

UNITED STATES FOOD & DRUG ADMINISTRATION

Current Good Manufacturing Practice, Certification, Postmarketing Safety Reporting, and Labeling Requirements for Certain Medical Gases

OMB Control No. 0910-0906 - NEW

RIN 0910-AH96 – Final Rule

SUPPORTING STATEMENT

**Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection request supports implementation of agency rulemaking **0910-AH96** entitled, “*Current Good Manufacturing Practice, Certification, Postmarketing Safety Reporting, and Labeling Requirements for Certain Medical Gases.*” The Food and Drug Administration (FDA, the Agency, or we) is establishing current good manufacturing practice (CGMP) regulations for certain medical gases to reflect differences in how these medical gases are manufactured, processed, packed, and held for both human and animal use compared to other drugs. The final rule also establishes new requirements for medical gas products with regard to labeling, safety reporting, and certification of designated medical gases (DMGs) for both human and animal use. Specifically, the rule introduces **21 CFR part 213** (CGMP for Medical Gases) and **21 CFR part 230** (Certification and Postmarketing Reporting for Designated Medical Gases). The rule also revises associated regulations found in 21 CFR part 210 (CGMP in Manufacturing, Processing, Packing, or Holding of Drugs; General) and 21 CFR part 211 (CGMP for Finished Pharmaceuticals) and makes conforming changes to regulations in 21 CFR parts 4, 16, 201, 314, and 514. The provisions include reporting, recordkeeping, and disclosure requirements.

The information collection also includes the following forms:

**Form FDA 3864**, *Request for Certification of Designated Medical Gas*, and **Form FDA 5025**, *Annual Report for Designated Medical Gas*.

We are therefore requesting approval for the information collection requirements of the final rule, as discussed in this supporting statement.

2. Purpose and Use of the Information Collection

Respondents to this information collection are entities that manufacture, process, pack, label, or distribute certain medical gases. Respondents also include those submitting certifications to FDA in accordance with certification requirements in 21 CFR part 230. We use the information collected to help determine compliance with regulatory provisions.

Our review also serves to establish accountability relating to the manufacturing and processing of medical gases, facilitating productive inspections, and enabling manufacturers to improve the quality of medical gases made available to consumers. In addition, the information collection facilitates product recall activities in the event a product recall becomes necessary.

Firms must make their records readily available for authorized inspection. FDA is authorized to inspect records under sections 301(f) and 704 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 331(f) and 374).

Moreover, current labeling regulations are part of FDA's strategic initiative to manage the risks of medical product use and to reduce adverse events involving products that the Agency regulates. These labeling requirements are intended to make it easier for healthcare practitioners to access, read, and use information in prescription drug labeling.

We believe that compliance with the regulations will reduce the number of adverse reactions resulting from medication errors due to misunderstood or incorrectly applied drug information.

### 3. Use of Improved Information Technology and Burden Reduction

Although the regulations do not prescribe specific automated recordkeeping methods, we believe all respondents will use electronic means to fulfill the information collection requirements. To comply with the requirements in 21 CFR part 230, applicants submit certification requests either in an appropriate electronic format through the NextGen portal or by submitting two paper copies of a signed, completed certification request form (**Form FDA 3864**) to our Center for Drug Evaluation and Research's (CDER's) Central Document Room, 5901B Ammendale Road, Beltsville, MD 20705.

### 4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information. We are establishing the information collection to support new regulatory requirements.

### 5. Impact on Small Businesses or Other Small Entities

The information collection poses no undue burden on small entities. At the same time, we assist small businesses by providing resources on our website at <https://www.fda.gov/industry/small-business-assistance> or for human drug products by contacting our staff in the CDER or for animal drug products by contacting the Center for Veterinary Medicine (CVM) at [AskCVM@fda.hhs.gov](mailto:AskCVM@fda.hhs.gov). Additionally, consistent with our analysis of impacts, we believe the regulations are better tailored for medical gases and may create small net cost savings for small entities.

### 6. Consequences of Collecting the Information Less Frequently

The information collection schedule is consistent with statutory and regulatory authorities.

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

No special circumstances are associated with this collection of information.

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

In accordance with section 3506(c)(2)(B) of the Paperwork Reduction Act of 1995 (PRA), FDA published a proposed rule in the Federal Register of May 23, 2022, and requested public comments on the proposed information collection. Comments received are discussed in the preamble to the final rule along with a Final Regulatory Impact Analysis (FRIA).

9. Explanation of Any Payment or Gift to Respondents

No remuneration is provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

*The Privacy Act of 1974*

In preparing this supporting statement, we consulted with our Privacy Office to ensure appropriate handling of information received:

Information collection associated with 21 CFR part 213 may include personally identifiable information (PII) consisting of work-related contact information and information in a resumé that is necessary when hiring qualified applicants, such as the applicant's name, home address, and employment qualifications. Collected information is stored at the vendor facility (compliant with the recordkeeping requirements) and is not sent to FDA. This information collection is not subject to the Privacy Act. Neither FDA nor the maintaining vendors use name or other PII to retrieve records from the stored collection.

Information collection associated with 21 CFR part 230 includes the following forms:

- **Form FDA 5025** – *Annual Report for Designated Medical Gas* required by 21 CFR 230.80 will collect PII consisting of: (1) name and the following work/professional context contact information about applicants (e.g., the legal person or individual or point of contact at a reporting entity): mailing address, telephone number, email address, fax number, title, and signature, and (2) name, title, signature and telephone number for a representative (if any) of the applicant.
- **Form FDA 3864** – *Request for Certification of Designated Medical Gas* established in 21 CFR 230.50 will collect PII consisting of: (1) name and the following work/professional context contact information about applicants: mailing address, telephone number, email address, fax number, title, and signature, and (2) name, title, signature and telephone number for a representative (if any) of the applicant.

Adverse event reporting will occur through FDA’s Electronic Submissions Gateway to the MedWatch Reporting Portal, currently approved in OMB control no. 0910-0291 for paper-based and electronic reporting. We continue to collect information required for the submission of adverse event reports (AERs) related to the use of a DMG in animals and information required for individual case safety reports (ICSRs) related to the use of a DMG in humans.

We have determined that none of the collections discussed in this section are subject to the Privacy Act of 1974, and the particular notice and other requirements of the Privacy Act do not apply. Specifically, FDA (including vendors or service providers acting on behalf of FDA) does not use names or any other personal identifiers to retrieve records from the information collected.

#### *The Freedom of Information Act (FOIA)*

Under FOIA (5 U.S.C. 552), the public has broad access to government documents. However, FOIA provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1) to (b)(9)). We will make the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy and the property rights of persons in trade and confidential, commercial, or financial information.

Certain data and information collected during an inspection of a drug manufacturing establishment to enforce compliance with the CGMP regulations are considered confidential and not releasable to the public. Confidentiality is maintained for trade secrets or maintained for 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 for the confidentiality of information contained in new drug applications (NDAs) and abbreviated new drug applications (ANDAs).

Confidentiality of the information submitted under these regulations is protected under 21 CFR 314.430, 21 CFR part 601, and 21 CFR part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under section 301(j) of the FD&C Act (21 U.S.C. 331(j)).

#### 11. Justification for Sensitive Questions

The information collection does not involve sensitive questions.

#### 12. Estimates of Annualized Burden Hours and Cost

##### *12a. Annualized Hour Burden Estimate*

The final rule introduces changes to FDA’s currently approved information collection inventory as follows:

**Product Jurisdiction and Combination Products (Final Rule 89 FR @ 51759)** – Agency regulations in 21 CFR parts 3 and 4 govern *Product Jurisdiction* and *Regulation of Combination Products*, respectively. Applicable information collections are approved in OMB control no.

0910-0523. While we believe the regulations impose no recurring burden, corresponding changes will revise the scope of the information collection to include the new requirements in 21 CFR part 4 regarding medical gases are marketed as part of a combination product.

**Labeling Requirements for Human Prescription Drug and Biological Products (Final Rule 89 FR @ 51760)** – Regulations in part 201 govern the statement of ingredients and declaration of net quantity of contents with regard to prescription drug product labeling. Applicable information collections are approved in OMB control no. 0910-0572. Covered firms must identify bulk or transport containers with the name of the product contained therein and that containers be accompanied by documentation that identifies the product as meeting applicable compendial standards. We estimate that 1,696 firms will label 4,000 containers, and assume 6 minutes (0.1 hours) is necessary to identify the containers with the name of the product and place documentation that identifies the product as meeting applicable compendial standards. Upon implementation of the final rule, we intend to revise the information collection to account for ongoing implementation of the new requirements as reflected below.

Estimated Annual Third-Party Disclosure Burden –  
Medical Gas Labeling (Table 2 from FINAL RULE)<sup>1</sup>

Activity; 21 CFR Section	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure (hours)	Total Hours
Labeling of bulk or transport containers used to hold designated medical gases; § 201.161(b).	1,696	2.36	4,000	0.1 (6 minutes)	400
Identify the owner of a designated medical gas container or a container of a medically appropriate combination of designated medical gases on the container label. If the container owner is not the manufacturer, packer, or distributor of the gas, identify that information on the label; § 201.328(d).	1,696	2.36	4,000	0.1 (6 minutes)	400
<b>TOTAL</b>			<b>8,000</b>		<b>800</b>

**Current Good Manufacturing Practice for Medical Gases; OMB Control No. 0910-0906 (89 FR @ 51760)**

Regulations in 21 CFR part 213 establish good manufacturing practice requirements applicable to medical gases, including recordkeeping requirements that provide for the preparation and retention of records, including the reporting of information to FDA or disclosures of information to the public. We estimate both one-time and recurring burden attributable to the new information collection provisions, as reflected below.

Estimated Annual Recordkeeping Burden –  
CGMP for Medical Gases (Tables 3 and 4 from FINAL RULE)

21 CFR part 213; Recordkeeping Requirement	No. of Recordkeepers	No. of Records per Recordkeep er	Total Annual Records	Average Burden per Recordkeepin g (hours)	Total Hours
One-time start-up SOPs	1,696	4	6,784	13	88,192
<u>Subparts A through I</u> - General provisions; Organization & personnel; Buildings & facilities; Product controls; Production & process controls; Packaging & labeling controls; Holding & distribution; Laboratory controls.	1,696	533.93	905,559	~0.24 (14 mins.)	221,158
<u>Subpart J</u> - Records; general requirements, specific records, & complaint files.	1,696	116.75	198,023	~ 0.78 (47 mins.)	154,802
<u>Subpart K</u> - Returned and salvaged medical gases.	1,696	1	1,696	0.65 (39 mins.)	1,102
<b>TOTAL</b>			<b>0</b>		<b>000</b>

**Certification and Postmarketing Reporting for Designated Medical Gases; OMB Control No. 0910-0906 (89 FR @ 51762)**

Regulations in 21 CFR part 230 establish general requirements applicable to designated medical gases, and set forth procedures for requesting medical gas certification, using **Form FDA 3864**, and prescribe annual reporting utilizing **Form FDA 5025**. The regulations also provide for requesting waivers from the electronic submission requirements. We estimate burden attributable to the new information collection provisions, as reflected below, including the requirement to prepare, retain, and submit information to FDA, and disclose information to the public.

Estimated Annual Recordkeeping Burden –  
Certification & Postmarket Reporting (Tables 5 and 6 from FINAL RULE)<sup>1</sup>

21 CFR part 230; Information Collection Activity	No. of Responden ts	No. of Responses per Responden t	Total Annual Response s	Average Burden per Response (hours)	Total Hours
230.50; certification submission requirements (Form FDA 3864)	5	1	5	3	15
230.70; supplements to certification	4	1	4	3	12
230.72; changes in ownership	2	2	4	2	8
230.80; annual reports (Form FDA 5025)	57	2.15	123	2	246
230.205; field alert reports	1,380	0.002	3	8	24
230.220; ICSR requirements (human designated medical gas)	1,430	1	858	20	11,664
230.230 adverse events (animal designated medical gas)	1,696	< 1	8	4	32
230.230; waivers from electronic submission requirement	1,696	< 1	16	5	80
<b>TOTAL</b>			<b>0</b>		<b>0</b>

*12b. Annualized Cost Burden Estimate*

Affected entities will incur costs with implementation of the final rule. Sections II.F.1, 2, 3, 4, and 5 of the FRIA discuss costs to industry for full compliance with the rule.

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

Capital costs of the rule include costs of relabeling, as discussed in Section F of the FRIA.

14. Annualized Cost to the Federal Government

We currently estimate the annual cost to the Federal government to be \$20,522.88, reflecting 144 hours multiplied by a fully-loaded wage rate of \$142.52, to develop **Forms FDA 3864** and **5025**.

15. Explanation for Program Changes or Adjustments

This is a new information collection request. The rulemaking introduces new information collections totaling 1,121,083 responses and 478,135 hours annually, a slightly upward adjustment from estimates included in our proposed rule, based on the most current analysis of impact data. We expect most of the burden to remain in OMB control no. 0910-0906, established to support this rulemaking and regulatory requirements in 21 CFR new parts 213 and 230; while we expect recurring burden attributable to the labeling of medical gases to be included in OMB control no. 0910-0572. The rule provides for an 18 month compliance period.

16. Plans for Tabulation and Publication and Project Time Schedule

We have no plans to publish or tabulate data collected from this 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 of this information collection.