UNITED STATES FOOD & DRUG ADMINISTRATION

Current Good Manufacturing Practice for
Positron Emission Tomography (PET) Drugs

OMB Control No. 0910-0667

SUPPORTING STATEMENT – **Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA, the agency, us or we) regulations pertaining to the Current Good Manufacturing Practice (CGMP) for Positron Emission Tomography (PET) drugs. PET is a medical imaging modality involving the use of a unique type of radiopharmaceutical drug product. Our CGMP regulations codified in part 212 (21 CFR part 212) are intended to ensure that PET drug products meet the requirements of the Federal Food, Drug, and Cosmetic Act (FD&C Act) regarding safety, identity, strength, quality, and purity. The CGMP requirements for PET drugs are issued under the provisions of the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 105-115). These CGMP requirements are designed according to the unique characteristics of PET drugs, including their short half-lives, and the fact that most PET drugs are produced at locations close to the patients to whom the drugs are to be administered.

The CGMP regulations require the establishment of written procedures as well as recordkeeping related to ongoing manufacturing of individual PET drugs, testing, and product release activities, including any third-party disclosure requirements for producing PET drugs. To estimate time spent to comply with the requirements, we relied on informal communications with PET producers, FDA staff visits to PET facilities, our familiarity with PET and general pharmaceutical manufacturing practices with application and supplement submissions, and various reports FDA received from 2016 through 2018.

We therefore request extension of OMB approval for the information collection provisions found in part 212 of our regulations (21 CFR 212) and discussed in this supporting statement.

2. Purpose and Use of the Information Collection

Respondents to the information collection are manufacturers of PET drugs. We use the information to ensure compliance with CGMP regulatory requirements applicable to PET drugs, including: personnel and resources; quality assurance (QA); equipment and facilities; control of components; in-process materials and finished products; production and process controls; laboratory controls; and acceptance criteria.

3. Use of Improved Information Technology and Burden Reduction

While the regulations cover record availability, quality, and retention, they do not prescribe a specific means of recordkeeping other than that records be reasonably accessible to FDA upon inspection. Because electronic submissions are the standard means of submitting information to the agency, however, we estimate most 85% respondents will use electronic means to fulfill the recordkeeping requirements. The agency accepts any recordkeeping method that complies with the applicable requirements.

Additionally, we have issued the following guidance documents to assist respondents to the information collection. All guidance documents are issued in accordance with our GGP regulations under 21 CFR part 10.115 and provide opportunity for comment at any time. All guidance documents are available from our website at www.fda.gov:

Clinical/Medical	Investigational New Drug Applications for Positron Emission Tomography (PET) Drugs (PDF - 369KB)
Procedural	FDA Oversight of PET Drug Products -- Questions and Answers (PDF - 499KB)
Procedural; Modernization Act	PET Drug Applications - Content and Format for NDAs and ANDAs: Attachment I: Sample formats for chemistry, manufacturing, and controls (CMC) sections 2011 (PDF - 614KB)
Procedural; Modernization Act	PET Drug Applications - Content and Format for NDAs and ANDAs_2011 (PDF - 429KB)
Pharmaceutical Quality/Manufacturing Standards (CGMP) and Small Entity Compliance Guide	PET Drugs--Current Good Manufacturing Practice (CGMP); Small Entity Compliance Guide (PDF - 229KB)
Procedural	Positron Emission Tomography (PET) Drug SPL

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection. Information collection is required in accordance with statutory provisions that are exclusively the responsibility of FDA pertaining to the manufacture and distribution of PET drugs, and pursuant to 21 CFR 212.

5. Impact on Small Businesses or Other Small Entities

Although the information collection applies to small and large businesses alike, we provide resources, including small business and industry assistance, to respondents on our website at https://www.fda.gov/industry/small-business-assistance and through staff within our Center for Drug Evaluation and Research (CDER). No undue burden is posed on small entities as a result of the information collection.

6. Consequences of Collecting the Information Less Frequently

The information collection schedule is consistent with statutory and regulatory requirements associated with the CGMP regulations applicable to PET drugs.

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

There are no special circumstances for this collection of 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), we published a 60-day notice inviting public comment in the Federal Register of March 14, 2019 (84 FR 9347). We received three letters in response. The comments submitted questioned the necessity of the proposed collection; suggested we allow both paper recordkeeping and simplified electronic report submission; questioned whether an Annual Product Review (APR) is required by the regulations; and identified an inadvertent printed error in one of our burden estimates. A detailed response to the comments was published in our 30-day notice of, where a summary is provided here:

FDA is Congressionally mandated to promulgate regulations that apply solely to PET drugs. Accordingly, requirements applicable to PET drugs are codified part 212 of our regulations (21 CFR 212). We therefore maintain that the information collection is necessary to ensure the promotion and protection of the public health. Also, as stated previously, the regulations prescribe no specific means for recordkeeping, however, records must be made reasonably accessible, as prescribed under 212.110(a). Regarding the question pertaining to Annual Product Review we defer to the regulations noting the applicable GMP review provisions. Finally, we are appreciative of the editorial comment regarding the discrepancy in a disclosure element as it appeared in the text and corresponding table. As correctly noted in the table and here in this supporting statement, we attribute 2.5 hours, representative of the industry average, for this information collection element which appears in Table x, row y below at *Question 12a*.

9. Explanation of Any Payment or Gift to Respondents

No remuneration is provided to respondents to the information collection.

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.

Upon review of the information collection with agency Privacy Act staff, we have concluded that information collection does not involve solicitation or collection of personally identifiable information (PII) by or on behalf of FDA/CDER. Specifically, we do not collect personally identifiable information (PII) and will not maintain records subject to the Privacy Act or otherwise operate a Privacy Act System of Records in relation to this specific collection.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

We estimate the burden of the information as follows:

Table 1.--Estimated One-Time Recordkeeping Burden for Corporate Firms[1]

Activity/Type of Respondent/21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	One-Time Records	Average Burden per Recordkeeper	Total Hours[2]
Batch Production and Control Records (§§ 212.20(c) and (e) and 212.50(a) and (b))	3	9	27	8	216
Equipment and Facilities Records (SOP) (§§ 212.20(c), 212.30(b) 212.50(d), and 212.60(f))	3	13	39	5	195
Records of Components, Containers, and Closures (SOP) (§§ 212.20(c) and 212.40(a) and (b))	3	2	6	8	48
Records of Components, Containers, and Closures (specifications data sheets) (§§ 212.20(c) and 212.40(a) and (b))	3	25	75	2	150
Out-of-Specification Investigations (SOP) (§§ 212.20(c) and 212.71(a))	3	1	3	8	24
Distribution Records (SOP) (§§ 212.20(c) and 212.90(a))	3	1	3	8	24
Complaints, Recalls (§§ 212.20(c) and 212.100(a))	3	3	9	8	72
Total					729

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Number rounded to the nearest whole number.

Table 2.--Estimated One-Time Recordkeeping Burden for Academia, Small Firms, and High-Risk Component Manufacturers [1]

Activity/Type of Respondent/21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	One-Time Records	Average Burden per Recordkeeper	Total Hours[2]
Batch Production and Control Records (§§ 212.20(c) and (e) and 212.50(a) and (b))	61	8	488	8	3,904
Equipment and Facilities Records (SOP) (§§ 212.20(c), 212.30(b) 212.50(d), and 212.60(f))	61	13	793	8	6,344
Records of Components, Containers, and Closures (specification only) (§§ 212.20(c) and 212.40(a) and (b))	61	25	1,525	2	3,050
Records of Components, Containers, and Closures (SOP) (§§ 212.20(c) and 212.40(a) and (b))	61	2	122	8	976
Out-of-Specification Investigations (SOP) (§§ 212.20(c) and 212.71(a))	61	1	61	8	488
Distribution Records (SOP) (§§ 212.20(c) and 212.90(a))	61	1	61	8	488
Complaints, Recalls (§§ 212.20(c) and 212.100(a))	52	3	156	8	1,248
Total					16,498

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Number rounded to the nearest whole number.

Table 3.--Estimated Annual Recordkeeping Burden for Corporate Firms[1]

Activity/21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeper	Total Hours[2]
Batch Production (Creating Manufacturing Records (creating batch-related records per year) (§§ 212.20(c) and (e) and 212.50(a) and (b))	115	144	16,560	0.50 (30 minutes)	8,280
Creating Any New Batch Records/Quality Records for New or Existing Drugs (§§ 212.20(c) and (e) and 212.50(a) and (b))	3	9	27	8	216
Equipment and Facilities Records (calibration and cleaning records systems) (§§ 212.30(b), 212.50(d), and 212.60(f))	115	164	18,860	0.50 (30 minutes)	9,430

Records of Components, Containers, and Closures (§§ 212.20(c) and 212.40(a) and (b))	115	24	2,760	0.50 (30 minutes)	1,380
Laboratory Testing Records (record laboratory test results) §§ 212.60(g), 212.61(b), and 212.70(d)(2) and (3)	115	144	16,560	0.50 (30 minutes)	8,280
Out-of-Specification Investigations (record events and investigations) (§ 212.71(b))	115	2	230	2	460
Complaints (§§ 212.100(b) and (c))	115	2	230	2	460
QA and Release of Batches	115	144	16,560	0.25 (15 minutes)	4,140
Distribution Records (§ 212.90(b))	115	144	16,560	0.25 (15 minutes)	4,140
Total					36,786

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Number rounded to the nearest whole number.

Table 4.--Estimated Annual Recordkeeping Burden for Academia and Small Firms[1]

Activity/21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeper	Total Hours[2]
Batch Production (creating manufacturing records) (filling batch related records per year) (§§ 212.20(c) and (e) and 212.50(a) and (b))	52	24	1,248	0.50 (30 minutes)	624
Creating Any New Batch Records/Procedures for New Drugs (§§ 212.20(c) and (e) and 212.50(a) and (b))	52	3	156	8	1,248
Equipment and Facilities Records (calibration and cleaning records) (§§ 212.30(b), 212.50(d), and 212.60(f))	52	34	1,768	0.50 (30 minutes)	884
Records of Components, Containers, and Closures (incoming acceptance tests) (§§ 212.20(c) and 212.40(a) and (b))	52	12	624	0.50 (30 minutes)	312
Laboratory Testing Records (QC test results) §§ 212.60(g), 212.61(b) and 212.70(d)(2) and (3)	52	24	1,248	0.50 (30 minutes)	624
Out-of-Specification Investigations (record events and investigations) (§ 212.71(b))	52	2	104	2	208

Complaints (Record events and investigations) (§§ 212.100(b) and (c))	52	2	104	2	208
QA and Release of Batches	52	24	1,248	0.25 (15 minutes)	312
Distribution Records (§ 212.90(b))	52	24	1,248	0.25 (15 minutes)	312
Total					4,732

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Number rounded to the nearest whole number.

Table 5.--Estimated Annual Recordkeeping Burden for High Risk Component Manufacturers[1]

Activity/21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeper	Total Hours[2]
Batch Production (creating manufacturing records and batch related records per year) (§§ 212.20(c) and (e) and 212.50(a) and (b))	9	12	108	0.50 (30 minutes)	54
Equipment and Facilities Records (calibration and cleaning records systems) (§§ 212.30(b), 212.50(d), and 212.60(f))	9	16	144	0.50 (30 minutes)	72
Records of Components, Containers, and Closures (incoming acceptance test) (§§ 212.20(c) and 212.40(a) and (b))	9	6	54	0.50 (30 minutes)	27
Laboratory Testing Records (record QC test results) §§ 212.60(g), 212.61(b) and 212.70(d)(2) and (3)	9	12	108	0.50 (30 minutes)	54
Out-of-Specification Investigations (Record events and investigations) (§ 212.71(b))	9	1	9	1	9
QA and Release of Batches	9	12	108	0.25 (15 minutes)	27
Distribution Records (§ 212.90(b))	9	12	108	0.25 (15 minutes)	27
Total					270

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Number rounded to the nearest whole number.

Table 6.--Estimated Annual Third-Party Disclosure Burden[1]

Activity/21 CFR Section	No. of Sterility Failure Incidents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Sterility Test Failure Notices (§ 212.70(e))	12	3[2]	36	2.5	90

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] There are two reports sent to FDA per incident and notification to receiving site.

Section 212.5(b) (21 CFR 212.5(b)) provides that for investigational PET drugs produced under an investigational new drug application (IND) and research PET drugs produced with approval of a Radioactive Drug Research Committee (RDRC), the requirement (FD&C Act) to follow CGMP is met by complying with the regulations under part 212 or complying with United States Pharmacopeia (USP) 32 Chapter 823. We believe that PET production facilities producing drugs under INDs and RDRCs are already substantially complying with the recordkeeping requirements of USP 32 Chapter 823 (see section 121(b) of FDAMA). Some IND and RDRC PET facilities also produce approved NDA (new drug application) and abbreviated new drug application (ANDA) PET drugs. While we do not have sufficient information to estimate burdens for all IND and RDRC PET facilities, our estimates have included those facilities that also produce NDA and ANDA PET drugs. Those facilities are included under academic and small firms.

A. One-Time Burden for Corporate Firms

We estimate corporate firms will have to employ one-time and ongoing annual recordkeeping. There are three major PET manufacturing corporations and most of the quality, manufacturing, and testing procedures are developed at the corporate level and then issued to the individual sites located in various States across the country. There are an estimated 115 such sites under three major corporations. Thus, the burden has been calculated for 3 recordkeepers instead of 115 individual sites.

It would take approximately 8 hours for each corporate firm to create one master batch record per drug, and an average of three PET drugs have been taken into consideration. We also estimate that approximately 3 firms will create and maintain approximately 27 records associated with production and quality testing for an average of 3 drugs, with a total recordkeeping burden of approximately 216 hours.

Sections 212.20(c), 212.30(b), 212.50(d), and 212.60(f) (21 CFR 212.20(c), 212.30(b), 212.50(d), and 212.60(f)) contain standard operating procedures (SOPs) dealing with equipment operation, maintenance, and cleaning, including maintenance of physical facilities.
It would take approximately 5 hours for each corporate firm to establish and maintain procedures for equipment and facility maintenance. We estimate that the 3 corporate firms

will establish and maintain 39 procedures, with a total recordkeeping burden of approximately 195 hours.

Sections 212.20(c) and 212.40(a) and (b) contain requirements on SOPs regarding receiving, testing, and accepting components. We estimate that the burden for corporate firms to create procedures for acceptance of raw materials and components would be approximately 8 hours and that there will be approximately three corporate firms performing these activities, with a total recordkeeping burden of approximately 48 hours. The burden for corporate firms to create component specification data sheets would be approximately 2 hours with approximately 3 corporate firms performing these activities, with a total recordkeeping burden of approximately 150 hours for approximately 25 component specification sheets for each firm.

Sections 212.20(c) and 212.71(a) and (b) require that PET drug firms establish procedures for investigating "deviations" and "out of specifications failures" of products during manufacturing and testing that do not conform to specifications and to conduct these investigations and record them as needed. We estimate that it will take approximately 8 hours for three corporate firms to establish one procedure, with a total recordkeeping burden of approximately 24 hours.

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 approximately 8 hours for each corporate firm to establish written procedures regarding distribution of PET drugs with a total of approximately three records, with a total recordkeeping burden of approximately 24 hours.

Sections 212.20(c) and 212.100(a), (b), and (c) require that PET drug firms establish and maintain written procedures for handling complaints and procedures for field alert reports (FARs). We estimate that each corporate firm will create three written procedures to establish complaints and FARs process and it will take approximately 24 hours for each corporate firm. A total of 72 hours will be required to create 27 procedures by 3 corporate firms.

B. One-Time Burden for Academia, Small Firms, and Precursors

There is a total of 52 sites combined for academic and small commercial firms, including some IND and RDRC sites. There are nine starting material/precursors/sterile raw material manufacturing entities who are required to follow selected regulations from part 212, according to the PET drug definition under section 121(a) of FDAMA and codified in section 201(ii)(1)(A) of the FD&C Act (21 U.S.C. 321(ii)(1)(A)). We will refer to them as high-risk component manufacturing firms in the tables.

It would take approximately 8 hours for each firm to perform the same activities as corporate firms regarding creating master batch records and manufacturing and quality procedures. We

estimate that there will be a total of approximately 488 records, with a total recordkeeping burden of approximately 3,904 hours.

It would take approximately 8 hours for each firm to create equipment and facility related procedures as corporate firms. We also estimate that there will be a total of approximately 793 records, with a total recordkeeping burden of approximately 6,344 hours.

We also estimate that the burden for each firm to create and maintain specification sheets would be approximately 2 hours and that there will be a total of approximately 61 firms performing these activities, with a total recordkeeping burden of approximately 3,050 hours. Furthermore, the burden for these firms to create and maintain procedures for acceptance of raw materials and components would be approximately 8 hours and that there will be a total of approximately 61 firms performing these activities, with a total recordkeeping burden of approximately 976 hours.

It would take approximately 8 hours for each firm to perform the same activities as corporate firms. We estimate that there will be a total of approximately 61 records, with a total recordkeeping burden of approximately 488 hours.

We estimate that 61 academia, small firms, and high-risk component manufacturers will create about one procedure related to deviations and out of specifications and that each firm will expend approximately 8 hours, for a total of 488 hours. Similarly, 488 hours will be spent for procedures on distribution of PET drugs. There will be 3 procedures created by each firm related to customer complaints, recalls, and FARs, with a total of 156 records from 52 sites and a total of 1,248 hours.

C. Annual Burden for Corporate Firms

In this section, we considered 115 individual corporate sites under the 3 major corporations in our estimates. These activities will be related to individual PET drugs manufactured at each of the sites located across the country. We estimate that it would take 30 minutes each to fill 144 batches (approximately 4 batches/month), for a total of 8,280 hours. In the second row of table 3, we have also estimated that on an annual basis, some new batch records or quality records may have to be created for newly introduced or existing drugs. It would take each firm approximately 24 hours for three new quality procedure/master batch records, with a total recordkeeping burden of approximately 216 hours for nine records from three corporate organizations.
We estimate that 115 individual corporate sites belonging to 3 major corporate entities will create 164 records for equipment maintenance, cleaning, calibration, and facilities maintenance records, with a total recordkeeping burden of 9,430 hours.

Sections 212.20(c) and 212.40(a) and (b) also set out requirements for raw material and component shipments received at the manufacturing facility on an ongoing basis. We estimate that the burden for each firm to create incoming raw material acceptance records for

2 shipments per month and 30 minutes per shipment will be 1,380 hours for 2,760 records from 115 sites.

Sections 212.60(g), 212.61(b), and 212.70(d)(2) and (3) set out requirements for documenting laboratory testing results from each PET drug manufactured referred to in laboratory testing, including final release testing. Each firm must keep records of different tests for each of their products. We estimate that approximately 115 corporate sites will document 144 records of cumulative quality control (QC) test results (one record with 5 to 6 tests included), with a total recordkeeping burden of approximately 8,280 hours.

We estimate that each firm will take approximately 1 hour to record out-of-specification (OOS) events and perform investigations for each incident. We also estimate an average of 2 "Out of Specification" investigations per firm, with a total of 230 records for "OOS" investigations from 115 sites, which results in a burden of 460 hours. This estimate includes any reprocessing or special release events, which are very rare.

Section 212.100(b) and (c) requires that PET drug firms document how each complaint is handled. We estimate that this will take approximately 2 hours for each site to document and investigate one complaint. We estimated 2 complaints per year per site, with a total expended hour of 460 hours for 115 individual sites. We believe the estimate is appropriate since not all sites receive complaints.

We also estimate annual recordkeeping for PET drug firms to perform quality assurance (QA) and release of manufactured PET drugs from the 115 corporate sites to be 4,140 hours, for a total of 144 released batches estimating 15 minutes per batch.

Section 212.90(b) requires that corporate firms maintain distribution records. We estimate that it will take each firm approximately 15 minutes to create a distribution record for each batch of PET drug products, with a total burden of approximately 4,140 hours for 144 released batches from 115 sites.

D. Annual Burden for Academia and Small Firms

It is estimated that each firm will expend the same amount of time to perform the same activities as corporate firms. Approximately 52 academia and small firms will fill 1,248 batch and production records, totaling 624 hours. For any new master batch record or quality procedures we have estimated 156 total records (3 per site), with a total of 1,248 hours.

For calibration and cleaning records like filling information in log books for each piece of equipment and documenting calibration records in each PET production firm, we estimate approximately 30 minutes on average for each piece of equipment for all firms. The calibration efforts are once per year per equipment, with estimated 10 pieces of equipment per site. We estimate that 52 academic and small firms will record a total of 884 hours for 34 records per site and a total of 1,768 records.

For §§ 212.20(c) and 212.40(a) and (b), approximately 1,768 raw material and component acceptance records will be filled on an ongoing annual basis. We estimate that the burden for each firm to create incoming raw material acceptance records for 12 shipments per year and 30 minutes per shipment will be 312 hours for 624 records from 52 sites.

We also estimate that approximately 52 academia and small firms will document 1,248 laboratory QC tests for 24 batches of drugs, with a total recordkeeping burden of approximately 624 hours.

We estimate that each firm will take approximately 1 hour each to record OOS and customer complaint events and perform investigations. We also estimate that an average of two "Out of Specification" and customer complaints and investigations per firm, with a total of 208 hours for each category. This estimate has included any reprocessing or special batch release events, which have been rarely observed.

We also estimate annual recordkeeping for PET drug firms to perform QA and release of manufactured PET drugs from 52 sites to be 312 hours, for a total of 24 batches per site released if estimating 15 minutes per batch.

Section 212.90(b) requires that corporate firms maintain distribution records. We estimate that it will take approximately 15 minutes to create a distribution record for each batch of PET drug products, with a total burden of approximately 312 hours for 24 batches per site.

E. Annual Burden for High-Risk Component Manufacturers

According to section 121(a) of FDAMA, the PET drug definition includes any non-radioactive or radioactive reagents, kits, nuclidic generators, target materials, synthesizers, and so forth. FDA performs risk assessments of each manufacturer and inspects such manufacturers. Sterile manufacturers and complex labels fall under this category, including sterile raw material or reagent manufactures. We have estimated nine such facilities based on inspections so far and have included them in this section. These manufacturers must comply with selected sections of part 212 since they are not final PET drug manufacturers. We will refer to them as high-risk component manufacturers in general in this document.

We estimate that it would take 9 high-risk component manufacturers about 30 minutes to fill each manufacturing batch records (12 per year) and that there will be a total of approximately 108 records, with a total recordkeeping burden of approximately 54 hours.
We also estimate that it will take nine component manufacturers 30 minutes to fill and create equipment and facilities related records, with a total recordkeeping burden of 72 hours.
We estimate that 9 high-risk component manufacturers will document 54 components, containers, and closures for incoming acceptance tests, with a total recordkeeping burden of approximately 27 hours.

We estimate that 9 high-risk component manufacturers will document 12 QC records related to 12 batches, with a total recordkeeping burden of approximately 54 hours.

We also estimate annual recordkeeping for PET drug firms to perform QA and release manufactured PET drugs from 9 sites to be 27 hours, for a total of 108 batches released, estimating 15 minutes per batch.

We further estimate that it would take each precursor 15 minutes to create and maintain distribution records and that there will be approximately 108 records, with a total recordkeeping burden of approximately 27 hours.

III. Process Verification

Section 212.50(f)(2) requires that any process verification activities and results be recorded. Process verification is usually performed as a one-time activity before a product is approved or if any major manufacturing process or equipment changes are made. This effort to conduct process verification has been estimated under annual new creation of master batch records and manufacturing and quality procedures in section II above.

IV. 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 uncommon, and we have them estimated under annual "OOS" investigations and final QA release efforts for each manufactured batch.

V. Reprocessing Procedures

Sections 212.20(c) and 212.71(d) require PET drug producers to establish and document procedures for reprocessing PET drugs. We rarely see any reprocessing option being submitted for application of such drugs and, if reprocessing occurs, we have estimated such rare events under annual QA release efforts.

VI. Third-Party Disclosure Burden

Section 212.70(e) requires that PET drug producers notify all receiving facilities if a batch fails sterility tests. FDA receives FARs reports based on confirmed sterility failures of released PET drugs. Based on our experience of such reporting, we estimated a total of 12 failures from all 167 sites (corporate, small firms, and academia). Therefore, we have estimated that 12 PET drug producers will file 2 reports to FDA and send a notification to the affected clinical/receiving site per year. PET drug producers would transmit the notice by email or Fax and submit the FARs notice to FDA electronically, with 2.5 hours per incident in total.

12b. Annualized Cost Burden Estimate

	Number of Establishments	Labor (Months)	Wage (Annual Salary)	Cost
RECORDS DAILY IMPLEMENTATION, AUDITS, UPDATES				
Academia and Small PET Producers	61	2.25	$164,300	$554,512.23
Commercial PET Producers	115	1.0	$164,300	$1,519,774.26
TRAINING:				
Academia and Small PET Producers	61	.11	$164,300	$27,109.49
Commercial PET Producers	115	.11	$164,300	$167,175.17
TOTAL				$194,284.66

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

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

14. Annualized Cost to the Federal Government

Costs for the information collection include periodic inspections of PET drug production facilities. Assuming 5 full-time employees are needed to conduct these inspections annually, we calculate $725,000 in total costs to the Federal Government.

15. Explanation for Program Changes or Adjustments

The information collection reflects adjustments. After a review of the information collection, we have increased the number of respondents based on the number of current production sites, and we have increased the time burden ascribed to some of the recordkeeping activities based on informal communications with industry. However, because fewer PET drug batches have been produced at the respective sites, the burden estimate reflects a decrease of 707,007 fewer records and 73,441 fewer hours, which we believe reflects the average burden for all respondents. We have also uploaded previously disclosed cost information for viewing at www.reginfo.gov.

16. Plans for Tabulation and Publication and Project Time Schedule

No tabulated results, or production or project schedules are associated with the information collection.

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

The OMB expiration date will be displayed as required by 5 CFR 1320.5.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.