UNITED STATES FOOD & DRUG ADMINISTRATION

Current Good Manufacturing Practice (CGMP):
Manufacturing, Processing, Packing, and Holding of Drugs; GMP for Finished Pharmaceuticals
(Including Medical Gases and Active Pharmaceutical Ingredients)

OMB Control No. 0910-0139

SUPPORTING STATEMENT – Part A: Justification:

1. Circumstances Making the Collection of Information Necessary

Section 301 of the Federal Food, Drug, and Cosmetic Act (FD&C Act; 21 U.S.C. 331) prohibits the introduction into interstate commerce any drug that is adulterated. This information collection supports Food and Drug Administration ("FDA, the agency, us or we") regulations that govern the manufacture, processing, packing, or holding of finished pharmaceuticals, including medical gases and active pharmaceutical ingredients (APIs). Under section 501(a)(2)(B) of 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 CGMP regulations. FDA is responsible for enforcing the FD&C Act as well as related statutes, including the Public Health Service Act, which governs regulation of biological products. 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.

Pharmaceutical or drug quality-related requirements appear in several parts of agency regulations. Regulations in 21 CFR part 210 set forth general GMP requirements applicable to drugs subject to 21 CFR parts 211, 225, 226; biological products for human use subject to 21 CFR parts 600 through 680; and human cell and tissue-based products subject to 21 CFR 1271. Regulations in 21 CFR part 211 set forth the minimum GMP for preparation of drug products, including medical gases and APIs and apply to drug products for administration to humans or animals; biological products for human use covered in parts 21 CFR parts 600-680; and human cells and tissue-based products covered in 21 CFR part 1271. The regulations enable a common understanding of the regulatory process by describing requirements that drug manufacturers, applicants, and FDA must follow, including recordkeeping subject to FDA inspection.

Under 21 CFR part 211 (see 21 CFR 211.94(e)(1)), specific requirements for medical gas containers and closures apply. Because a number of injuries and deaths resulted from medical gases not being produced or handled properly, we established the applicable regulations (0910-AC53). To assist respondents with these provisions we also developed the draft guidance document, "*Current Good Manufacturing Practice for Medical Gases*" (June 2017). The guidance is being issued consistent with our Good Guidance Practice regulations in 21 CFR 10.115, which provide for public comment at any time. While we intend to finalize the guidance, we believe that guidance regarding regulations applicable to medical gases is useful to respondents to the information collection.

We therefore request extension of OMB approval for the information collection provisions in 21 CFR parts 210 and 211, along with the associated guidance discussed in this supporting statement.

2. Purpose and Use of the Information Collection

Section 704 of the FD&C Act (21 U.S.C. 374) provides for inspections by FDA to ensure compliance with statutory and regulatory requirements. 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

Although the regulations do not prescribe specific recordkeeping methods, we believe all respondents will use electronic means to fulfill the information collection requirements. We strive to increase the utility of agency operating systems and databases to improve all aspects of information collection activities as our resources permit. On our website we discuss data submission standards and therefore recommend respondents adopt recordkeeping practices in light of related data submissions that may be contemplated.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection.

5. Impact on Small Businesses or Other Small Entities

The information collection poses no undue burden on small entities. To help small businesses comply with agency regulations we provide assistance and resources through agency staff and information available from 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 the Federal Register of March 3, 2021 (86 FR 12466), we published a 60-day notice soliciting comment on the proposed collection of information. One comment was received requesting clarification on FDA's basis in calculating its burden estimate. In response to the comment we discussed in our 30-day notice of June 10, 2021 (86 FR 30960), the information upon which we

relied. At the same time, the comment offered no formula or method upon which alternative figures might be derived. We informed all readers that details regarding all approved information collections currently in use by FDA, were available at https://www.reginfo.gov/public/. We also explained that, with regard to this information collection specifically, our estimate of burden as defined in 44 U.S.C. 3502(2), is based on our experience with routine inspections, informal communications with industry, and our experience with the collection. Finally, we also communicated that, as noted in our 60-day notice, we adjusted our figures to account for burden that API and finished dosage manufacturers may incur acknowledging that the applicable recordkeeping requirements are discussed in associated agency guidance[1] and apply to these respondents.

9. Explanation of Any Payment or Gift to Respondents

There are no incentives, payments, or gifts associated with this information collection.

10. Assurance of Confidentiality Provided to Respondents

In preparing this supporting statement, we consulted with our Privacy Office to ensure appropriate identification and handing of information collected. This ICR does not collect personally identifiable information (PII) or information of a personal nature. We further determined that the information collection is not subject to the Privacy Act of 1974 and the particular notice and other requirements of the Privacy Act do not apply. FDA (including vendors or service providers acting on behalf of FDA) does not use name or any other personal identifier to retrieve records from the information collected.

Under the Freedom of Information Act (FOIA) (5 U.S.C. 552), the public has broad access to certain information, but FOIA also provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1-9)). FDA will make the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy, the property rights of persons in trade and confidential commercial or financial information. At the same time, certain data and information collected during an inspection of drug manufacturing establishments for the purpose of enforcing compliance with CGMP regulations are considered confidential and not releasable to the public, nor information collection subject to review and approval under the PRA as it pertains to information collection during the course of administrative actions by the agency. 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

The collection of information does not involve questions of a sensitive.

[1] See the guidance document, "*Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients; Guidance for Industry*" (September 2016). While we do not believe the guidance includes information collection beyond that already required by the regulations, we have adjusted our estimate to include this set of respondents.

12. Estimates of Annualized Burden

12a. Estimated Annualized Hour Burden

Table 1.--Estimated Annual Recordkeeping Burden--APIs, Finished Pharmaceuticals, and Medical Gases[1,2]

Section 501(a)(2)(B) of the FD&C Act; Parts 210 and 211	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
CGMP API Manufacturers	1,260	256	322,560	0.82 (49.2 minutes)	264,499
CGMP Finished Pharmaceuticals Manufacturers (excludes medical gases)	3,270	299	977,730	0.64 (38 minutes)	625,747
CGMP Medical Gases Manufacturers	2,284	280	639,520	0.62 (37 minutes)	396,502
Total			1,939,810		1,286,748

[1] There are no capital or operating and maintenance costs associated with the information collection.
[2] Records and burden per activity have been averaged and rounded.

As noted previously, our figures are based on our experience with the information collection along with agency data and reflect burden we attribute to the applicable recordkeeping requirements and to those respondents we believe may incur such burden. These activities include, among others, establishing and maintaining standard operating procedures; the need to consult outside experts; recommendations pertaining to documenting equipment cleaning and maintenance; and requirements and recommendations pertaining to master production records, control records, and distribution records.

12b. Annualized Cost Burden Estimate

We calculated annualized cost burden by multiplying the total number of annualized hours by an hourly wage rate $85 applicable to a Pharmaceutical Industry employee, for a total of $111,886,690.

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

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

14. Annualized Cost to the Federal Government

We allocate approximately 375 full-time-employees (FTEs) annually to ensuring compliance with the statutory and regulatory requirements. Using 2018 Office of Personnel Management and U.S. Bureau of Labor Statistics data and assuming a fully loaded annual salary of $175,000, we calculate an annual cost to the Federal government of $65,625,000.

15. Explanation for Program Changes or Adjustments

We have made adjustments to the information collection. We retitled the collection to better align with agency regulations its intended to support. Also, to demonstrate products comply with applicable requirements, API manufacturers must maintain CGMP records and therefore we have included them in our accounting of respondents to the information collection. We have also reorganized the IC elements by subset of applicable recordkeeping, rather than by regulatory provision. These adjustments apply as follows:

- a decrease of 29,073 hours and 1,762 records annually for CGMP for finished pharmaceutical manufacturers, excluding those manufacturers of medical gases;
- a decrease of 486 hours and 1,574 records annually for medical gas manufacturers; and
- our inclusion of API manufacturers in this collection represents an addition of 264,499 hours and 322,560 records prepared.

The result is an overall increase of 319,224 responses and 234,940 hours annually to the information collection.

16. Plans for Tabulation and Publication and Project Time Schedule

This information collected will not be published or tabulated.

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

The OMB expiration date will be displayed as required.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.