

INFORMATION COLLECTION

SUPPORTING STATEMENT

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

JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

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 FD&C 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 FD&C 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 FD&C 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 Collection

Information about the safety or effectiveness of a diagnostic radiopharmaceutical enables 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 FD&C Act and section 351 of the PHS Act.

3. Use of Improved Information Technology and Burden Reduction

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--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 in Electronic Format--Prescription Drug Advertising and Promotional Labeling" (January 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--Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications" (June 2008). 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, issued by all centers in FDA, discusses general issues common to all types of electronic regulatory submissions.
- "Providing Regulatory Submissions in Electronic Format--Content of Labeling" (April 2005). This 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

4. Efforts to Identify Duplication and Use of Similar Information

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. Impact on Small Businesses or Other 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 of Collecting the Information 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. Special Circumstances Relating to 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. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In the Federal Register of June 10, 2011 (76 FR 34079), 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. Explanation of Any Payment or Gift to Respondents

No payment or gift was provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

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. Justification for Sensitive Questions

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

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

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	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response (in hours)	Total Hours
315.4, 315.5, and 315.6	2	1	2	2,000	4,000
TOTAL					4,000

12b. Annualized Cost Burden Estimate

The estimated annual cost to respondents is \$300,000.

Activity	Hours	Cost per hour	Total Cost
Reporting	4,000	\$75.00	\$300,000

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 \$75.00/hour, including benefits and overhead, who is responsible for preparing the safety and effectiveness portions of an application or supplement.

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

There are no capital, start-up, operating, or maintenance costs associated with this information collection.

14. Annualized Cost Burden to the Federal Government

FDA estimates that approximately 22 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 \$160,000, the total Federal burden would be \$3,520,000.

15. Explanation for Program Changes or Adjustments

There are no changes in burden hours.

16. Plans for Tabulation and Publication and Project Time Schedule

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

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

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

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

PAPERWORK REDUCTION ACT SUBMISSION

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

<p>1. Agency/Subagency originating request</p> <p style="padding-left: 20px;">DHHS/FDA</p>	<p>2. OMB control number b. <input type="checkbox"/> None</p> <p style="padding-left: 20px;">a. 0910-0409</p>
<p>3. Type of information collection (<i>check one</i>)</p> <p>a. <input type="checkbox"/> New Collection</p> <p>b. <input type="checkbox"/> Revision of a currently approved collection</p> <p>c. <input checked="" type="checkbox"/> Extension of a currently approved collection</p> <p>d. <input type="checkbox"/> Reinstatement, without change, of a previously approved collection for which approval has expired</p> <p>e. <input type="checkbox"/> Reinstatement, with change, of a previously approved collection for which approval has expired</p> <p>f. <input type="checkbox"/> Existing collection in use without an OMB control number</p> <p style="padding-left: 20px;">For b-f, note Item A2 of Supporting Statement instructions</p>	<p>4. Type of review requested (<i>check one</i>)</p> <p>a. <input checked="" type="checkbox"/> Regular submission</p> <p>b. <input type="checkbox"/> Emergency - Approval requested by <u>at close of con</u></p> <p>c. <input type="checkbox"/> Delegated</p>
	<p>5. Small entities</p> <p>Will this information collection have a significant economic substantial number of small entities? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>
	<p>6. Requested expiration date</p> <p>a. <input checked="" type="checkbox"/> Three years from approval date b. <input type="checkbox"/> Other <u>Spec</u></p>
<p>7. Title: Regulations for In Vivo Radiopharmaceuticals Used for Diagnosis and Monitoring</p>	
<p>8. Agency form number(s) (<i>if applicable</i>)</p>	
<p>9. Keywords <u>drugs</u></p>	
<p>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.</p>	
<p>11. Affected public (<i>Mark primary with "P" and all others that apply with "X"</i>)</p> <p>a. <input type="checkbox"/> Individuals or households d. <input type="checkbox"/> Farms</p> <p>b. <input checked="" type="checkbox"/> Business or other for-profit e. <input type="checkbox"/> Federal Government</p> <p>c. <input type="checkbox"/> Not-for-profit institutions f. <input type="checkbox"/> State, Local or Tribal Government</p>	<p>12. Obligation to respond (<i>check one</i>)</p> <p>a. <input type="checkbox"/> Voluntary- (guidance document)</p> <p>b. <input type="checkbox"/> Required to obtain or retain benefits</p> <p>c. <input checked="" type="checkbox"/> Mandatory</p>
<p>13. Annual recordkeeping and reporting burden</p> <p>a. Number of respondents <u>2</u></p> <p>b. Total annual responses <u>2</u></p> <p style="padding-left: 20px;">1. Percentage of these responses collected electronically <u> </u></p> <p>c. Total annual hours requested <u>4,000</u></p> <p>d. Current OMB inventory <u>4,000</u></p> <p>e. Difference <u> 0</u></p> <p>f. Explanation of difference</p> <p style="padding-left: 20px;">1. Program change</p> <p style="padding-left: 20px;">2. Adjustment <u> </u></p>	<p>14. Annual reporting and recordkeeping cost burden (<i>in thousands of dollars</i>)</p> <p>a. Total annualized capital/startup costs</p> <p>b. Total annual costs (O&M)</p> <p>c. Total annualized cost requested</p> <p>d. Current OMB inventory</p> <p>e. Difference</p> <p>f. Explanation of difference</p> <p style="padding-left: 20px;">1. Program change</p> <p style="padding-left: 20px;">2. Adjustment</p>
<p>15. Purpose of information collection (<i>Mark primary with "P" and all others that apply with "X"</i>)</p> <p>a. <input type="checkbox"/> Application for benefits e. <input type="checkbox"/> Program planning or management</p> <p>b. <input type="checkbox"/> Program evaluation f. <input type="checkbox"/> Research</p> <p>c. <input type="checkbox"/> General purpose statistics g. <input checked="" type="checkbox"/> Regulatory or compliance</p> <p>d. <input type="checkbox"/> Audit</p>	<p>16. Frequency of recordkeeping or reporting (<i>check all that apply</i>)</p> <p>a. <input type="checkbox"/> Recordkeeping b. <input type="checkbox"/> Third party disclosure</p> <p>c. <input checked="" type="checkbox"/> Reporting</p> <p style="padding-left: 20px;">1. <input checked="" type="checkbox"/> On occasion 2. <input type="checkbox"/> Weekly 3. <input type="checkbox"/> Monthly</p> <p style="padding-left: 20px;">4. <input type="checkbox"/> Quarterly 5. <input type="checkbox"/> Semi-annually 6. <input checked="" type="checkbox"/> Annually</p> <p style="padding-left: 20px;">7. <input type="checkbox"/> Biennially 8. <input type="checkbox"/> Other (describe)</p>

<p>17. Statistical methods Does this information collection employ statistical methods <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>	<p>18. Agency Contact (person who can best answer questions about the content of this submission) Name: <u>Elizabeth Berbakos</u> Phone: <u>301-796-3792</u></p>
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