

As stated in Section 1 above, the proposed rule would require the sponsor to report to FDA information it possesses regarding the possible falsification of data. The information a sponsor should report to FDA includes the following:

- The name of the person who has, or may have, falsified data;
- The last known address(es) and phone number(s) of that person;
- The specific identity of the potentially affected study, including, when applicable, application information such as the application number, investigational protocol number, study title, study site(s), and study dates; and
- Information suggesting that falsification occurred and describing the falsification.

In addition, FDA is considering requiring that additional information, such as the NCT number assigned to a study when an applicable clinical trial is registered with ClinicalTrials.gov, be reported.

The sponsor would be required to report this information to the appropriate FDA center promptly, but no later than 45 calendar days after the sponsor becomes aware of the information.

Table 1 of this document provides an estimate of the annual reporting burdens associated with the proposed rule (the rule does not include any recordkeeping requirements). Based on data concerning the number of reports of falsification received annually by FDA, the agency estimates that it will receive approximately 73 reports of falsification of data per year. We base this estimate on the fact that CDER receives approximately 20 reports a year from sponsors, CBER receives approximately 30 per year, and CDRH receives approximately 15. There are approximately three incidents a year concerning nonclinical laboratory studies. CFSAN receives approximately three reports a year concerning food additive petitions and color additive petitions. CFSAN has received no reports concerning nutrient content claims, health claims, or new dietary ingredients. CVM receives approximately two reports a year.

We estimate that it will take approximately 5 hours to prepare and submit to FDA each report. We base this estimate on the time it would take a sponsor to gather the information to report to FDA, contact us to report the information, and meet with us to present the report, if necessary.

TABLE 1.--ESTIMATED ANNUAL REPORTING BURDEN

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
58.11(a)	3	1	3	5	15
71.1(k)	1	1	1	5	5
101.69(p)	0	0	0	0	0
101.70(k)	0	0	0	0	0
170.101(f)	1	1	1	5	5
171.1(o)	1	1	1	5	5
190.6(g)	0	0	0	0	0
312.56(e)	50	1	50	5	250
511.1(c)(1)	2	1	2	5	10
571.1(l)	0	0	0	0	0
812.46(d)	15	1	15	5	75
Total	73	7	73	35	365

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

Costs:

Section VI of the proposed rule, Analysis of Impacts, estimates that it will take about 5 hours to prepare and report this information about possible falsification to the agency. We are uncertain of the average number of these reports to expect annually. We estimate that we may receive 73 reports per year in compliance with this rule. We are basing this estimate on several types of information, including reports received from sponsors of errors and reports of suspensions and terminations of clinical investigators. Because most errors do not involve falsification and because investigators may be suspended or terminated for reasons other than for falsifying data, this estimate of 73 reports is likely to be greater than the number the agency would actually receive. At a benefit-adjusted hourly wage rate of about $42 for a regulatory affairs official, these assumptions imply a cost of $210 per report and a total annual cost of about $15,330 per year ($42 times 365 hours). As mentioned previously, we expect the total number of reports of falsified data, and therefore the total cost, to be lower.

13. Estimates of Other Total Annual Cost Burden to Respondents and Recordkeepers

There are no other costs, including capital costs or operating and maintenance costs, associated with this collection of information.

14. Annualized Cost to the Federal Government

As stated under No. 12 above, we estimate that the agency will receive approximately 73 reports of falsification of data per year. We estimate approximately 1 hour for FDA personnel to review each submission on falsification of data, for a total of approximately 73 hours. If the average loaded wage for an FDA reviewer is approximately $75 per hour, the Federal burden would be $5,475.

15. Explanation for Program Changes or Adjustments

The requirement to report falsification or possible falsification of data would be added to the following FDA regulations:

- Good laboratory practice for nonclinical laboratory studies (21 CFR part 58),
- Color additive petitions in part 71 (21 CFR part 71),
- Petitions for nutrient content claims and petitions for health claims in part 101 (21 CFR part 101),
- Information in a premarket notification for a food contact substance in part 170 (21 CFR part 170),
- Food additive petitions (21 CFR part 171),
- Dietary supplement premarket notifications (21 CFR part 190),
- Investigational new drug applications (21 CFR part 312),
- New animal drugs for investigational use (21 CFR part 511),
- Animal food additive petitions (21 CFR part 571), and
- Investigational device exemptions (21 CFR part 812).

Thus, this is a new information collection and does not amend any current approval.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no time schedules, publications, and analysis plans.

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

There is no display of the expiration date.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no certifications needed.