

**REPORT TO CONGRESS**

**REVIEW OF FEDERAL DRUG REGULATIONS  
WITH REGARD TO MEDICAL GASES**

**Required by Section 1112(a)(2) of the  
Food and Drug Administration Safety and Innovation Act of 2012 (Public  
Law 112-144)**

**Department of Health and Human Services  
Food and Drug Administration**

## **EXECUTIVE SUMMARY**

Section 1112 of the Food and Drug Administration Safety and Innovation Act (FDASIA) required that the Food and Drug Administration (FDA) determine whether any changes to the Federal drug regulations are needed concerning medical gases and submit a report to Congress regarding any such changes, after obtaining input from medical gas manufacturers and other interested members of the public. FDA has obtained stakeholder input and conducted a review of Federal drug regulations to determine whether any changes are needed regarding the regulation of medical gases.

After extensive deliberation, FDA has determined that although some regulation changes are necessary to implement the medical gas labeling provisions contained in FDASIA, the current regulatory framework is adequate and sufficiently flexible to appropriately regulate medical gases. FDA can continue to work within this framework to appropriately regulate these products. In addition to the applicable regulations, FDA relies on guidance documents, development of appropriate inspection practices and inspector training, and interaction with industry trade associations, state regulators, and other stakeholders on an as-needed basis in regulating medical gases.

FDA will continue to evaluate the need for regulatory changes on an ongoing basis. New questions and concerns may arise as FDA, the regulated industry, and the public gain experience with the practical results of certifying designated medical gases as approved human and animal drug products. FDA expects to maintain open communication with industry, members of Congress, and other stakeholders as appropriate, and we will continue to evaluate and address medical gas issues as needed.

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## **I. INTRODUCTION**

Under section 1112 of the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-144, July 9, 2012), the Food and Drug Administration (FDA or the Agency) has obtained stakeholder input and conducted a review of Federal drug regulations to determine whether any changes are needed regarding the regulation of medical gases. FDA requested and received input from medical gas manufacturers and other interested stakeholders on this issue, including extensive written comments and comments received during a public meeting and several follow-up meetings.

Following extensive deliberation, FDA has determined that although some regulation changes are necessary to implement the medical gas labeling provisions contained in FDASIA, the current regulatory framework is adequate and sufficiently flexible to appropriately regulate medical gases. Although the current regulatory framework applicable to drug products is not a perfect fit in all respects for medical gases, FDA's experience regulating these products over many years supports our conclusion that we can continue to work within this framework to appropriately regulate these products. In addition to the applicable regulations, FDA relies on guidance documents, development of appropriate inspection practices and inspector training, and interaction with industry trade associations, state regulators, and other stakeholders on an as-needed basis in regulating medical gases.

As it has in the past (see, e.g., the 2006 proposed rule addressing medical gas mix-ups discussed below), FDA may in the future determine that rulemaking is necessary to address specific issues affecting medical gases. There is, however, no compelling need to undertake the sweeping regulatory makeover requested by the medical gas industry.

## **II. REQUIREMENT TO REVIEW FEDERAL DRUG REGULATIONS**

FDASIA was enacted on July 9, 2012. Title XI, Subtitle B of FDASIA, "Medical Gas Product Regulation," includes three sections that address the regulation of medical gases (sections 1111-1113). Section 1111 added new sections 575, 576, and 577 to the Federal Food, Drug, and Cosmetic Act (the FD&C Act). Among other things, these new sections establish a streamlined approval process for oxygen, nitrous oxide, and certain other "designated medical gases" for certain uses (indications).<sup>1</sup>

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<sup>1</sup> For more information, see the draft guidance for industry *Certification Process for Designated Medical Gases*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM332136.pdf>. In the *Federal Register* of December 18, 2012 (77 FR 74852), FDA announced the availability of this draft guidance. The draft guidance describes how FDA plans to implement the new certification process.

Section 1112 of FDASIA required that FDA determine whether any changes to the Federal drug regulations are needed concerning medical gases and submit a report to Congress regarding any such changes, after obtaining input from medical gas manufacturers and other interested members of the public. Section 1112 also requires that any regulation changes that may result from the review be issued no later than 48 months after enactment of FDASIA (i.e., by July 9, 2016). Section 1113 provides rules of construction for sections 1111-1112.

#### **A. *Federal Register* Notices Inviting Public Comments**

On November 23, 2012, FDA issued a *Federal Register* (FR) notice establishing a docket for public commenters to submit information related to FDA's implementation of FDASIA's medical gas provisions.<sup>2</sup> As of March 4, 2015, FDA has received two comments in response to the notice that are related to the regulation review:<sup>3</sup> one from the office of U.S. Representative Pete Olson, and one from Air Liquide USA LLC (Air Liquide), a medical gas manufacturer. Both comments addressed FDA's new authority to add additional gases to the list of designated medical gases under section 575(1)(H) of the FD&C Act and expressed concern that doing so could undermine pending investigational new drug applications (INDs) or investigational new animal drug applications (INADs), if any, for the gas or gases in question. Air Liquide also proposed regulations to address this concern.<sup>4</sup>

On March 22, 2013, FDA issued a notice requesting comments on whether any potential changes to Federal drug regulations are necessary for medical gases.<sup>5</sup> As of March 4, 2015, FDA has received comments from four organizations: the National Association of Boards of Pharmacy (NABP), the Compressed Gas Association (CGA), the Gases and Welding Distributors Association (GAWDA) (joint comments), and the American Association of Respiratory Care (AARC).

- The NABP comments requested changes to the treatment of medical gases under the Federal drug regulations regarding state licensing of wholesale drug distributors found in 21 CFR part 205, and provided a copy of NABP's *Model Rules for the Licensure of Medical Gas and Medical Gas Related Equipment*

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<sup>2</sup> *Federal Register* (FR) notice, "Provisions of the Food and Drug Administration Safety and Innovation Act Related to Medical Gases; Establishment of a Public Docket" (77 FR 70166, November 23, 2012).

<sup>3</sup> Although unrelated to the regulation review, we note that CGA and GAWDA submitted a copy of a previous (September 2012) letter to FDA regarding their suggestions for the certification guidance to this docket as well. See "Draft Guidance for Industry on Certification of Designated Medical Gases; Availability," available at <http://www.regulations.gov> (Docket No. FDA-2012-D-1197).

<sup>4</sup> Copies of these comments are available at <http://www.regulations.gov> (Docket No. FDA-2012-N-1090).

<sup>5</sup> FR Notice, "Provisions of the Food and Drug Administration Safety and Innovation Act Related to Medical Gases; Request for Comments Regarding Regulations" (78 FR 17611, March 22, 2013).

### *Wholesale Distributors.*

- The CGA and GAWDA comments proposed numerous specific changes to the Federal drug regulations currently found in 21 CFR parts 201, 205, 210, 211, and 314. Among other things, these regulations address drug labeling (part 201); state licensing of wholesale drug distributors (part 205); current good manufacturing practice (parts 210 and 211); and postmarket reporting, including adverse event reporting (part 314). The initial comments also generally requested that changes be made to the regulations found in 21 CFR part 207 (registration and listing of drug manufacturers). A supplemental comment by CGA and GAWDA submitted in September 2013 provided more detail on requested changes to part 207. CGA and GAWDA also sent a letter to FDA regarding the regulation review in April 2014 (discussed in more detail below), and submitted a copy of the letter to the public docket in June 2014.
- The AARC comments did not request specific changes, but requested that FDA issue regulations (rather than guidance) to implement the FDASIA medical gas provisions.<sup>6</sup>

### **B. Public Meeting**

In their comments, CGA and GAWDA requested that FDA hold a public meeting concerning the regulation review. FDA agreed that a public meeting was warranted.

Following publication of a FR notice,<sup>7</sup> FDA held a public meeting on December 6, 2013, to obtain additional stakeholder input on whether any changes to the Federal drug regulations are needed for medical gases. Presentations by CGA and GAWDA (the only members of the public who requested the opportunity to present their views at the meeting) were followed by an extensive question and answer session between industry representatives (including but not limited to CGA and GAWDA officials) and a panel of FDA staff from relevant program areas.

In addition to discussing their proposed regulation changes, medical gas industry representatives present at the meeting also provided a few comments and questions regarding the new approval process for designated medical gases. Among other things, they requested (consistent with the comments from Representative Pete Olson and Air Liquide mentioned above, and with congressional correspondence received from Representatives Pete Olson and Gene Green) that FDA clarify how the Agency will make

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<sup>6</sup> Copies of these comments are available at <http://www.regulations.gov> (Docket No. FDA-2013-N-0260).

<sup>7</sup> In the *Federal Register* of November 1, 2013 (78 FR 65588), FDA issued a public meeting notice, “Medical Gas Regulation Review; Announcement of Public Meeting.”

determinations under its authority to add additional gases to the list of designated medical gases.<sup>8</sup> These commenters expressed concern that adding new gases to the list of designated medical gases could undermine legitimate pending INDs or INADs, if any, for the gas or gases in question, and asked FDA to issue regulations addressing this.

### **C. Additional Stakeholder Input**

At the December 2013 meeting, CGA and GAWDA requested follow-up meetings with FDA regarding the regulation review. In February 2014, FDA staff met with CGA and GAWDA. Based on the discussion, these stakeholders were invited to submit a narrower and more targeted list of proposed regulation changes that they considered most important.

CGA and GAWDA sent a letter with a revised list of requests to FDA in April 2014.<sup>9</sup> The letter categorized the initial regulation requests according to which of them CGA and GAWDA believe to require regulation changes (most) and which they believe could be addressed by guidance or other agency actions (a few). The letter also described CGA's and GAWDA's views regarding potential safety concerns related to certain current regulations. We have considered the views and concerns expressed in the letter in connection with the Section 1112 review.

## **III. RESULTS OF REGULATION REVIEW**

FDA has been able to appropriately regulate medical gases using existing Federal drug regulations and a variety of additional mechanisms including but not limited to guidances, training of inspectors, and interaction with industry stakeholders on an as-needed basis.

FDA has reviewed and considered all the comments and information submitted by stakeholders in connection with this regulation review and has reviewed the current regulations. We appreciate the stakeholder comments and concerns, and we recognize the significant work reflected in the suggested regulation changes and other information submitted by CGA and GAWDA, as well as other stakeholders. After extensive deliberation, we have determined that the current regulatory framework is adequate and sufficiently flexible to regulate medical gases, and that FDA can continue to work within this current framework to appropriately regulate these products. In light of this determination and given the multiple competing public health priorities and obligations that place demands on agency resources, we have concluded that the sweeping

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<sup>8</sup> See section 575(1)(H) of the FD&C Act.

<sup>9</sup> A copy of the letter is available at <http://www.regulations.gov> (Docket No. FDA-2013-N-0260) (see Document No. FDA-2013-N-0260-0006, a copy of a letter dated April 21, 2014 from CGA and GAWDA to Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, FDA).

rulemaking initiative requested by CGA and GAWDA is not necessary.<sup>10</sup>

We do, however, intend to make certain changes to our regulations (discussed below), and we remain open to future rulemaking as necessary to address specific issues. We further intend to continue to take other agency action as appropriate, including updating and revising guidances, reviewing and updating inspector training and procedures, and communicating with the regulated industry, state regulators, and other stakeholders as necessary.

### **A. FDA Regulation of the Medical Gas Industry**

FDA has historically regulated the medical gas industry through a range of agency actions, including publication of guidance for industry, internal training of inspection staff regarding the application of labeling and current good manufacturing practice (CGMP) regulations to medical gases, interaction with industry trade associations (CGA and GAWDA)<sup>11</sup> and other stakeholders on an as-needed basis, outreach to state regulatory agencies,<sup>12</sup> and, where necessary, rulemaking to address specific issues. In 2006, for example, we proposed targeted modifications of the CGMP and labeling regulations regarding medical gases.<sup>13</sup> The proposed changes would, among other things, reduce the chance that containers of industrial or other gases could be inappropriately connected to medical oxygen supply systems, and would make the contents of medical gas containers more readily identifiable. The chief impetus for this proposal was information regarding medical gas mix-ups (e.g., the inappropriate administration of an

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<sup>10</sup> Although the CGA and GAWDA joint revised rulemaking requests (submitted April 2014) were somewhat scaled back from those groups' initial joint proposal, both sets of requests, if adopted, would result in the creation of a separate regulatory scheme for medical gases, and our conclusion (stated in the text above) applies equally to both their initial and revised rulemaking requests.

<sup>11</sup> We note that the medical gas industry also sets guidelines for its own members, such as by developing numerous industry-wide standards, which are communicated to members via guidance and information provided by its primary trade associations, CGA and GAWDA. CGA is a member of the American National Standards Institute (ANSI) and is an ANSI-accredited American Standards Developer for the compressed gas industry. CGA publishes both topic-specific papers and a general treatise on the compressed gas industry, including sections on its views regarding compliance with Federal and State regulations, and frequently provides training for its members. See, e.g., <http://www.cganet.com/publications.php>.

<sup>12</sup> For example, since 2007, FDA has included a model Medical Gas Partnership Agreement as one of several available Federal-State regulatory partnerships. See Current Partnership Agreements, Appendix A: Model (Standard) Medical Gas Partnership Agreement, available at <http://www.fda.gov/ForFederalStateandLocalOfficials/PartnershipsContracts/CurrentPartnershipAgreements/ucm115984.htm>.

<sup>13</sup> Proposed rule, "Medical Gas Containers and Closures; Current Good Manufacturing Practice Requirements" (71 FR 18039, April 10, 2006) (Container-Closure Proposed Rule).



industrial gas to a patient intended to receive a medical gas) that resulted in serious patient injuries and deaths.<sup>14</sup>

Following the passage of FDASIA, the Agency implemented the new streamlined certification process for designated medical gases that was created by that Act. Implementation of this process has been successful. As of March 4, 2015, over 60 designated medical gas products have been certified. This process has allowed medical gas manufacturers to seek and obtain approval for previously unapproved drug products via a certification process. Under the FD&C Act, as amended by FDASIA, a certified gas is deemed to have in effect an approved new drug application (NDA) or new animal drug application (NADA) for certain specified indications (see section 576(a)(3)(A)(i) of the FD&C Act).

In December 2012, FDA issued draft guidance to industry regarding the new certification process and FDA's plans for implementation.<sup>15</sup> Among other things, the guidance discusses which products may be certified as designated medical gases, who should submit a certification request, what information should be submitted, how FDA will evaluate and act on the request, and how FDA plans to enforce the new certification requirement.

FDA inspections of the medical gas industry have resulted in a lower rate of cited violations than occurs in the drug industry generally, particularly in recent years.<sup>16</sup> Overall, this inspection history has resulted in a lower regulatory burden on medical gas firms than on many other drug manufacturing firms with regard to inspections (e.g., medical gas firms are inspected less frequently than many other types of drug manufacturers).<sup>17</sup>

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<sup>14</sup> Id.

<sup>15</sup> Supra note 1.

<sup>16</sup> For example, FDA inspections of medical gas firms currently result in citations on an FDA Form 483 (Inspectional Observations) in only 38 percent of those inspections, as opposed to 45 percent for non-medical gas drug firms (see presentation by FDA at FDA's Public Meeting on Medical Gas Regulation Review, December 6, 2013; transcript available at <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM380960.pdf> (see pp. 9-13)).

<sup>17</sup> In FDA's experience, medical gas facilities have generally proven to have fewer violations than other drug manufacturing firms. Accordingly, these facilities make up only about 10 percent of FDA drug product compliance inspections even though they constitute 54 percent of FDA's current drug product facility compliance inventory (sites eligible for inspection). These facilities account for less than 1 percent of Agency enforcement actions. Id.

## B. Regulatory Changes FDA May Undertake

As noted above, FDA has received written comments proposing changes to regulations found in 21 CFR parts 201, 205, 207, 210, 211, and 314. Among other things, these regulations address drug labeling (part 201); state licensing of wholesale drug distributors (part 205); registration and listing of drug manufacturers (part 207); current good manufacturing practices (parts 210 and 211); and post-market reporting, including adverse event reporting (part 314). FDA has conducted an extensive review of all of these comments and the underlying regulations. We have also considered the oral presentations and discussion at the December 2013 public meeting as well as other stakeholder communications, including the February 2014 meeting with CGA and GAWDA and the related April 2014 letter from CGA and GAWDA.

FDA has determined that the following regulation changes are or may be needed regarding medical gases:

- *Part 201: Warning Label Statements.* FDA agrees with stakeholder comments that changes to the current warning label regulation for medical gases (21 CFR § 201.161) may be appropriate. Specifically, changes may be appropriate to implement the new labeling exemption for designated medical gases in section 576(a)(3)(ii) of the FD&C Act, which is conditioned on, among other things, including “a warning statement concerning the use of the medical gas as determined by the Secretary by regulation” (section 576(a)(3) (ii)(II) of the FD&C Act).

Please note that there are also specific labeling regulations for animal drugs (see, e.g., 21 CFR § 201.105). FDA plans to make any corresponding changes to these animal drug regulations as appropriate.

- *Part 314: Adverse Event Reporting.* FDA disagrees with stakeholder comments that designated medical gases should be entirely exempt from the periodic postapproval reporting requirements generally applicable to all approved drugs. However, FDA is considering the appropriate frequency and content of such reporting for designated medical gases, and will continue to consider whether changes specific to designated medical gases are necessary as FDA and the medical gas industry gain practical experience with the regulation of medical gases as NDA products. As noted above, FDA has considered, and will continue to consider, stakeholder input on this issue.

Please note that there are parallel post-approval regulations for animal drugs, including adverse event reporting requirements (see, e.g., 21 CFR part 514). Although no public comments have been submitted regarding post-approval requirements for animal drugs, FDA will also continue to consider if any changes to these regulations are needed in connection with its evaluation of adverse event reporting for designated medical gases for human use.

### C. Review of Remaining Stakeholder Rulemaking Requests

FDA also considered the remaining rulemaking requests<sup>18</sup> raised by stakeholders. After an extensive review of these requests, FDA has concluded that for the most part, the current regulatory framework is adequate and sufficiently flexible to appropriately regulate medical gases.

This conclusion was reached with an awareness of the Agency's competing priorities, including the fulfillment of a number of important Congressional mandates. FDASIA, for example, in addition to its medical gas provisions, includes numerous mandates for FDA, including implementation of two new user fee programs (for generic and biosimilar drug products) and the development of a regulatory framework for breakthrough and other innovative drug products. In addition, the recently-passed Drug Supply Chain Security Act of 2013 creates important obligations for FDA relating to the oversight of compounding of human drugs and outlines critical steps to build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the United States.

FDA considered each comment received suggesting a regulatory change related to medical gases. Changes that were not deemed necessary at this time generally fall into the following categories:

- **The current regulation is sufficiently flexible as written.** For many suggested changes, although FDA agrees with commenters that a certain regulation should not be applied to medical gases under some circumstances, it is our view that the current regulation, as written, already allows sufficient flexibility to address the concerns raised. In those cases where clarification of FDA's application of the regulation to medical gases may be needed, FDA believes the issue either could be, or already is, adequately addressed in guidance and inspection procedures. For example, a proposed change to 21 CFR § 211.87 (retesting of approved components, drug product containers, and closures) would completely exempt designated medical gases from that regulation. We believe the regulation is applicable in some situations (e.g., gas containers with previous industrial use, cylinders left open), and the current text ("shall be retested or reexamined, as appropriate") already provides sufficient regulatory flexibility to apply the regulation as appropriate to medical gases.

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<sup>18</sup> The comments from other entities generally addressed a single issue also addressed by CGA and GAWDA. For example, NABP addressed State licensing requirements for wholesale drug distributors, and AARC addressed issuing regulations instead of guidance. On the general docket, Representative Pete Olson and Air Liquide submitted comments addressing the IND process and new designated medical gases under section 575(1)(H) of the FD&C Act.

- **The issue of concern is specific to an operation in which the regulated party is not engaged.** Similarly, in the case of some suggested changes FDA agrees that a certain regulation should not be applied to medical gases, but disagrees that a regulatory change is necessary because existing regulation 21 CFR § 210.2(b) already provides that CGMP regulations apply only to operations in which the regulated party is engaged. That regulation states that “[i]f a person engages in only some operations subject to the regulations in this part...[and in Parts 211, 225, and 226]..., and not in others, that person need only comply with those regulations applicable to the operations in which he or she is engaged.” So, for example, a suggested change to 21 CFR § 211.42 (design and construction features) would add a new subsection specific to medical gases. Commenters state that this is to address a concern regarding the requirement of aseptic processing for non-sterile medical gases (required by 21 CFR § 211.42 (c)(10)). However, most medical gases are non-sterile, and in such cases, per operation of 210.2(b), FDA would not apply 211.42(c)(10) to them as the manufacturer is not engaging in the operation of producing a sterile drug product.<sup>19</sup>
- **FDA can accomplish the goals of the proposed changes without rulemaking.** For certain suggested changes, FDA agrees with the commenters that the regulation generally should not be applied to medical gases. For example, we agree that expiration dating (21 CFR 211.137), calculation of yield (21 CFR 211.103), and component reconciliation records (21 CFR 211.184(c)) requirements are generally not well-suited for medical gases. However, FDA does not agree that revising these regulations is necessary because FDA can adequately address these issues by other means, including guidance for industry and appropriate inspector training and inspection procedures.
- **The regulation is already under review as part of other rulemakings.** For other suggested changes, FDA is already reviewing the regulation under separate rulemaking proceedings.<sup>20</sup> In some cases, the medical gas industry has separately provided comments on those proposed rules. In those cases, FDA will address the relevant issues as part of the ongoing rulemaking processes associated with the rule in question.

For example, in response to FDA’s solicitation of input from medical gas manufacturers and other interested persons as part of the regulation review, CGA

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<sup>19</sup> In those cases where the medical gas product is intended to be a sterile product, the aseptic processing requirement would apply as written.

<sup>20</sup> See, e.g., Proposed rule, “Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated under a Biologics License Application, and Animal Drugs” (71 FR 51276, August 29, 2006) (eDRLS Proposed Rule); the Container-Closure Proposed Rule, *supra* note 14, and Proposed rule, “Safety Reporting Requirements for Human Drug and Biological Products” (68 FR 12406 -12497, March 14, 2003).

and GAWDA have provided numerous written and oral comments, questions, and proposed changes regarding 21 CFR part 207 (registration and listing of drug manufacturers). FDA has previously issued a proposed rule addressing the electronic drug establishment registration and listing system (eDRLS),<sup>21</sup> which includes multiple FDA-proposed revisions to part 207, and CGA, GAWDA, and other representatives of the medical gas industry submitted numerous comments regarding that rulemaking. In addition, industry representatives have communicated with FDA staff regarding specific questions about application of the current registration requirements to medical gases. FDA will consider these comments and questions regarding registration and listing for medical gases, as appropriate, in connection with the eDRLS rulemaking.

Similarly, as noted above, in 2006 FDA issued a proposed rule that includes modifications of certain CGMP regulations regarding medical gas containers and closures and a change to the preexisting medical gas labeling regulation at § 201.161.<sup>22</sup> Several of the suggested changes submitted as part of the general medical gas regulation review are related to that proposed rulemaking, and will be considered in connection with that rulemaking.

- **Consideration of additional designated medical gases does not require rulemaking.** Finally, regarding the request by some commenters that FDA codify the process of determining when a medical gas other than those enumerated in FDASIA could be deemed appropriate for certification as a designated medical gas (as contemplated in new section 575(1)(H) of the FD&C Act), such determinations will be made on a case-by-case basis. As FDA has already indicated several times to stakeholders and others concerned about this issue, FDA will carefully consider the possible negative impacts on new drug development of designating a new medical gas. FDA believes that at this time, regulations on the topic are not needed.

#### IV. CONCLUSION

We appreciate the comments and concerns submitted by stakeholders, and recognize the significant work reflected in the suggested regulation changes and other information submitted. After extensive deliberation, we have concluded that the current regulatory framework is adequate and sufficiently flexible to appropriately regulate medical gases and that we can continue to work within this framework to appropriately regulate these products. As noted above, however, we do intend to make certain regulation changes and we remain open to future rulemaking as necessary to address specific issues. We further intend to continue to take other Agency action as appropriate, including updating and

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<sup>21</sup> See the eDRLS Proposed Rule, *id.*

<sup>22</sup> See the Container-Closure Proposed Rule, *supra* note 14.

revising guidances, reviewing and updating inspector training and procedures, and communicating with the regulated industry, state regulators, and other stakeholders as necessary.

We will continue to evaluate the need for regulatory changes on an ongoing basis. New questions and concerns may arise as FDA, the regulated industry, and the public gain experience with the practical results of certifying designated medical gases as approved human and animal drug products. FDA expects to maintain open communication with industry, members of Congress, and other stakeholders as appropriate, and we will continue to evaluate and address medical gas issues as needed.