SUPPORTING STATEMENT
CURRENT GOOD MANUFACTURING PRACTICES
FOR POSITRON EMISSION TOMOGRAPHY DRUGS
OMB CONTROL NO. 0910-

A **Justification**

1. **Circumstances Making the Collection of Information Necessary**

FDA is issuing regulations on current good manufacturing practice (CGMP) for positron emission tomography (PET) drug products. The regulations are intended to ensure that PET drug products meet the requirements of the Federal Food, Drug, and Cosmetic Act (the act) regarding safety, identity, strength, quality, and purity. We are promulgating these CGMP requirements for all PET drugs under the provisions of the Food and Drug Administration Modernization Act of 1997 (the Modernization Act).

Positron emission tomography is a medical imaging modality involving the use of a unique type of radiopharmaceutical drug product. The majority of PET drug products are injected intravenously into patients for diagnostic purposes. Most PET drugs are produced using cyclotrons and other production equipment at locations that are close to the patients to whom the drugs are administered (for example, in hospitals or academic institutions). Due to their short half-lives, PET drugs usually are administered to patients within a few minutes or hours of production.

Under section 501(a)(2)(B) of the act, a drug is adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with CGMP regulations to ensure that such drug meets the requirements of the act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess. FDA has the authority under section 701(a) of the act to issue regulations for the efficient enforcement of the act regarding CGMP procedures for manufacturing, processing, and holding drugs and drug products. Our CGMP requirements for non-PET drug products are set forth in 21 CFR parts 210 and 211. The CGMP regulations help ensure that drug products meet the statutory requirements for safety and have their purported or represented identity, strength, quality, and purity characteristics. The recordkeeping requirements in the CGMP regulations provide FDA with the necessary information to perform its duty to protect public health and safety. CGMP requirements establish accountability in the manufacturing and processing of drug products, provide for meaningful FDA inspections, and enable manufacturers to improve the quality of drug products over time. The CGMP recordkeeping requirements also serve preventive and remedial purposes and provide crucial information if it is necessary to recall a drug product.

The requirements that are the subject of this information collection are as follows:

A. Investigational and Research PET Drugs

Section 212.5(b)(2) provides that for investigational PET drugs produced under an IND and research PET drugs produced with approval of an RDRC, the requirement under the act to follow current good manufacturing practice is met by complying with the regulations in part 212 or with USP 32 Chapter <823>.

B. Batch Production and Control Records

Sections 212.20(c) through (e), 212.50(a) through (c), and 212.80(c) set out requirements for batch and production records as well as written control records.

C. Equipment and Facilities Records

Sections 212.20(c), 212.30(b), 212.50(d), and 212.60(f) contain requirements for records dealing with equipment and physical facilities.

D. Records of Components, Containers, and Closures

Sections 212.20(c) and 212.40(a) through (b) and (e) contain requirements on records regarding receiving and testing of components, containers, and closures.

E. Process Verification

Section 212.50(f)(2) requires that any process verification activities and results be recorded.

F. Laboratory Testing Records

Sections 212.20(c), 212.60(a) through (b) and (g), 212.61(a) through (b), and 212.70(a) through (b) and (d) set out requirements for documenting laboratory testing and specifications referred to in laboratory testing, including final release testing and stability testing.

G. Sterility Test Failure Notices

Section 212.70(e) requires PET drug producers to notify all receiving facilities if a batch fails sterility tests.

H. Conditional Final Releases

Section 212.70(f) requires PET drug producers to document any conditional final releases of a product.

I. Out-of-Specification Investigations

Sections 212.20(c) and 212.71(a) and (b) require PET drug producers to establish procedures for investigating products that do not conform to specifications and conduct these investigations as needed.

J. Reprocessing Procedures

Sections 212.20(c) and 212.71(d) require PET drug producers to establish and document procedures for reprocessing PET drugs.

K. Distribution Records

Sections 212.20(c) and 212.90(a) require that written procedures regarding distribution of PET drug products be established and maintained.

L. Complaints

Sections 212.20(c) and 212.100 require that PET drug producers establish written procedures for dealing with complaints, as well as document how each complaint is handled.

2. Purpose and Use of the Information Collection

The regulations are intended to ensure that approved PET drug products meet the requirements of the act as to safety, identity, strength, quality, and purity. The regulations address the

following CGMP issues: Personnel and resources; quality control; facilities and equipment; control of components, in-process materials and finished products; production and process controls; laboratory controls; acceptance criteria; labeling and packaging controls; distribution controls; complaint handling; and recordkeeping.

3. Use of Improved Information Technology and Burden Reduction

Generally, records required by CGMP regulations are designed and maintained by drug manufacturers. Because the CGMP regulations provide great latitude on how these requirements are to be achieved, manufacturers are allowed to establish their own methods of recordkeeping. FDA accepts any recordkeeping method which meets the objectives of 21 CFR parts 210, 211, and proposed part 212. For example, drug manufacturing establishments may use automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems that will perform a function satisfactorily, to comply with these recordkeeping requirements.

4. Efforts to Identify Duplication and Use of Similar Information

Other FDA regulations affecting drug manufacturers do not duplicate the CGMP regulations. The information required by the CGMP regulations is not available from any other source except the manufacturer. No other government agency collects these data.

5. Impact on Small Businesses or Other Small Entities

Section IV of the final rule, Analysis of Economic Impacts, analyzes the impact on small businesses or other small entities:

> The rule affects producers of PET drugs, including certain hospitals, clinics, colleges and universities, and producers of in vivo diagnostic substances. According to the Small Business Administration (SBA), pharmaceutical preparation manufacturers with 750 or fewer employees, electromedical and electrotherapeutic apparatus manufacturers with 500 or fewer employees, drugs and druggists' sundries wholesalers with 100 or fewer employees, and for-profit hospitals, clinics, colleges, and universities with $29 million or less in revenue are considered small businesses or entities. To estimate the number of U.S. establishments producing PET drugs, we combined a list of PET centers with cyclotrons from the Academy of Molecular Imaging (AMI) with a list of PET manufacturing facilities from the Society of Nuclear Imaging in Drug Development, which has since merged with the AMI, and added additional facilities that we identified. We have identified 101 establishments operated by 51 PET drug producers. In over one-third of the cases, the PET drug is produced by a hospital. In other instances, a corporate producer manages production under contract at one or more hospitals with cyclotrons.

PET drugs are also produced at independent establishments by corporate producers or small regional producers. Total producer numbers continue to increase as the current corporate producers expand their number of establishments and more independent regional producers enter the market.

Using information from the American Hospital Association (AHA), we characterized 28 of the hospital producers as one of the following establishment types:

- Government, non-Federal;
- Government, Federal;
- Non-Government not-for-profit;
- Investor-owned (for-profit).[1]

The AHA data did not include information for eight hospitals associated with large colleges or universities, but for this analysis, these were assumed to be not-for-profit because approximately 93 percent of all 4-year higher education institutions are public or nonprofit institutions.[2] Census data reports indicate that private hospitals (with more than 100 employees) average gross revenues of about $36.8 million in 1997. This figure inflates to about $57.7 million using the Consumer Price Index (CPI) for medical care from 1997 to 2007. Considering that hospitals producing PET drugs probably are larger than the average private hospital, we consider it very likely that the two private hospitals producing PET drugs have annual revenues over $29 million and are therefore not considered small entities.[3] In instances where PET drug producer information is not available, this analysis assumes that the PET drug producer is owned by the hospital in which it is located.

Two of the three domestic corporate PET drug producers exceed the SBA employee limits within their respective business classifications to qualify as small businesses. Employee data were not available for the other domestic corporation or any of the 11 regional commercial producers, and we therefore assume that these may be small businesses.

In total, the 51 identified producers of PET drugs are classified as follows: 6 Federal, 6 State, 34 small entities, and 5 large entities. Most of those that were considered small entities were classified as such because they are not-for-profit organizations, not because they met the employee or revenue limits for small businesses. It should be noted that an entity's identification as small or large in this analysis does not necessarily indicate the volume of PET drugs it produces or the share of the market it holds.

Most, if not all, of the PET drug producers currently employ individuals who possess skills necessary to establish written procedures and prepare documentation as required by

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1 "AHA Guide to the Health Care Field, 1997-98 Edition," Healthcare Infosource, Inc., a subsidiary of the American Hospital Association.

2 "The Nation: Colleges and Universities," The Chronicle of Higher Education, 1999-2000, Almanac Issue, volume XVI, no. 1, p. 7, August 27, 1999.

3 "Hospital Statistics," table 3, pp. 8-9, Health Forum, An American Hospital Association Company, 1999.

this rule. Some may choose, as mentioned above, to contract with an outside consultant to manage their compliance with the rule.

At most, a single PET drug producer may incur one-time and annual costs of approximately $57,900 and $32,400, respectively, per production facility. The hospital and regional commercial producers will incur these higher per-facility costs because these establishments are expected to have higher noncompliance rates with the written procedure and recordkeeping requirements. The total of the maximum one-time and annual costs per producer equates to significantly less than 1 percent of the $111 million ($70.8 million inflated by the CPI for medical care from 1997 to 2007) average annual gross revenue per nonprofit hospital. In addition, most of the hospitals that are affected by this rule are affiliated with large universities whose total revenues are expected to be much higher than the $111 million figure cited. The estimated compliance cost represents an even smaller portion of a percent of the entire university's revenues. Revenue data were not available for the one possibly small corporate producer. This company is expected to incur annual costs of approximately $70,100 and one-time costs of about $16,800. The 11 regional commercial producers are expected to incur one-time and annual costs of approximately $57,900 per producer and $32,400 per production facility. We lack sufficient data to estimate the expected compliance costs as a percentage of revenues for the regional commercial producers. Although no comments on the proposed rule directly addressed our estimates of the expected impact of compliance costs on small facilities, it is possible that this final rule will have a significant effect on these small entities.

6. Consequences of Collecting the Information Less Frequently

The frequency for the collection of information is based upon FDA's statutory responsibility to assure the availability of uniformly high quality drug products to the nation. FDA assures compliance with CGMP recordkeeping requirements by conducting drug establishment inspections, as authorized by section 704 (21 U.S.C. 374) of the act, to review and evaluate the adequacy of records. Drug manufacturers are, in general, scheduled for these comprehensive on-site inspections once every two years. Inspections are scheduled more frequently when there have been compliance problems. FDA investigators are authorized to examine and to copy and verify these records in order to document evidence of deviation should an enforcement case go to litigation. It would be impossible to ensure compliance with section 501(a)(2)(B) of the act (21 U.S.C.351 (a)(2)(B)) if industry were not required to maintain these records.

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

There is no inconsistency with the requirements of section 1320.5.

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

Section 121 of the Modernization Act contains several provisions affecting the regulation of PET drugs. Section 121(d) directed us to terminate the application of three Federal Register documents:

- A notice entitled "Regulation of Positron Emission Tomography Radiopharmaceutical Drug Products; Guidance; Public Workshop"(60 FR 10594, February 27, 1995). This notice stated that traditional CGMP requirements in parts 210 and 211 were applicable to PET drugs.
- A notice that announced the availability of a draft guideline on the production of PET drugs (60 FR 10593, February 27, 1995).
- A final rule authorizing us to approve exceptions or alternatives to the application of CGMP requirements to the production of PET drugs (62 FR 19493, April 22, 1997).

We terminated the application of these three documents in a notice (62 FR 66636) and final rule (62 FR 66522) published in the December 19, 1997, issue of the Federal Register.

Section 121(c)(1)(A) of the Modernization Act directs us to establish appropriate approval procedures and CGMP requirements for PET drugs. Section 121(c)(2) of the Modernization Act provides that FDA cannot require the submission of a new drug application (NDA) or abbreviated new drug application (ANDA) for a PET drug product until 2 years after the day we publish a final rule establishing CGMP requirements for PET drug products.

Section 121(c)(1)(B) of the Modernization Act states that, in adopting CGMP and approval requirements, we must take due account of any relevant differences between not-for-profit institutions that compound PET drugs for their patients and commercial manufacturers of such drugs.

Section 121(c)(1)(B) also directs us, as we develop PET drug CGMP requirements and approval procedures, to consult with patient advocacy groups, professional associations, manufacturers, and physicians and scientists who make or use PET drugs. We have taken the following steps in developing the PET drug CGMP regulations:

- We presented our initial tentative approach to PET drug CGMP requirements and responded to numerous questions and comments about that approach at a public meeting on February 19, 1999.
- We announced the availability of preliminary draft regulations on PET drug CGMP requirements in the September 21, 1999, issue of the Federal Register (64 FR 51274).
- We held a public meeting to discuss the preliminary draft regulations on September 28, 1999.
- After considering the comments on the preliminary draft regulations, we announced the availability of a preliminary draft proposed rule on PET drug CGMP requirements in the April 1, 2002, issue of the Federal Register (67 FR 15344).
- We also announced the availability of a draft guidance on "PET Drug Products--Current Good Manufacturing Practice for Positron Emission Tomography" on April 1, 2002 (67 FR 15404), and a revised draft guidance on September 20, 2005.
- We held a public meeting to discuss the preliminary draft proposed rule and draft guidance on May 21, 2002.
- We issued a proposed rule for public comment on September 20, 2005 (70 FR 55038).

All comments received on the proposed rule are summarized and responded to in the final rule. The comments that pertained to the information collection are summarized and responded to under section 12 below.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

Certain data and information collected during an inspection of a drug manufacturing establishment for the purpose of enforcing compliance with the CGMP regulations are 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, certain sections of 21 CFR 314.430 provide confidentiality of information contained in NDAs and ANDAs.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Hour Burden and Costs

12a. Annualized Hour Burden -

In accordance with the Modernization Act, the final rule establishes CGMP requirements for PET drugs. The CGMP requirements are designed to take into account the unique characteristics of PET drugs, including their short half-lives and the fact that most PET drugs are produced at locations that are very close to the patients to whom the drugs are administered. The estimated annual recordkeeping and third-party disclosure burden is based on there being 51 PET drug producers operating 36 hospital or academic facilities and 65 commercial facilities for a total of 101 PET drug production facilities.

The CGMP regulations are intended to ensure that approved PET drugs meet the requirements of the act as to safety, identity, strength, quality, and purity. The regulations address the following matters: Personnel and resources; quality assurance; facilities and equipment; control of components, in-process materials, and finished products; production and process controls; laboratory controls; acceptance criteria; labeling and packaging controls; distribution controls; complaint handling; and recordkeeping.

The CGMP regulations establish several recordkeeping requirements and a third-party

disclosure requirement for the production of PET drugs. In making our estimates of the time spent in complying with these requirements, we relied on communications we have had with PET producers, visits by our staff to PET facilities, and our familiarity with both PET and general pharmaceutical manufacturing practices.

Table 1 of this document provides an estimate of the annual recordkeeping burdens associated with the final rule. Table 2 of this document provides an estimate of the annual third-party disclosure burdens associated with the final rule. All of our burden estimates are based on there being 101 PET production facilities, with each of the 36 academic or hospital facilities producing 3 different PET drug products and each of the 65 commercial facilities producing 1 PET drug, resulting in an estimated 173 total PET drugs. Our estimates are also based on a 250-day work year with an average yearly production of 500 batches for each facility. We have also taken into account that time spent on recording procedures, processes, and specifications may be somewhat higher in the year in which these records are first established and correspondingly lower in subsequent years, when only updates and revisions will be required.

A. Investigational and Research PET Drugs

Section 212.5(b)(2) provides that for investigational PET drugs produced under an IND and research PET drugs produced with approval of an RDRC, the requirement under the act to follow current good manufacturing practice is met by complying with the regulations in part 212 or with USP 32 Chapter 823. We believe that PET production facilities producing drugs under INDs and RDRCs are currently substantially complying with the recordkeeping requirements of USP 32 Chapter 823 (see section 121(b) of the Modernization Act), and accordingly, we have not estimated any recordkeeping burden for this provision of the rule.

B. Batch Production and Control Records

Sections 212.20(c) through (e), 212.50(a) through (c), and 212.80(c) set out requirements for batch and production records as well as written control records. We estimate that it would take 20 hours annually for each PET production facility to prepare and maintain written production and control procedures and to create and maintain master batch records for each PET drug produced. We also estimate that there will be a total of 173 PET drugs produced, with a total estimated recordkeeping burden of 3,460 hours. We estimate that it would take a PET production facility an average of 30 minutes to complete a batch record for each of 500 batches. Our estimated burden for completing batch records is 25,250 hours.

C. Equipment and Facilities Records

Sections 212.20(c), 212.30(b), 212.50(d), and 212.60(f) contain requirements for records dealing with equipment and physical facilities. We estimate that it would take 1 hour to establish and maintain these records for each piece of equipment in each PET production facility. We estimate that the total burden for establishing procedures for these records would be 1,515 hours. We estimate that recording maintenance and cleaning information would take 5 minutes a day for each piece of equipment, with a total recordkeeping burden of 31,436 hours.

D. Records of Components, Containers, and Closures

Sections 212.20(c) and 212.40(a), (b), and (e) contain requirements on records regarding receiving and testing of components, containers, and closures. We estimate that the annual burden for establishing these records would be 202 hours. We estimate that each facility would receive 36 shipments annually and would spend 10 minutes per shipment entering records. The annual burden for maintaining these records would be 604 hours.

E. Process Verification

Section 212.50(f)(2) requires that any process verification activities and results be recorded. Because process verification is only required when results of the production of an entire batch are not fully verified through finished-product testing, we believe that process verification will be a very rare occurrence, and we have not estimated any recordkeeping burden for documenting process verification.

F. Laboratory Testing Records

Sections 212.20(c), 212.60(a), (b), and (g), 212.61(a) through (b), and 212.70(a), (b), and (d) set out requirements for documenting laboratory testing and specifications referred to in laboratory testing, including final release testing and stability testing. We estimate that each commercial PET production facility will need to establish procedures and create forms for 20 different tests for the 1 product they produce. Each hospital and academic PET drug production facility will need to establish procedures and create forms for a total of 34 different tests for the 3 products they produce. We estimate that it will take each facility an average of 1 hour to establish procedures and create forms for one test. The estimated annual burden for establishing procedures and creating forms for these records is 2,525 hours, and the annual burden for recording laboratory test results is 8,383 hours.

G. Sterility Test Failure Notices

Section 212.70(e) requires PET drug producers to notify all receiving facilities if a batch fails sterility tests. We believe that sterility test failures might occur in only 0.05 percent of the estimated 50,500 batches of PET drugs produced each year (about 25 times each year). Therefore, we have estimated that each PET drug producer will need to provide 0.25 sterility test failure notice per year to receiving facilities. The notice would be provided using e-mail or facsimile transmission and should take no more than 1 hour.

H. Conditional Final Releases

Section 212.70(f) requires PET drug producers to document any conditional final releases of a product. We believe that conditional final releases will be fairly uncommon, but for purposes of the PRA, we estimated that each PET production facility would have one conditional final release a year and would spend 1 hour documenting the release and notifying receiving facilities.

One comment expressed concern about the estimate of the frequency of conditional final release of PET drug products. The comment noted that the preamble to the proposed rule stated that conditional final release should not be necessary except in “very rare circumstances”; the comment also noted the statement in the preamble that repeated conditional final releases based on the unavailability of equipment that is difficult to envision failing or that is easily replaced could be considered to be a failure to take “reasonable efforts * * * to ensure that the problem does not recur” within the meaning of proposed § 212.70(f)(1)(v). The comment disagreed with the estimate of one conditional final release per year for each facility, stating that there appeared to be no consideration for size or production volume. The comment maintained that the use of conditional release should be tracked by producers to look for trends in equipment failures that need corrective actions, and the diligence applied in these corrective actions should be the measure for taking reasonable efforts to ensure that the problem does not recur.

FDA believes that the estimate of one conditional final release per year per facility is an appropriate average number because we believe that many facilities might have no conditional

final releases while others might have only a few. We agree with the comment that an assessment of "reasonable efforts" to prevent recurrence of a malfunction involving analytical equipment, under § 212.70(f)(1)(iv) of the final rule, would not focus primarily on the specific number of equipment failures. Instead, the reasonableness of the efforts relates to the steps that a producer takes to remedy a particular equipment problem and to identify and address trends in equipment malfunctions.

I. Out-of-Specification Investigations

Sections 212.20(c) and 212.71(a) and (b) require PET drug producers to establish procedures for investigating products that do not conform to specifications and conduct these investigations as needed. We estimate that it will take 1 hour annually to record and update these procedures for each PET production facility. We also estimate, for purposes of the PRA, that one out-of-specification investigation would be conducted at each facility each year and that it would take 1 hour to document the investigation.

One comment maintained that the number of out-of-specification investigations is significantly underestimated (at one investigation per facility each year). The comment stated that a true failure might only occur once each year but an out-of-specification investigation is necessary each time a single item in the final product testing process results in a nonconformance to specifications. The comment stated that because quality control on each batch is executed quickly, most out-of-specification conditions are directly due to operator or equipment failure and are rectified by retesting. The comment maintained that out-of-specification investigations actually occur two to three times per month; therefore, the comment recommended that we use an estimate of 36 investigations per facility each year.

FDA agrees with the comment's reasoning and we have revised the annual frequency of out-of-specification investigations from 1 to 36, which results in an annual hourly burden of 3,636 (101 producers times 36 investigations times 1 hour for documentation equals 3,636 hours).

J. Reprocessing Procedures

Sections 212.20(c) and 212.71(d) require PET drug producers to establish and document procedures for reprocessing PET drugs. We estimate that it will take 1 hour a year to document these procedures for each PET production facility. We did not estimate a separate burden for recording the actual reprocessing, both because we believe it would be an uncommon event and because the recordkeeping burden has been included in our estimate for batch production and control records.

K. Distribution Records

Sections 212.20(c) and 212.90(a) require that written procedures regarding distribution of PET drug products be established and maintained. We estimate that it will take 1 hour annually to establish and maintain records of these procedures for each PET production facility. Section 212.90(b) requires that distribution records be maintained. We estimate that it will take 15 minutes to create an actual distribution record for each batch of PET drug products, with a total burden of 12,625 hours for all PET producers.

L. Complaints

Sections 212.20(c) and 212.100 require that PET drug producers establish written procedures for dealing with complaints, as well as document how each complaint is handled. We estimate that establishing and maintaining written procedures for complaints will take 1 hour

annually for each PET production facility and that each facility will receive one complaint a year and will spend 30 minutes recording how the complaint was dealt with.

Table 1.— Estimated Recordkeeping Burden

21 CFR Section	No. of Record-keepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Record-keeper	Total Hours	Total Capital Costs	Total Operating & Mainten-ance Costs
212.20(c) and (e), 212.50(a) and (b)	101	1.71	173	20	3,460		
212.20(d) and (e), 212.50(c), 212.80(c)	101	500	50,500	.5	25,250		
212.20(c), 2.30(b), 212.50(d), 212.60(f)	101	15	1,515	1	1,515		
2.30(b), 212.50(d), 212.60(f)	101	3,750	378,750	.083	31,436		
212.20(c), 212.40(a) and (b)	101	2	202	1	202		
212.40(e)	101	36	3,636	.166	604		
212.20(c), 212.60(a) and (b), 212.61(a), 212.70(a), (b), (d)	101	25	2,525	1	2,525		
212.60(g), .61(b), 212.70(d)(2) and (d)(3)	101	500	50,500	.166	8,383		
212.70(f)	101	1	101	1	101		
212.20(c), 212.71(a)	101	36	3636	1	3636		
212.71(b)	101	1	101	1	101		
212.20(c), 212.71(d)	101	1	101	1	101		
2.20(c), 212.90(a)	101	1	101	1	101		
212.90(b)	101	500	50,500	.25	12,625		
212.20(c), 212.100(a)	101	1	101	1	101		
212.100(b) & (c)	101	1	101	.5	50		
					90,191		

Table 2. Estimated Annual Third-Party Disclosure Burden

	Number of Respondents	Number of Responses per Respondent	Total Responses	Hours per Response	Total Hours
212.70(e)	101	.25	25	1	25

[1] There are no capital costs or operating and maintenance costs associated with this information collection.

Costs -

The following cost analysis is taken from section IV of the final rule, Analysis of Economic Impacts:

Costs By Recordkeeping Requirement				
	Number of Establishments	Labor (Months)	Wage (Year Salary)[1]	Cost[2]
-- Establishment/Write SOPs				
Academic PET Producers	47	3	$164,300	$2,574,000
Commercial PET Producers	4	1	$164,300	$55,000
-- Training on SOPs				
Academic PET Producers	53	.23	$164,300	$168,000
Commercial PET Producers	48	.23	$164,300	$152,000
-- Total One-Time Costs				$2,949,000
-- Daily Implementation, Audits, Updates				
Academic PET Producers	53	2.25	$164,300	$1,633,000
Commercial PET Producers	48	1.0	$164,300	$657,000
-- Training				
Academic PET Producers	53	.11	$164,300	$84,000
Commercial PET Producers	48	.11	$164,300	$76,000
-- Total Annual Costs				$2,450,000

[1] Salary includes 35 percent increase for benefits.
[2] Cost totals may not sum due to rounding.

Total one-time costs are estimated at about $2.95 million (annualized at $720,000 over 5 years), and re-occurring or annual costs at about $2.45 million.

The 53 hospital and regional commercial PET drug production establishments will incur about $2.74 million in one-time costs and $1.72 million in annual costs. The annualized (annualized one-time costs plus annual costs) cost per facility is estimated at about $43,600. The 48 corporate PET drug production facilities will incur about $207,000 and $733,000 in one-time and annual costs, respectively. Total annualized (annualized one-time costs plus annual costs) costs per corporate establishment are estimated at about $16,300. Total annualized costs for all producers are estimated at $3,170,000.

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

There are no other costs associated with this collection of information.

14. Annualized Cost to the Federal Government

- Number of PET inspections per year is 60:

We estimate that there are about 120 PET drug production facilities in the U.S. and we will be inspecting 50% of the facilities on an annual basis. The 50% are derived from the fact that FDA is mandated by Congress to inspect each facility once every 2 years, as resources and priority allows. PET drugs are injectables and are classified as a high priority.

- Operational cost estimate is 2 operational FTEs:

Assuming that FDA investigators receive appropriate training in conducting PET inspections, and 1 FDA investigator conducts an inspection, it should not take more than an average of 1 day to prepare for the inspection, 2 days to complete an inspection, and 1 day to finish the inspection report -- 60 inspections x 32 hours/inspection = 1920 hours = 2 operational FTEs (based on 1 operational FTE = 980 hours)

- Supportive cost estimate is 4 supportive FTEs:

The supportive cost includes administrative support in ORA (review, travel) and in CDER (compliance officer/reviewer participation) -- 2 operational FTEs x 2 = 4 supportive FTEs (based on the standard ratio used by FDA, supportive cost = 2 x operational cost)

In summary:

Total FTEs (operational and supportive) = 2 operational FTEs + 4 supportive FTEs = 6 FTEs

Total cost per year: 6 FTE X $145,000/FTE = $870,000

15. Explanation for Program Changes or Adjustments

There are no changes because this is a final rule and OMB has not yet issued an approval number.

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.