U.S. Food & Drug Administration
Current Good Manufacturing Practices (CGMP)
for Finished Pharmaceuticals, and CGMP for Medical Gases

OMB Control No. 0910-0139

SUPPORTING STATEMENT **Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA, us or we) regulations regarding finished pharmaceuticals and biological products, including drug product containers and closures for medical gas. Under Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 351(a)(2)(B)), 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 current good manufacturing practice (CGMP) regulations. FDA is responsible for enforcing the FD&C Act as well as related statutes, including the Public Health Service (PHS) Act. Congress enacted these laws to ensure that covered products meet applicable requirements regarding the safety, identity and strength, and the quality and purity characteristics they purport or are represented to possess, and are labeled with adequate warnings and instructions for use.

The pharmaceutical or drug quality-related regulations appear in several parts of Title 21 (Food and Drugs) CFR, including sections in parts 1-99, 200-299, 300-499, 600-799, and 800-1299. The regulations enable a common understanding of the regulatory process by describing requirements to be followed by drug manufacturers, applicants, and FDA. This particular information collection supports regulations codified at 21 CFR Part 210: *Current Good Manufacturing Practice (CGMP) in manufacturing, processing, packing, or holding of drugs* that include general recordkeeping requirements applicable to drug products. The information collection also supports regulations codified at 21 CFR Part 211: *Current Good Manufacturing Practice for Finished Pharmaceutical*s which sets forth "*minimum [CGMP] for preparation of drug products (excluding positron emission tomography drugs) for administration to humans or animals*." Under 21 CFR Part 211 (see 21 CFR Part 211.180) specific requirements for medical gas containers and closures are also found in the regulations, which were finalized by rulemaking on November 18, 2016 (82 FR 81685) (see 21 CFR Part 211 Subpart E). Finally, the information collection also supports regulations codified under 21 CFR Subchapter F: Biologics: Part 610 – *General Biologicals Products Standards*; and Part 680 – *Additional Standards for Miscellaneous Products*. Specifically, parts 610 and 680 (21 CFR parts 610 and 680) reference certain CGMP regulations in part 211: §§ 610.12(g), 610.13(a)(2), 610.18(d), 680.2(f), and 680.3(f).

These regulations set forth information collection requirements that allow FDA to meet its public health protection responsibilities. Products that fail to comply with CGMP requirements may be rendered adulterated under section 501(a)(2)(B) of the FD&C Act. We therefore request extension of OMB approval for the information collection found under 21 CFR Parts

211, 610, and 680 as identified and discussed in this supporting statement; and associated guidance documents developed to assist respondents with the regulatory requirements.

2. Purpose and Use of the Information Collection

Consistent with the regulations, records maintained shall be made readily available for authorized inspection. FDA is authorized to inspect these records under section 704 of the FD&C Act (21 U.S.C. 374) (and its enforcement section under section 301(f) of the FD&C Act 21 U.S.C. 331(f)). We use the information to help determine compliance with regulatory requirements established to ensure the safety and efficacy of the covered products. Our review also serves to establish accountability in the manufacturing and processing of drug products, facilitate productive inspections, and enable manufacturers to improve the quality of drug products made available to consumers. The information collection also facilitates product recall activities in the event a product recall becomes necessary.

3. Use of Improved Information Technology and Burden Reduction

While the regulations do not prescribe specific recordkeeping methods, we believe all respondents will use electronic means to fulfill the information collection requirements. Also, to assist respondents with the information collection requirements for medical gases, we developed a draft guidance for industry entitled, "*Current Good Manufacturing Practice for Medical Gases*." The guidance document discusses our recommendations regarding compliance with applicable requirements found in the regulations as they apply to these products. We believe the recommendations, when followed, will help respondents focus their information collection activities most efficiently with regard to demonstrating regulatory compliance.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection. As previously mentioned, GMP or quality system (QS) regulations appear in several parts of Title 21 (Food and Drugs) of the CFR. This collection covers provisions associated with requirements for finished pharmaceuticals under 21 CFR Part 211. Related collection OMB Control No. 0910-0585: *Medical Gas Containers and Closures; Current Good Manufacturing Practice Requirements* was established in support of recently finalized rulemaking (RIN 0910-AC53) and expires May 31, 2020. Before the next extension/renewal of either collection will consider how best to consolidate the information collections.

5. Impact on Small Businesses or Other Small Entities

Any exemption or exceptions to the regulations would threaten the assurance of product safety and thus pose unreasonable potential threats to the public health. At the same time, we do not believe the information collection imposes undue burden on small entities. However, we provide assistance to small businesses through agency staff and published resources, available on our website at www.fda.gov.

6. Consequences of Collecting the Information Less Frequently

The information collection schedule is consistent with statutory provisions and applicable regulations.

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

There are no special circumstances for the 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), FDA published a 60-day notice for public comment in the Federal Register of December 14, 2017 (82 FR 58811). FDA received no comments that pertained to the information collection. At the same time, we engage with respondents to the information collection both formally and informally through seminars, conferences, workshops, academia and other forums to encourage open communication on evolving standards and other topics related to safe drug product manufacturing and quality assurance.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift was 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 subparagraphs 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 Burden Hours and Costs

12a. Annualized Hour Burden Estimate

We estimate the hourly burden of the information collection as follows:

Table 1.- Estimated Annual Recordkeeping Burden[1]

21 CFR Section; Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Avg. Burden per Recordkeeping (in hours)[1]	Total Hours
SOP Maintenance	3,270		3,270	25	81,750
New Startup SOPs	50	25	1,250	20	25,000
211.34; Consultants	3,270	0.25	818	5	4090
211.67(c); Equipment cleaning and maintenance	3,270	50	163,500	0.25	40,875
211.68; Changes in master production and control records or other records	3,270	2	6,540	1	6,540
211.68(a); Automatic, mechanical, and electronic equipment	3,270	10	32,700	0.5	16,350
211.68(b); Computer or related systems	3,270	5	16,350	0.25	4,088
211.72; Filters	416	0.25	104	1	104
211.80(d); Components and drug product containers or closures	3,270	0.25	818	0.1	82
211.100(b); Production and process controls	3,270	3	9,810	2	19,620
211.105(b); Equipment identification	3,270	0.25	818	0.25	205
211.122(c); Labeling and packaging material	3,270	50	163,500	0.25	40,875
211.130(e); Labeling and packaging facilities	3,270	50	163,500	0.25	40,875
211.132(c); Tamper-evident packaging	1,613	20	32,260	0.5	16,130
211.132(d); Tamper-evident packaging	1,613	0.2	323	0.5	162
211.137; Expiration dating	3,270	5	16,350	0.5	8,175
211.160(a); Laboratory controls	3,270	2	6,540	1	6,540
211.165(e); Test methodology	3,270	1	3,270	1	3,270
211.166; Stability testing	3,270	2	6,540	0.5	3,270
211.173; Laboratory animals	33	1	33	0.25	8
211.180(e); Production, control, and distribution records	3,270	0.2	654	0.25	164
211.180(f); Procedures for notification of regulatory actions	3,270	0.2	654	1	654
211.182; Equipment cleaning and use log	3,270	2	6,540	0.25	1,635
211.184; Component, drug product container, closure, and labeling records	3,270	3	9,810	0.5	4,905

21 CFR Section; Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Avg. Burden per Recordkeeping (in hours)[1]	Total Hours
211.186; Master production and control records	3,270	10	32,700	2	65,400
211.188; Batch production and control records	3,270	25	81,750	2	163,500
211.192; Discrepancies in drug product production and control records	3,270	2	6,540	1	6,540
211.194; Laboratory records	3,270	25	81,750	0.5	40,875
211.196; Distribution records	3,270	25	81,750	0.25	20,438
211.198; Compliant files	3,270	5	16,350	1	16,350
211.204; Returned drug products	3,270	10	32,700	0.5	16,350
Total			979,492		654,820

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

Based on our experience with the collection and a review of our data, we estimate the CGMP provisions apply to 3,270 firms and use this figure to calculate the respective recordkeeping activities. In addition, we assume some existing firms will expand into new manufacturing areas and that startup firms will need to create SOPs. As reflected above, we estimate 50 firms will create up to 25 SOPs each for a total of 1,250 records, and that it will take 20 hours per recordkeeper to create 25 new SOPs for a total of 25,000 hours. In addition, estimated burden for information collection activity associated with regulations under 21 CFR §§ 610.12(g), 610.13(a)(2), 610.18(d), 680.2(f), and 680.3(f) is included in the burden estimates under §§ 211.165, 211.167, 211.188, and 211.194, as appropriate.

Table 2 reflects burden associated with the same recordkeeping requirements as they apply to medical gas containers and closures, as regulations covering these products have recently been amended.

Table 2.--Estimated Annual Recordkeeping Burden (Medical Gases)[1]

21 CFR Section; Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Avg. Burden per Recordkeeping (in hours)[1]	Total Hours
SOP Maintenance	2,284	0.65	1,485	25	37,125
New startup SOPs	100	25	2,500	20	50,000
211.34; Consultants	2,284	0.25	571	0.5	286
211.67(c); Equipment cleaning and maintenance	2,284	32.5	74,230	0.25	18,558
211.68; Changes in master production and control records or other records	2,284	2	4,568	1	4,568
211.68(a); Automatic, mechanical, and electronic equipment	2,284	10	22,840	0.5	11,420
211.68(b); Computer or related systems	2,284	5	11,420	0.25	2,855
211.72; Filters	2,284	0.25	571	1	571

21 CFR Section; Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Avg. Burden per Recordkeeping (in hours)[1]	Total Hours
211.80(d); Components and drug product containers or closures	2,284	0.25	571	0.1	57
211.100(b); Production and process controls	2,284	3	6,382	2	13,704
211.105(b); Equipment identification	2,284	0.25	571	0.25	143
211.122(c); Labeling and packaging material	2,284	50	114,200	0.25	28,550
211.130(e); Labeling and packaging facilities	2,284	50	114,200	0.25	28,550
211.132(c); Tamper-evident packaging	2,284	20	45,680	0.5	22,840
211.132(d); Tamper-evident packaging	2,284	0.2	457	0.5	229
211.137; Expiration dating	2,284	3.25	7,423	0.33	2,450
211.160(a); Laboratory controls	2,284	2	4,568	1	4,568
211.165(e); Test methodology	2,284	1	2,284	1	2,284
211.166; Stability testing	2,284	1.3	2,969	0.33	980
211.173; Laboratory animals	2,284	1	2,284	0.25	571
211.180(e); Production, control, and distribution records	2,284	0.2	457	0.25	114
211.180(f); Procedures for notification of regulatory actions	2,284	0.2	457	1	457
211.182; Equipment cleaning and use log	2,284	1.3	2,969	0.16	475
211.184; Component, drug product container, closure, and labeling records	2,284	1.95	4,454	0.33	1,470
211.186; Master production and control records	2,284	10	22,840	2	45,680
211.188; Batch production and control records	2,284	16.25	37,115	1.3	48,250
211.192; Discrepancies in drug product production and control records	2,284	2	4,568	1	4,568
211.194; Laboratory records	2,284	25	57,100	0.5	28,550
211.196; Distribution records	2,284	25	57,100	0.25	14,275
211.198; Complaint files	2,284	5	11,420	1	11,420
211.204; Returned drug products	2,284	10	22,840	0.5	11,420
Total			641,094		396,988

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

12b. Annualized Cost Burden Estimate

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Pharmaceutical industry average wage grade for maintaining this information collection	1,051,808	$85.00	$89,403,680

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 to the Federal Government

FDA allocates approximately 283 full-time-employees (FTE's) annually to ensure industry compliance with the information collection. Using 2018 OPM and BOL data and assuming a fully-loaded annual salary of $175,000, we calculate the annual cost to the Federal government is 49,525,000.

15. Explanation for Program Changes or Adjustments

The information collection reflects changes and adjustments. The collection has been revised to include new requirements applicable to medical gas containers and closures resulting from rulemaking (0910-AC53). Also, we have reorganized and consolidated previously itemized recordkeeping burdens found in the tables of our 60- and 30-day Federal Register notices as they will appear at www.reginfo.gov. We believe this will better assist the reader in understanding fluctuations to the information collection. In doing so, we discovered and made corrections to nominal calculation errors that appeared in our notices and we regret this oversight. Cumulatively, these changes and adjustments have resulted in an increase to the collection of 319,491 annual responses and 169,605 burden hours.

16. Plans for Tabulation and Publication and Project Time Schedule

We have no such plans for the information collection.

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 exceptions to the certification.