INFORMATION COLLECTION

SUPPORTING STATEMENT

Regulations for In Vivo Radiopharmaceuticals Used for Diagnosis and Monitoring - 0910-0409

JUSTIFICATION

1. Circumstances of Information Collection

The information collection requirements contained in 21 CFR 315.4, 315.5, and 315.6 require manufacturers of diagnostic radiopharmaceuticals to submit information that demonstrates the safety and effectiveness of a new diagnostic radiopharmaceutical or of a new indication for use of an approved diagnostic radiopharmaceutical.

In response to the requirements of section 122 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) (P.L. 105-115), FDA, in the Federal Register of May 17, 1999 (64 FR 26657), published a final rule amending its regulations by adding provisions that clarify FDA=s evaluation and approval of in vivo radiopharmaceuticals used in the diagnosis or monitoring of diseases. The regulation describes the kinds of indications of diagnostic radiopharmaceuticals and some of the criteria that the agency would use to evaluate the safety and effectiveness of a diagnostic radiopharmaceutical under Section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) (the

act) and section 351 of the Public Health Service Act (42 U.S.C. 262) (the PHS Act). Information about the safety or effectiveness of a diagnostic radiopharmaceutical enables FDA to properly evaluate the safety and effectiveness profiles of a new diagnostic radiopharmaceutical or a new indication for use of an approved diagnostic radiopharmaceutical.

The rule clarifies existing FDA requirements for approval and evaluation of drug and biological products already in place under the authorities of the act and the PHS act. The information, which is usually submitted as part of a new drug application (NDA) or biologics license application (BLA) or as a supplement to an approved application, typically includes, but is not limited to, nonclinical and clinical data on the pharmacology, toxicology, adverse events, radiation safety assessments, and chemistry, manufacturing, and controls. The content and format of an application for approval of a new drug are set forth in 21 CFR 314.50. Under 21 CFR part 315, information required under the act and needed by FDA to evaluate the safety and effectiveness of in vivo radiopharmaceuticals still needs to be reported.

2. Purpose and Use of the Information

Information about the safety or effectiveness of a diagnostic radiopharmaceutical enable the agency to properly evaluate the safety and effectiveness profiles of a new diagnostic radiopharmaceutical or a new indication for use of an approved diagnostic radiopharmaceutical, as required under section 505 of the act and section 351 of the PHS Act.

3. Use of Improved Information Technology

In the Federal Register of December 11, 2003, FDA issued a final rule amending FDA regulations governing the format in which certain

labeling is required to be submitted for review with NDAs, certain BLAs, ANDAs, supplements, and annual reports. The final rule requires the electronic submission of the content of labeling (i.e., the content of the package insert or professional labeling, including all text, tables, and figures) in NDAs, certain BLAs, ANDAs, supplements, and annual reports electronically in a form that FDA can process, review, and archive.

The following guidances for industry have been developed to improve the use of information technology in the submission of marketing applications for human drugs and related reports:

- "Providing Regulatory Submissions in Electronic Format--NDAs" (January 28, 1999). This guidance provides information on how to submit a complete archival copy of an NDA in electronic format and applies to the submission of original NDAs as well as to the submission of supplements and amendments to NDAs.
- "Providing Regulatory Submissions in Electronic Format--General Considerations" (January 28, 1999). This guidance includes a description of the types of electronic file formats that the agency is able to accept to process, review, and archive electronic documents. The guidance also states that documents submitted in electronic format should enable the user to: (1) Easily view a clear and legible copy of the information; (2) print each document page by page while maintaining fonts, special orientations, table formats, and page numbers; and (3) copy text and images electronically into common word processing documents.

- “Providing Regulatory Submissions to the Center for Biologics Evaluation and Research (CBER) in Electronic Format” (November 12, 1999). This guidance provides information to assist applicants in submitting documents in electronic format for review and archive purposes as part of a BLA, product license application (PLA), or establishment license application (ELA).
- "Providing Regulatory Submissions in Electronic Format-—Prescription Drug Advertising and Promotional Labeling" (January 31, 2001). This draft guidance discusses issues related to the electronic submission of advertising and promotional labeling materials for prescription drug and biological products.
- "Providing Regulatory Submissions in Electronic Format-—ANDAs" (June 27, 2002). This guidance discusses issues related to the electronic submission of ANDAs and supplements and amendments to those applications.
- "Providing Regulatory Submissions in Electronic Format-—Annual reports for NDAs and ANDAs" (August 2003). This guidance discusses issues related to the electronic submission of annual reports for NDAs and ANDAs.
- "Providing Regulatory Submissions in Electronic Format-—Postmarketing Periodic Adverse Drug Experience Reports" (June 2003). This guidance discusses general issues related the electronic submission of postmarketing periodic adverse drug experience reports for NDAs, ANDAs, and BLAs.
- "Providing Regulatory Submissions in Electronic Format-—Human

Pharmaceutical Product Applications and Related Submissions" (August, 2003). This draft guidance discusses issues related to the electronic submission of ANDAs, BLAs, INDs, NDAs, master files, advertising material, and promotional material.

- "Providing Regulatory Submissions in Electronic Format-–General Considerations" (October 2003). This draft guidance discusses general issues common to all types of electronic regulatory submissions.
- "Providing Regulatory Submissions in Electronic Format-–Content of Labeling" (February 2004). This draft guidance discusses issues related to the submission of the content of labeling in electronic format for marketing applications for human drug and biological products.

These guidance documents are available at FDA's web site http://www.fda.gov/cder/guidance/index.htm.

4. Efforts to Identify Duplication

FDA is the only agency that requires the filing of an application for the marketing of diagnostic radiopharmaceuticals for human use. No other component of the agency or other government agencies require similar information or data to be filed. The information to be submitted under the regulations is not available from any other source.

5. Involvement of Small Entities

FDA requires the equal application of its regulations. While FDA does

not believe it can apply different standards with respect to statutory requirements, FDA does provide special help to small businesses. CDER provides assistance to small businesses subject to FDA's regulatory requirements.

6. Consequences if Information Collected Less Frequently

Manufacturers submit applications for approval of a diagnostic radiopharmaceutical to obtain permission to market the product in interstate commerce. Less frequent collection of information or other methods of reducing the frequency of information would not provide the information needed by FDA to properly evaluate the safety and effectiveness of a diagnostic radiopharmaceutical or a new indication for use of an approved diagnostic radiopharmaceutical.

7. Consistency with the Guidelines in 5 CFR 1320.5

An applicant may be required to submit to FDA proprietary trade secrets or other confidential information when submitting a license application or supplement. FDA has instituted security measures to protect confidential information received from manufacturers and will, to the extent permitted by law, protect this information.

8. Consultation Outside the Agency

In the Federal Register of April 28, 2008 (73 FR 22956), FDA published a notice that provided a comment period for the public on the information collection provisions. No comments were received on the

information collection.

9. Remuneration of Respondents

No payment or gift was provided to respondents.

10. Assurance of Confidentiality

The confidentiality of the information received by FDA under the final rule would be consistent with the Freedom of Information Act and the agency's regulations under 21 CFR Part 20. Manufacturers seeking to market a diagnostic radiopharmaceutical or a new indication for use for an approved diagnostic radiopharmaceutical might be required to reveal proprietary information or trade secrets to gain FDA approval of the product or new indication. However, such information is deleted from the application before it is released under the Freedom of Information Act and FDA regulations.

11. Questions of a Sensitive Nature

Questions of a sensitive nature are not applicable to this information collection.

12. Estimates of Annualized Hour Burden to Respondents

Based on the number of submissions (that is, human drug applications and/or new indication supplements for diagnostic radiopharmaceuticals) that FDA receives, FDA estimates that it will receive approximately 2 submissions annually from 2 applicants. The hours per response refers

to the estimated number of hours that an applicant would spend preparing the information required by the regulations. Based on FDA=s experience, the agency estimates the time needed to prepare a complete application for a diagnostic radiopharmaceutical to be approximately 10,000 hours, roughly one-fifth of which, or 2,000 hours, is estimated to be spent preparing the portions of the application that would be affected by these regulations. The regulation does not impose any additional reporting burden for safety and effectiveness information on diagnostic radiopharmaceuticals beyond the estimated burden of 2,000 hours because safety and effectiveness information is already required by '314.50 (collection of information approved by OMB under OMB Control Number 0910-0001). In fact, clarification in these regulations of FDA=s standards for evaluation of diagnostic radiopharmaceuticals is intended to streamline overall information collection burdens, particularly for diagnostic radiopharmaceuticals that may have well-established, low-risk safety profiles, by enabling manufacturers to tailor information submissions and avoid unnecessary clinical studies. Table 1 of this document contains estimates of the annual reporting burden for the preparation of the safety and effectiveness sections of an application that are imposed by existing regulations. This estimate does not include the actual time needed to conduct studies and trials or other research from which the reported information is obtained.

Table 1 - Estimated Annual Reporting Burden

21 CFR Section	Number of Respon-dents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
315.4, 315.5, and 315.6	2	1	2	2,000	4,000
TOTAL					4,000

13. Estimates of Annualized Cost Burden to Respondents

The estimated annual cost to respondents is $200,000.

Activity	Hours	Cost per hour	Total Cost
Reporting	4,000	$74.00	$296,000

FDA estimates that it should require an average of 2,000 hours of staff time per applicant to organize and submit the required safety and effectiveness information portions of a new application or supplement to an approved application. The estimate is based on an average hourly wage of a regulatory affairs specialist, at a pay rate of $74.00/hour, including benefits and overhead, who is responsible for preparing the safety and effectiveness portions of an application or supplement.

14. Estimates of Annualized Cost Burden to the Government

FDA estimates that approximately 14 FTEs are devoted to the review of NDAs and supplements that we receive as a result of §§ 315.4, 315.5, and 315.6. Based on an average FTE cost for CDER of $145,000, the total Federal burden would be $2,030,000.

15. Changes in Burden

There are no changes in burden.

16. Time Schedule, Publication, and Analysis Plans

There are no tabulated results to publish for this information collection.

17. Exemption for Display of Expiration Date

FDA is not seeking approval to exempt the display of the expiration date of the OMB approval.

18. Certifications

There are no exceptions to Item 19 of OMB Form 83-I.

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PAPERWORK REDUCTION ACT SUBMISSION

Please read the instructions before completing this form. For additional forms or assistance in completing this form, contact your agency's Paperwork Clearance Officer. Send two copies of this form, the collection instrument to be reviewed, the supporting statement, and any additional documentation to: Office of Information and Regulatory Affairs, Office of Management and Budget, Docket Library, Room 10102, 725 17th Street NW, Washington, DC 20503.

1. Agency/Subagency originating request DHHS/FDA	2. OMB control number b. [ ] None a. 0910-0409
3. Type of information collection (*check one*) a. [ ] New Collection b. [ ] Revision of a currently approved collection c. [X] Extension of a currently approved collection d. [ ] Reinstatement, without change, of a previously approved collection for which approval has expired e. [ ] Reinstatement, with change, of a previously approved collection for which approval has expired f. [ ] Existing collection in use without an OMB control number For b-f, note Item A2 of Supporting Statement instructions	4. Type of review requested (*check one*) a. [x] Regular submission b. [ ] Emergency - Approval requested by at close of comment period c. [ ] Delegated 5. Small entities Will this information collection have a significant economic impact on a substantial number of small entities? [ ] Yes [x] No 6. Requested expiration date a. [X] Three years from approval date b. [ ] Other Specify:____/__
7. Title: Regulations for In Vivo Radiopharmaceuticals Used for Diagnosis and Monitoring	
8. Agency form number(s) (*if applicable*)	

9. Keywords drugs

10. Abstract: 21 CFR 315.4, 315.5, and 315.6 require manufacturers of diagnostic radiopharmaceuticals to submit information that demonstrates the safety and effectiveness of a new diagnostic radiopharmaceutical or of a new indication for use of an approved diagnostic radiopharmaceutical.

11. Affected public (*Mark primary with "P" and all others that apply with "x"*)

a. ___ Individuals or households
b. _x__ Business or other for-profit
c. ___ Not-for-profit institutions
d. ___ Farms
e. ___ Federal Government
f. ___ State, Local or Tribal Government

12. Obligation to respond (*check one*)

a. [ ] Voluntary- (guidance document)
b. [ ] Required to obtain or retain benefits
c. [x] Mandatory

13. Annual recordkeeping and reporting burden

a. Number of respondents 2
b. Total annual responses 2
1. Percentage of these responses collected electronically ___
c. Total annual hours requested 4,000
d. Current OMB inventory 4,000
e. Difference 0
f. Explanation of difference
1. Program change
2. Adjustment __

14. Annual reporting and recordkeeping cost burden *(in thousands of dollars)*

a. Total annualized capital/startup costs _____
b. Total annual costs (O&M) _____
c. Total annualized cost requested _____
d. Current OMB inventory _____
e. Difference _____
f. Explanation of difference
1. Program change _____
2. Adjustment _____

15. Purpose of information collection (*Mark primary with "P" and all others that apply with "X"*)

a. __ Application for benefits
b. __ Program evaluation
c. __ General purpose statistics
d. __ Audit
e.__ Program planning or management
f.__ Research
g._x_ Regulatory or compliance

16. Frequency of recordkeeping or reporting *(check all that apply)*

a. [ ] Recordkeeping
b. [ ] Third party disclosure
c. [x] Reporting
1. [x] On occasion
2. [ ] Weekly
3. [ ] Monthly
4. [ ] Quarterly
5. [ ] Semi-annually
6. [X] Annually
7. [ ] Biennially
8. [ ] Other (describe) _____

17. Statistical methods

Does this information collection employ statistical methods

[ ] Yes [x] No

18. Agency Contact (person who can best answer questions regarding the content of this submission)

Name: _____

Phone: _____

OMB 83-I