Regulations for In Vivo Radiopharmaceuticals Used for Diagnosis and Monitoring

0910-0409

SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

FDA is requesting OMB approval of the information collection requirements contained in 21 CFR 315.4, 315.5, and 315.6. These regulations 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 (Pub. L. 105-115), FDA published a final rule in the Federal Register of May 17, 1999 (64 FR 26657), which amended its regulations by adding provisions that clarify the Agency'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 § 314.50 (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

FDA has issued several guidance documents for industry that are intended to improve the use of information technology in the submission of marketing applications for human drugs and related reports. 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 accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of 7/21/2014 (79 FR 42337). 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 may 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, the Agency estimates that it will receive approximately two submissions annually from two 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 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.

FDA estimates the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
In Vivo Radio-pharmaceuticals Used for Diagnosis and Monitoring 315.4, 315.5, and 315.6	2	1	2	2,000	4,000

12b. Annualized Cost Burden Estimate

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

Activity	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
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 approximately $75.00/hour, 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 $250,000, the total Federal burden would be $5,500,000.

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.