UNITED STATS FOOD & DRUG ADMINISTRATION

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

OMB Control No. 0910-NEW
RIN 0910-AH96

SUPPORTING STATEMENT – **Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information supports agency rulemaking 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 issuing a proposed rule to establish current good manufacturing practice (CGMP) regulations for certain medical gases. The proposed rule also establishes new requirements for medical gas products with regard to labeling, safety reporting, and certification of designated medical gases (DMGs)

We are therefore requesting approval for the information collection requirements applicable to the proposed regulatory requirements and 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. We will use the information collected to help determine compliance with regulatory requirements established to ensure that the covered products: (1) are safe and have the identity and strength and (2) meet the quality and purity characteristics, which they purport or are represented to possess.

Our review also serves to establish accountability relating to the manufacturing and processing of drug products, facilitating productive inspections, and enabling manufacturers to improve the quality of drug products 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 these 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 current regulations do not prescribe specific recordkeeping methods, FDA believes that all respondents will use electronic means to fulfill their information collection requirements.

To comply with the requirements in the proposed regulations, applicants must submit certification requests either in an appropriate electronic format or by submitting two paper copies of a signed, completed certification request form to our Center for Drug Evaluation and Research's (CDER's) Central Document Room. FDA has not identified an electronic format or submission portal by which respondents can submit certification requests, and we do not have an approved FDA form for paper submissions; however, we intend to identify an electronic format or submission type and have an approved FDA form for paper submission upon publication of the final rule.

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 and through contacting our staff in the Center for Drug Evaluation and Research (CDER). Additionally, consistent with our analysis of impacts, we believe the proposed 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 requirements.

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

As required by section 3506(c)(2)(B) of the Paperwork Reduction Act of 1995 (PRA), FDA is publishing a proposed rule, including an analysis of the proposed information, and inviting public comment.

9. Explanation of Any Payment or Gift to Respondents

We do not provide payment or gifts to respondents.

10. Assurance of Confidentiality Provided to Respondents

In preparing this supporting statement, we consulted with our Privacy Office to ensure that the information collected is appropriately identified and handled. For information collection

associated with proposed 21 CFR part 213, information collected 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.

For information collection associated with proposed 21 CFR part 230, respondents will submit information to FDA using two new forms once the draft forms have been approved by OMB: (1) Annual Report for Designated Medical Gas (21 CFR 230.80) and (2) Request for Certification of Designated Medical Gas. The Annual Report for Designated Medical Gas (21 CFR 230.80) form 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.

Similarly, the Request for Certification of Designated Medical Gas form 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.

We propose to collect information required for the submission of adverse event reports (AERs) related to the use of a designated medical gas in animals and information required for individual case safety reports (ICSRs) related to the use of a designated medical gas in humans.

AERs: FDA's Center for Veterinary Medicine

The patients for which AERs are submitted are typically animals. As such, no privacy protection applies to the information collection. Submissions regarding AERs may include the following: (1) reporter's name, (2) veterinarian's name, (3) business name, (4) telephone number, (5), email address, and (6) mailing address.

ICSRs

We will collect, by way of ICSRs, the following information for patients: the name, date of birth, email address, mailing address, telephone number, medical records number, and medical notes. We will collect work contact information for FDA personnel (permanent and contract employees). In addition, we will collect professional contact information (telephone, email, and mailing address) for the point of contact submitting the required report. Submitters may choose to include PII in the ICSR, such as personal history, names of individuals, or descriptions of actions associated with an adverse event.

The PII described above is discussed in FDA's regulations codified at 21 CFR 310.305 and 314.80, and we currently have approval under OMB control numbers 0910-0001 (Applications for FDA Approval to Market a New Drug) and 0910-0230 (Adverse Experience Reporting for Drug Products). We also have approval for paper and electronic submissions under OMB control numbers 0910-0291 (FDA Medwatch: Adverse Event and Product Experience Reporting System) and 0910-0645 (FDA Adverse Event and Products Experience Reports), respectively.

FDA has 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.

Under the Freedom of Information Act (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)). FDA 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 Federal Food, Drug, and Cosmetic 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

Labeling Requirements for Prescription Drugs; OMB Control No. 0910-0572 – Revision

Table 1 – Estimated Annual Disclosure Burden

Activity; Proposed CFR Section	No. of Respondents	No. of Disclosures per Respondent[1]	Total Annual Disclosures[1]	Average Burden per Disclosure	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
On the container label, identify the owner of a designated medical gas container or a container of a medically appropriate combination of designated medical gases. If the container owner is not the manufacturer, packer, or distributor of the gas,	1,696	2.36	4,000	0.1 (6 minutes)	400

identify that information on the label; § 201.328(d)					
Total			8,000		800

[1]Totals have been rounded to the nearest whole number.

Regulations in part 201 govern the statement of ingredients and declaration of net quantity of contents with regard to prescription drug product labeling.

The proposed revisions to the regulations would require that firms 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. Bulk or transport containers are excluded from the proposed definition of final use containers. Because these large containers are removed from the point of care and we do not expect that patients and healthcare practitioners will use them directly to administer designated medical gas, FDA does not believe that firms' bulk or transport containers need to bear the information that we would require under proposed § 201.161(a). However, to prevent mix-ups, it is essential that the identity of the gas inside such containers is evident to individuals who handle and transport the containers. FDA expects that these proposed requirements will help prevent mix-ups and ensure that recipients of medical gases in bulk or transport containers are provided information indicating that such gases meet applicable compendial standards.

Based on our experience with similar information collections, we estimate that 1,696 firms will label 4,000 containers and assume firms will expend 6 minutes (0.1 hours) to identify the containers with the name of the product and place documentation that identifies the product as meeting applicable compendial standards, totaling 400 hours annually.

Proposed § 201.328(d) would provide that the owner of a designated medical gas container or a container of a medically appropriate combination of designated medical gases may be identified on the container. This statement may appear on a separate sticker or decal on the container (that is, it need not be contiguous with other labeling on the container), but if the container owner is not the manufacturer, packer, or distributor of the gas, that information shall be clearly stated. FDA recognizes the complex distribution system for designated medical gases and medically appropriate combinations of designated medical gases and the importance of each entity in the distribution chain being clearly identified so that patients and healthcare professionals can contact the appropriate entity if necessary. We intend for this provision to help ensure that appropriate entities can be contacted about quality issues or adverse events. In addition, the proposed labeling requirement would facilitate the return of cylinders to owners who may not also be medical gas manufacturers. FDA proposes that including the container owner's information will not cause the container owner to be a "relabeler" for purposes of FDA's registration and listing requirements.

Based on our experience with similar information collections, we estimate that 1,696 firms will identify on a designated medical gas container or a container of a medically appropriate combination of designated medical gases the name of the container owner who may not also be the manufacturer, packer, or distributor of the gas. We assume firms would include this label on 4,000 containers and will expend 6 minutes (0.1 hours) to perform this activity, totaling 400 hours annually.

Table 2.--Estimated Annual Recordkeeping Burden

Activity; Proposed CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper[1]	Total Annual Records[1]	Average. Burden per Recordkeeping	Total Hours
New Start Up SOP; § 213.42	1,696	1	1,696	13	22,048
SOP Maintenance; § 213.42	1,696	1	1,696	0.65 (39 minutes)	1,102
New Start Up SOP; § 213.208	1,696	1	1,696	13	22,048
SOP Maintenance § 213.208	1,696	1	1,696	0.65 (39 minutes)	1,102
Documentation of completion of training; § 213.25(a)	1,696	10	16,960	0.083 (5 minutes)	1,408
Consultants' records of sufficient education, training, and experience, or any combination thereof; § 213.34	1,696	0.336	571	0.5 (30 minutes)	286
Firms' records of equipment maintenance and cleaning; § 213.67(c)	1,696	43.7676	74,230	0.25 (15 minutes)	18,557
Maintain records for modifications to automatic, mechanical, and electronic equipment; § 213.68(d)	1,696	6.734	11,420	0.25 (15 minutes)	2,855
Receipt and storage of incoming designated medical gases; § 213.82(a)	1,380	417	575,460	0.25 (15 minutes)	143,865
Records of rejected components; § 213.89	1,380	24.2	33,400	0.083 (5 minutes)	2,772
Maintain records for each shipment received of each different labeling and packaging material indicating receipt, examination, and whether accepted	1,696	43.7676	74,230	0.25 (15 minutes)	18,558

or rejected; § 213.122(c)					
Document results of inspections in the batch production records; § 213.130(e)	1,696	67.334	114,200	0.25 (15 minutes)	28,550
Maintain written records so that data therein can be used for evaluating, at least annually, the quality standards of each medical gas to determine the need for changes in specifications or manufacturing or control procedures; § 213.180(d)	1,696	0.27	457	0.25 (15 minutes)	114
Maintain record of equipment cleaning and use log maintenance; § 213.182	1,696	1.76	2,969	0.16 (10 minutes)	475
Maintain records for components, medical gas containers and closures, and labeling; § 213.184	1,696	2.626	4,454	0.33 (19.8 minutes)	1,470
Maintain master production and control records; § 213.186	1,696	13.467	22,840	2	45,680
Maintain batch production and control records; § 213.189	1,696	21.883	37,115	1.3 (78 minutes)	48,250
Maintain record of the investigation; § 213.192(a)	1,696	2.69	4,568	1	4,568
Maintain laboratory records; § 213.194(b) through (e))	1,696	33.667	57,100	0.5 (30 minutes)	28,550
Maintain distribution records; § 213.196	1,696	33.667	57,100	0.25 (15 minutes)	14,275
Maintain written records of each complaint; §	1,696	6.733	11,420	1	11,420

213.198(b)					
Total			1,105,278		417,953

[1] Totals have been rounded to the nearest whole number.

FDA proposes to establish part 213 setting forth CGMP requirements applicable to medical gases. If finalized, part 213 would apply to entities that manufacture a medical gas and would also establish requirements applicable to firms that subsequently combine, commingle, refill, or distribute medical gases.

The proposed regulations include recordkeeping requirements pertaining to personnel qualifications and responsibilities of persons who are engaged in the manufacturing, processing, packing, or holding of a medical gas.

Provisions under proposed § 213.42(c) include recordkeeping to document the development and implementation of written procedures to ensure that firms maintain a clean condition for any building used to manufacture, process, pack, or hold a medical gas so as to ensure the safety, identity, strength, quality, and purity of the gas. Firms would need to develop written procedures that apply to maintaining and cleaning buildings. Based on available data, we estimate 1,696 firms will each develop and implement written procedures to maintain and clean buildings. We assume it will take 13 hours to perform this activity, totaling 22,048 hours annually. Firms would also maintain these procedures. Based on available data, we estimate 1,696 firms would each maintain written procedures to maintain and clean buildings. We assume it will take 39 minutes (0.65 hours) to perform this activity, totaling 1,102 hours annually.

Similarly, under proposed § 213.208, firms would be required to develop and implement written procedures for the holding, testing, and use of salvaged medical gases. Based on available data, we estimate 1,696 firms will develop and implement written procedures for the holding, testing, and use of salvaged medical gases. We assume it will take 13 hours for firms to perform this activity, totaling 22,048 hours annually. Based on available data, 1,696 firms will prepare written procedures (1 procedure each) for the holding, testing, and use of salvaged medical gases. We assume it takes 0.65 hours to perform this activity, totaling 1,102 hours annually.

The proposed regulations would provide that employee training be included in the firm operations. Recordkeeping would be established to demonstrate that qualified individuals conduct training on a continuing basis and with sufficient frequency to allow employees to remain familiar with applicable requirements. Based on available data, we estimate that 1,696 firms will prepare written documentation pertaining to employee training. We assume 10 employees per firm will create 16,960 records (10 records per firm) and that it will take 5 minutes (0.083 hours) to prepare the records, for a total of 1,408 hours annually.

Under proposed § 213.34, records demonstrating that consultants have sufficient education, training, and experience, or any combination thereof, to advise on the subject for which they are retained will be required. Based on available data, we estimate that 1,696 firms will maintain 571 records of consultants' education, training, and experience, or any combination thereof and assume it will take 30 minutes (0.5 hours) to perform this activity, totaling 286 hours annually.

Based on available data, we estimate that 1,696 firms will maintain 74,230 records of equipment maintenance and cleaning and assume it will take 15 minutes (.25 hours) to perform this activity, totaling 18,557 hours annually.

Based on available data, we estimate 1,696 firms will develop and implement 11,420 written procedures for automatic, mechanical, and electronic equipment and assume firms will expend 15 minutes (0.25 hours) to perform this activity, totaling 2,855 hours annually.

As provided for in the proposed regulations, if an incoming designated medical gas is obtained from a supplier other than the original manufacturer, the shipment would also need to include specific information. To ensure the reliability of appropriate assessment and testing, firms will be required to establish and maintain a program to ensure the reliability of the supplier's capabilities through appropriate assessment and testing procedures. Based on assumptions found in our Preliminary Regulatory Impact Analysis (PRIA), we estimate that 1,380 firms would verify and document records upon receipt of a designated medical gas. We assume firms will maintain 575,460 records (417 records each (1 delivery per week of oxygen for 1 year (52 deliveries) plus 1 delivery per night of nitrogen for 1 year (365 deliveries)). We further assume firms will expend 15 minutes (0.25 hours) each (104 hours in total for each firm) to perform this activity, totaling approximately 143,865 hours annually.

Proposed § 213.89 would require that firms identify and control rejected components, containers, and closures under a quarantine system designed to prevent their use in operations for which they are unsuitable. Proposed § 213.89 also applies to incoming designated medical gases. Quarantine systems would not need to include physical quarantining because other methods can adequately ensure that unsuitable products are not used. Based on assumptions found in section II.F.4.b of the PRIA, we estimate that 1,380 downstream firms would need to assess and document 33.4 million medical gas components, containers, and closures annually. We assume that firms would reject 0 to 0.1 percent of all containers. These firms will maintain a total of 33,400 records of rejected components and we assume will expend 5 minutes (0.083 hours) to perform this activity, totaling 2,772 hours annually.

Under proposed § 213.122(c), firms would need to maintain records for each shipment received of each different labeling and packaging material indicating receipt, examination, and whether accepted or rejected. Based on available data, we estimate 1,696 firms will prepare 74,230 records to document each shipment received of each different labeling and packaging material indicating receipt, examination, and whether accepted or rejected. We assume it will take 15 minutes (0.25 hours) to perform this activity, totaling 18,558 hours annually.

Under proposed 213.130(e), firms would need to document results of inspections concerning packaging and labeling in the batch production records. Based on available data, we estimate 1,696 firms will document results of inspections in the batch production records in approximately 114,200 records. We assume it will take 15 minutes (0.25 hours) per record to perform this activity, totaling 28,550 hours annually.

As described in section V.B.11 in the preamble of the proposed rule and under proposed § 213.180(d), firms would need to maintain written records so that data therein can be used for evaluating, at least annually, the quality standards of each medical gas to determine the need for changes in specifications or manufacturing or control procedures. Based on available data, we estimate 1,696 firms will prepare 457 records. We assume it will take 15 minutes (0.25 hours) to perform this activity, totaling 114 hours annually.

Under proposed § 213.182 and as described in section V.B.11 in the preamble of the proposed rule, firms would need to maintain a written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use. Based on available data, we

estimate 1,696 firms will prepare 2,969 records documenting major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use. We assume it will take 10 minutes (0.16 hours) to perform this activity, totaling 475 hours annually.

As described in section V.B.11 in the preamble of the proposed rule and under proposed § 213.184, firms would need to maintain certain records concerning components, medical gas containers and closures, and labeling. Based on assumptions found in our PRIA, we estimate 1,696 firms will prepare 4,454 records for components, medical gas containers and closures, and labeling. We assume firms will expend 19.8 minutes (0.33 hours) to perform this activity, totaling 1,470 hours annually.

As discussed in section V.B.11 in the preamble of the proposed rule and based on estimates for the number of firms calculated throughout the PRIA, under proposed § 213.186, to ensure uniformity from batch to batch, firms would need to prepare, date, and sign master production and control records for each medical gas. Based on data from existing information collection requests and estimates for the number of firms calculated throughout the PRIA, we estimate 1,696 firms will prepare and maintain approximately 22,840 master production and control records and assume it will require 2 hours for firms to perform this activity, totaling 45,680 hours annually.

Under proposed § 213.189 and as described in section V.B.11 in the preamble of the proposed rule, firms would need to maintain batch production and control records. These records would need to include documentation that the firm has accomplished each significant step in the manufacturing, processing, packing, or holding of the medical gas produced. Based on data from existing information collection requests and estimates for the number of firms calculated throughout the PRIA, we estimate 1,696 firms will prepare and maintain 37,115 batch production and control records. We assume it will require 78 minutes (1.3 hours) for firms to perform this activity, totaling 48,250 hours annually.

Section V.B.11 in the preamble of the proposed rule and proposed § 213.192(a) describe production record review. Per paragraph (a), firms would need to maintain a written record of the investigation and include the conclusions and followup. Based on data from existing information collection requests and estimates for the number of firms calculated throughout the PRIA, we estimate 1,696 firms will prepare and maintain 4,568 laboratory records and that it will require 1 hour for firms to perform this activity, totaling 4,568 hours annually.

Under proposed § 213.194(b) through (e) and as described in section V.B.11 in the preamble of the proposed rule, firms would need to maintain certain laboratory records. Based on available data, we estimate 1,696 firms will prepare and maintain 57,100 laboratory records and assume it will require 30 minutes (0.5 hours) for firms to perform this activity, totaling 28,550 hours annually.

As described in section V.B.11 in the preamble of the proposed rule, proposed § 213.196 describes certain proposed requirements for distribution records. Based on available data, we estimate 1,696 firms will prepare and maintain 57,100 distribution records and assume it will require 15 minutes (0.25 hours) for firms to perform this activity, totaling 14,275 hours annually.

Under proposed § 213.198(b), firms would be required to maintain written records of each complaint regarding medical gases. Our full discussion is shown in section V.B.11 in the preamble of the proposed rule. Based on assumptions found in our PRIA, we estimate 1,696 firms will maintain 11,420 records of complaints. We assume it will require approximately 1 hour for firms to perform this activity, totaling 11,420 hours annually.

Certification Process and Postmarketing Quality and Safety Reporting; OMB Control No. 0910-NEW

Table 3.--Estimated Annual Reporting Burden

Activity; Proposed CFR Section	No. of Respondents	No. of Responses per Respondent[1]	Total Annual Responses[1]	Average Burden per Response (in hours)	Total Hours
Submission of certification requests and certification form that includes any resubmissions and amendments to pending requests; § 230.50	5	1	5	3	15
Submission of supplements to certification requests and other changes; § 230.70	4	1	4	3	12
Submission of requests to transfer ownership of certification, including new address and the owner's submission of any change in the conditions in the granted certification; § 230.72	2	2	4	2	8
Annual reports; § 230.80	50	2.16	108	2	216
Field alert reports; § 230.205	1,380	0.002	3	8	24
CDER: Submission of ICSRs (§ 230.220(a) through (d))	1,430	0.12	172	6	1,032
CDER's maintenance of records for human designated medical gas ICSR requirements (§ 230.220(e))	1,430	0.48	686	16	10,976
CVM's recordkeeping requirements related to adverse event reports (§ 230.230(c))	1,696	0.0044	7.5	5	37.5
CVM: Submission of adverse event reports; § 230.230	1,696	0.0044	7.5	5	37.5
CVM: Waiver request from electronic submission requirement; § 230.230	1,696	0.0044	7.5	5	37.5
Total			1,004.5		12,395.5

[1] Totals have been rounded to the nearest whole number.

Proposed § 230.50 (see section V.C.2 in the preamble of the proposed rule) would establish the general requirements for requesting a designated medical gas certification for all submission types and would outline the information that must be included in certification request submissions.

The proposed regulations would require applicants to include facility information in certification requests. Such information would include, among others, name and address of the original manufacturing facility or facilities where the gas is or will be manufactured.

Proposed section 230.50 would also provide for the submission of additional information if FDA deems it appropriate to determine whether a medical gas meets the definition of a designated medical gas. This information would generally be in the form of a written request by FDA for the additional information.

Based on assumptions found in our PRIA, we estimate that five respondents will submit a total of five certification requests annually, including certification forms for original and resubmissions. We assume each certification request will require 3 hours to prepare and submit, totaling 15 hours annually.

Under proposed § 230.65, applicants would be allowed to withdraw a certification request that has not been deemed granted. An applicant could notify FDA that it withdraws its certification request at any time before the certification is deemed granted. Upon an applicant's withdrawal of a certification request, FDA would retain the certification request, and if the applicant requests a copy via a FOIA request, FDA would provide it pursuant to the fee schedule in FDA's public information regulations. Since the passage of FDASIA, FDA has received several certification requests but has not received any withdrawal requests. FDA has no other data on which to provide a burden estimate. Therefore, the Agency does not expect to receive withdrawal requests except in exceedingly rare situations.

Proposed § 230.70, as discussed in section V.C.3 in the preamble of the proposed rule would require applicants to submit a supplement if any information in the granted certification has changed. The proposed regulation would prescribe information to be included in a supplement submission.

Based on our experience with similar information collections, we estimate four applicants will submit supplements and assume each submission will require 3 hours to prepare, totaling 12 hours annually.

Proposed § 230.72 would govern changes in ownership of a granted certification. An example of when a change in ownership could occur is during a merger or acquisition. Upon a change in ownership, the regulations would require that both the new and previous owner notify FDA.

Based on related submissions received by FDA over the last few years and averaged, we estimate two respondents will submit four letters or other supporting documents, and assume it will take 2 hours to complete this task, totaling 8 hours annually.

To assist respondents with the proposed submission requirements associated with proposed § 230.80 (annual reports), we are developing an annual report form.

Based on our records and informal requests received upon announcing this rulemaking, we estimate that 50 applicants will submit to FDA 108 annual reports (a total of 108 reports). We assume firms will expend 2 hours to perform this activity, totaling 216 hours annually.

Our estimate associated with proposed requirements in § 230.205 for field alert reporting for designated medical gases is based on our experience with similar reports that FDA received in 2019 and 2020.

We estimate that 1,380 applicants and nonapplicants will submit to FDA three FARs. We assume respondents will expend approximately 8 hours to perform this activity, totaling 24 hours annually.

Proposed § 230.210 would require that applicants and nonapplicants promptly review all safety information that the applicant or nonapplicant receives or otherwise obtains from any source (including both foreign and domestic sources). Applicants and nonapplicants would generate reports from their review and submit them under proposed §§ 230.220 and 230.230.

As described under proposed § 230.220(a) through (d) (see section V.D.4 in the preamble of the proposed rule), firms would be required to submit ICSRs associated with the use of a designated medical gas in humans.

Proposed § 230.220 (see section V.D.4 in the preamble of the proposed rule) would contain requirements for the submission of ICSRs associated with the use of a designated medical gas in humans. Under proposed § 230.220(a)(1), applicants and nonapplicants would be required to submit each ICSR as soon as possible, but no later than 15 calendar days from the date the applicant or nonapplicant has met the reporting criteria under proposed § 230.220(b) and acquired a minimum data set for an ICSR for that adverse event.

Under proposed § 230.220(a)(3), applicants and nonapplicants would submit new information they receive or otherwise obtain about a previously submitted ICSR to FDA. The proposed regulation would prescribe reporting schedules to ensure FDA becomes aware of any new information that arises about the adverse event.

Based on assumptions found in our PRIA and a review of safety report data, we estimate that 1,430 applicants and nonapplicants will submit to FDA 172 ICSRs annually. We assume it will take 6 hours for respondents to perform this activity, totaling 1,032 hours annually.

Proposed § 230.220(b) would describe the types of ICSRs that applicants and nonapplicants would need to report for human use. Under proposed § 230.220(b)(1), applicants and nonapplicants would be required to submit ICSRs for serious adverse events. Under proposed § 230.220(b)(2), FDA proposes to require an applicant to report to FDA, in a timeframe established by FDA, ICSRs for any adverse events that would not be required under proposed § 230.220(b)(1) upon notification by FDA.

Proposed § 230.220(e) would prescribe content and format requirements for records pertaining to human designated medical gas adverse events. For a period of 10 years from the initial receipt of information, each applicant or nonapplicant would be required to maintain records of information relating to adverse events, whether or not submitted to FDA. These records would need to include raw data, correspondence, and any other information relating to evaluating and reporting adverse event information that is received or otherwise obtained by the applicant or nonapplicant. Upon written notice by FDA, the applicant or nonapplicant would need to submit any and all of these records to FDA within 5 calendar days after receipt of the notice. The applicant or nonapplicant would need to permit any authorized FDA employee, at reasonable times, to access, copy, and verify the established and maintained records described in this section.

Based on available data, we estimate that 1,430 manufacturers will create 686 records pertaining to human designated medical gas requirements and that it would take approximately 16 hours to perform this activity, totaling 10,976 hours.

Proposed § 230.220(c) and (d) would include additional requirements for the content and format of ICSRs.

Based on available data, we assume all firms (1,696) will distribute designated medical gases for human and animal use and invite comment on our assumption.

Under proposed § 230.230(a)(1), an applicant or nonapplicant would need to submit serious adverse events related to the use of a designated medical gas in animals to FDA as soon as possible but no later than 15 calendar days from first receiving the information. The applicant or

nonapplicant would need to submit the report to FDA in electronic format as described under proposed § 230.230(b)(1) of this section, unless the applicant or nonapplicant obtains a waiver under proposed § 230.230(b)(2) of this section or FDA requests the report in an alternate format.

Under proposed § 230.230(a)(2), upon notification by FDA, applicants and nonapplicants would need to submit reports of adverse events associated with the use of a DMG in animals that do not qualify for reporting under proposed § 230.230(a)(1) of this section. The notice would specify the adverse events to be reported and the reason for requiring the reports.

We estimate approximately 7.5 records will be submitted per year and estimate that it will take approximately 5 hours to perform this activity, totaling 37.5 hours. We also estimate that approximately 7.5 reports will be maintained yearly and estimate it will take 5 hours to perform this activity, totaling 37.5 hours.

Under proposed § 230.230(b)(2), an applicant or nonapplicant could request, in writing, a temporary waiver of the electronic submission requirements under proposed § 230.230(b)(1). An applicant or nonapplicant would need to provide the initial request by telephone or email to the Center for Veterinary Medicine's (CVM's) Division of Veterinary Product Safety, with prompt written followup submitted as a letter to the granted certification or certifications. FDA would grant waivers on a limited basis for good cause shown. If FDA grants a waiver, the applicant or nonapplicant would need to comply with the conditions for reporting specified by FDA upon granting the waiver.

We estimate approximately 7.5 waiver requests will be submitted annually and estimate it will take 5 hours to perform this activity, totaling 37.5 hours annually.

12b. Annualized Cost Burden Estimate

If we finalize the proposed rule, affected entities will incur costs. Sections II.F.1., 3, 4, and 5 of the PRIA discusses costs to industry.

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

No capital costs or operating and maintenance costs are associated with this information collection.

14. Annualized Cost to the Federal Government

Proposed part 230 would govern the process for applicants to: (1) file a certification request that includes the contents of the certification request, (2) submit supplements to a certification, and (3) withdraw a certification request. The proposed rule also requires that applicants submit a streamlined annual report and includes the required contents and timing for submission of the annual report.

As stated in section II.F.6.b of the PRIA, we assume that approximately 9 FDA forms committee employees would expend approximately 8 hours each to develop and approve the certification form, which would include the certification statement. We use the 2019 FDA-wide full-time employee (FTE) value to estimate the fully loaded wage rate of $131.32. To estimate the total one-time cost for the FDA forms committee to create the certification request form, we use the primary estimate of $9,455.

As stated in II.F.6.d of the PRIA, we assume that approximately 9 FDA forms committee employees would expend approximately 8 hours to develop and approve the annual report form. We use 2019 FDA-wide FTE value to estimate the fully loaded wage rate of $131.32. To estimate the total annual cost for the FDA forms committee to create the certification request form, we use the primary estimate of $9,455.

In total, FDA allocates approximately 144 hours (9 employees x 8 hours for each form x 2 forms) to develop and approve. We calculate the annual cost to the Federal government as $18,910.

Table 9. One-Time Cost for FDA to Create Certification Request Two Forms

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Costs
FDA staff – certification form and annual report form	144	$131.32	18,910

15. Explanation for Program Changes or Adjustments

This is a new information collection.

16. Plans for Tabulation and Publication and Project Time Schedule

We will not publish or tabulate this information collection.

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

We will display the OMB expiration date as required by 5 CFR 1320.8(b)(1) and 1320.5(a)(1)(iii)(C).

18. Exceptions to Certification for Paperwork Reduction Act Submissions

No exceptions to the certification are associated with this information collection.