Medical Gas Containers and Closures;
Current Good Manufacturing Practice Requirements

SUPPORTING STATEMENT Part A
OMB Control No. 0910-NEW
RIN 0910-AC53

Terms of Clearance: None

A. Justification

1. Circumstances Making the Collection of Information Necessary

This information collection supports rulemaking by the Food and Drug Administration (FDA or we). The chief impetus for this rulemaking was a number of incidents in which a medical gas container holding a gas other than oxygen was erroneously connected to a health care facility's oxygen supply system, leading to serious injuries and deaths. There have also been reports of serious injuries attributable to contamination of high-pressure medical gas cylinders with residue of industrial cleaning solvents, likely as a result of inadequate cleaning during conversion of the cylinder from industrial to medical use. Accordingly, FDA proposed certain regulatory requirements intended to (1) reduce the likelihood of the wrong gas being attached to a gas supply system or container (and in particular to reduce the likelihood of a gas other than oxygen being connected to an oxygen supply system), (2) make the contents of medical gas containers more easily and accurately identifiable, and (3) reduce the risk of contamination of medical gases. Additionally, FDA proposed including medical air, oxygen, and nitrogen among, and excluding cyclopropane and ethylene from, those gases intended for drug use that are conditionally exempt from certain labeling requirements as described in 21 CFR 201.161. Accordingly, therefore, we are requesting OMB approval of the information collection provisions at 21 CFR Parts 201 and 211 as described below.

2. Purpose and Use of the Information Collection

These requirements are intended to increase the likelihood that the contents of medical gas containers are accurately identified and to reduce the likelihood of the wrong gas being connected to a gas supply system or container.

3. Use of Improved Information Technology and Burden Reduction

The final rule contains no restrictions on and FDA encourages the use of improved information technology to reduce the burden on third party disclosure and recordkeeping requirements.

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

Section VI of the final rule discusses the impact on small entities. The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the final rule imposes new burdens on small entities, FDA cannot certify that the final rule will not have a significant economic impact on a substantial number of small entities. The rule imposes new costs to small entities, and FDA estimates the rule's one-time costs to roughly range between 0.0001 percent to 0.13 percent of average annual revenues.

6. Consequences of Collecting the Information Less Frequently

Information collection schedule is consistent with regulatory requirements. We believe this imposes minimal burden on respondents while at the same time ensuring that medical gas containers are accurately identified and that we can effectively reduce the likelihood of the wrong gas being connected to a gas supply system or container.

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

Information collection is consistent with the requirements of section 5 CFR 1320.5.

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

On April 10, 2006 (71 FR 18039), FDA issued a proposed rule to amend our Current Good Manufacturing Practice regulations. On November 18, 2016 (81 FR 81685) finalized the rule, including a discussion at Section IV of the comments we received and our responses. None of the comments pertained to the information collection analysis. Comment 23 raised issues about the recordkeeping requirements as analyzed in section VI of the final rule, Analysis of Impacts. All comments may be found under Docket No. FDA-2005-N-0343.

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.

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 Estimates

A gas listed at 21 CFR 201.161(a) is exempt from certain labeling requirements if its labeling bears, among other things, a warning statement that conforms to § 201.161(a)(1). Section 201.161(a)(1)(i) specifies the content to be included in a warning statement for oxygen, § 201.161(a)(1)(ii) specifies the content to be included in a warning statement for medical air, and § 201.161(a)(1)(iii) specifies the content to be included in a warning statement for nitrogen, carbon dioxide, helium, nitrous oxide, and any medically appropriate combinations of any of the gases listed in § 201.161(a). FDA believes most medical gases are already labeled in a manner that complies with § 201.161(a) as finalized. Furthermore, because § 201.161(a) provides the warning statement content to be included in medical gas labeling, the inclusion of these warning statements on medical gas labeling is not considered a "collection of information" for PRA purposes. See 5 CFR 1320.3(c)(2) (providing that "the public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public is not included" within the definition of "collection of information").

Under § 201.328(a)(1), each portable cryogenic medical gas container must be conspicuously marked with a 360° wraparound label identifying its contents. The identity of the medical gas held in the container must be printed on the label in one of the following ways: using lettering that appears in the standard color designated for the gas in § 201.328(c) and that is printed against a white background, or using lettering that appears in white against a background that is painted in the standard color for the gas as designated in § 201.328(c). The lettering for the name of the gas on the label must be at least 2 inches high; the name of the gas must be printed continuously around the label and be capable of being read around the entire container; the label must be on the sidewall of the container, as close to the top of the container as possible but below the top weld seam; and, if the shoulder portion of a portable cryogenic gas container is colored, the color used must be the standard color or colors designated in § 201.328(c) for the gas or gases held within the container.

Under § 201.328(a)(2), the 360° wraparound label required in § 201.328(a)(1), or a separate label, must include in conspicuous lettering the phrase "For Medical Use", "Medical Gas," or some similar phrase. Finally, under § 211.94(e)(2), the wraparound label must be affixed to the container in a manner that does not interfere with other labeling and such that it is not susceptible to becoming worn or inadvertently detached during normal use, and the wraparound label must be reasonably resistant to fading, durable when exposed to atmospheric conditions, and not readily soluble in water.

FDA's database of establishments that manufacture medical gases includes about 2,500 such establishments. We estimate that there are approximately 35,000 portable cryogenic containers in medical gas service that are subject to the labeling requirements at § 201.328(a). As discussed in the Analysis of Impacts, FDA conservatively estimates that all manufacturers will choose to comply with § 201.328(a) by removing any existing wraparound labels from all portable cryogenic containers and replacing them with wraparound labels that meet all of the requirements at § 201.328(a). Thus, on average, each manufacturer would need to add labels (or re-label) approximately 14 containers (35,000 ÷ 2,500). FDA estimates that approximately 6 minutes would be required to remove any existing wraparound label and attach a new wraparound label to each container. Thus, the total burden third-party disclosure burden hours associated with § 201.328(a)(1) and (2) is approximately 3,500 hours (2,500 x 14 x .10 hours).

Section 201.328(a)(1)(v) also provides that a portable cryogenic cylinder may only be colored in the color or colors designated in § 201.328(c) if the gas or gases held within the container correspond to that color or those colors. Alternatively, the container may be colored in a light-reflective color such as white (or some other color which is not an FDA-designated gas color), or simply not colored at all. Based on discussions with subject matter experts, we estimate that few to no cryogenic containers will require re-coloring as a result of this requirement, and that, accordingly, there is no third-party disclosure burden associated with this requirement.

Under § 201.328(b), high-pressure medical gas cylinders must be colored on the shoulder with the colors designated in § 201.328(c) for the gas contained in the cylinder, and such colors must be visible when viewed from the top of the cylinder. Under § 211.94(e)(2), the materials used for coloring medical gas containers must be reasonably resistant to fading, durable when exposed to atmospheric conditions, and not readily soluble in water. Based on information contained in the Analysis of Impacts, we estimate that as many as 10% of the estimated 24.6 million high-pressure cylinders in medical service will require coloring or re-coloring to comply with § 201.328(b). Thus, on average, each manufacturer would need to color 984 containers (2.46 million ÷ 2,500). Based on information contained in the ERG Report, we conservatively estimate that it will take an average of 6 minutes to color a cylinder. Thus, the total third-party disclosure burden hours associated with § 201.328(b) is approximately 246,000 hours (2,500 x 984 x .10 hours).

Section 211.94(e)(1) requires that portable cryogenic medical gas containers that are not manufactured with permanent gas use outlet connections must use a locking device or other method to ensure that the gas use outlet connection on the container cannot be readily removed or replaced except by the manufacturer. The locking device or other method used would be considered part of the container closure, and manufacturers must maintain records in accordance with § 211.184 for such articles.

As discussed in the Analysis of Impacts, FDA conservatively estimates that manufacturers will need to secure the gas use outlets of as many as 1,750 portable cryogenic

containers to bring them into compliance with the final rule. Each manufacturer would have annual § 211.184 records maintenance activities incident to bringing, on average, 0.7 containers into compliance with the secure gas use outlet connection requirement (1,750 ÷ 2,500). As discussed in the proposed rule, FDA estimates record maintenance costs associated with this work to average two minutes (0.033 hours) per container. Thus, the total annual burden of § 211.184 records maintenance activities incident to bringing portable cryogenic containers into compliance with § 211.94(e)(1) of the final rule is estimated to be approximately 58 hours (2,500 x 0.7 x .033 hours).

FDA estimates the burden for the collection of information as follows:

Table 1 — Estimated One-Time Third-Party Disclosure Burden[1]

21 CFR Section	No. of Respondents	No. of Disclosures per Respondent	Total Disclosures	Average Burden per Disclosure	Total Hours
§201.328(a)(1) and (2), and §211.94(e)(2); portable cryogenic medical gas container labels and colors	2,500	14	35,000	.10	3,500
§201.328(b) and, §211.94(e)(2); high-pressure medical gas cylinder colors	2,500	984	2,460,000	.10	246,000
Total					249,500

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

Table 2 — Estimated Annual Recordkeeping Burden1

21 CFR Section	No. of Record-keepers	No. of Records per Recordkeeper	Total Records	Avg. Burden Per Recordkeeper	Total Hours
§211.184 and §211.94(e)(1); records maintenance re: secure gas use outlet connection requirement	2,500	0.7	1,750	.033	58

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

12b. Annualized Cost Burden Estimates

Section VI of the final rule, Analysis of Impacts, explains that the industry costs resulting from this rulemaking are attributed to coloring medical gas containers, complying with the 360◦ wraparound label requirement for portable cryogenic containers, and requiring gas-specific use outlet connections on portable cryogenic containers to be permanently attached to the valve body (e.g., by silver brazing) or otherwise attached to the valve body using a locking mechanism or other appropriate device so that only the manufacturer can readily remove or replace them.

Using a standard 10 year time period, the annualized costs are estimated to range between $0.18 million to $1.5 million using a 3 percent discount rate and $0.21 million to $1.8 million using a 7 percent discount rate.

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

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

14. Annualized Cost to the Federal Government

We believe the information collection imposes nominal cost to the government that will be absorbed by existing resource allocations. Under OMB Control No. 0910-0139 FDA already has information collection authority regarding CGMP-related regulatory activities, including inspections, policy, and enforcement activities.

15. Explanation for Program Changes or Adjustments

This is a new information collection.

16. Plans for Tabulation and Publication and Project Time Schedule

Information collected under this rulemaking will not be tabulated or published.

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

The agency does not seek an exemption from displaying the expiration date.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.