Compressed Gas Association
The Standard For Safety Since 1913

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POSITION STATEMENT

APPROPRIATE AND EFFECTIVE REGULATIONS FOR MEDICAL GASES WITHIN 21 CFR PARTS 201, 205, AND 210/211

Question

Consistent with Section 1112 of the 2012 *Food and Drug Administration Safety and Innovation Act*'s (FDASIA) Congressional direction to the Federal Food and Drug Administration (FDA), what modifications need to be made to the existing regulations to make them appropriate and effective for designated medical gases or combinations thereof for labeling, wholesale distribution, and good manufacturing practice (GMP) compliance?

Answer

This position statement reflects the Compressed Gas Association's (CGA) consensus position for how the FDA's regulations for finished pharmaceuticals found in Title 21 of the U.S. *Code of Federal Regulations* (21 CFR) Parts 201 (labeling), 205 (wholesale distribution), and 210 and 211 (GMPs), should be revised for designated medical gases or combinations thereof. This position is consistent with established and long standing industry practice yielding safe and efficacious designated medical gases and consistent with the Congressional intent in the FDASIA identifying the need for revisions to 21 CFR [1, 2].[1]

This position statement is intended to be used by the industry to assist in communicating its positions on labeling, wholesale distribution, and GMPs when federal and state inspectors apply regulations that are either unnecessary or unsafe for designated medical gases or combinations thereof during facility inspections. A copy of this position statement has been provided to FDA's Center for Drug Evaluation and Research (CDER) Office of Compliance and is consistent with the proposed regulatory changes CGA provided to FDA in May 2013. As of the printing of this document FDA has not communicated disagreement or questioned any recommended change.

This position statement contains the positions presented to FDA in CGA's May 2013 letter proposing specific changes to 21 CFR Parts 201, 205, and 210/ 211 to make them effective and appropriate. To facilitate communication and assure consistent rationales to enforcement personnel, the industry developed the proposed changes to the existing regulations and those that are appropriate for designated medical gases. The sections within this document which cover the regulations are formatted to provide the current regulation, the current regulation modified to be appropriate for designated medical gases, and an explanation why there is a difference.

NOTE—CGA's modifications to the regulations identify new text with underlines and deleted text with strikeouts.

This position statement is intended to address requirements for:

- Designated medical gases or combinations thereof; and
- Other medical gas as defined in Section 575(2) of FDASIA that may be approved via a New Drug Application (NDA) or Abbreviated New Drug Application (ANDA) for which the sponsor has shown through a science based risk management plan that the positions detailed in this document are appropriate.

This position statement is not intended to address requirements for:

- Medical gases approved via an NDA or ANDA prior to July 8, 2012; or
- Medical gases approved in the future via an NDA or ANDA that contain the same active ingredient moiety as a medical gas approved via an NDA or ANDA prior to July 8, 2012.

[1] References are shown by bracketed numbers and are listed in order of appearance in the reference section.

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Compliance with 21 CFR § 201 Labels and Labeling

The 21 CFR Part 201 section specifically associated with medical gases, 21 CFR 201.161, was developed in the 1970's and the following significant modifications address additional medical gases contained in FDASIA and eliminate gases that are not. The FDA Draft Guidance for Industry on Certification Process for Designated Medical Gases (FDA–2012–D-1197) references a 1987 Compliance Policy Guide (CPG 435.100) and a 1972 proposed rule on oxygen labeling. That 1972 proposed rule, implementing a proposed policy, was never adopted and was subsequently officially rescinded. The industry standards based on safety for labeling are and have been very different from the rescinded proposed rule that was referenced in the draft certification guidance and are reflected in the changes to § 201.161.

In addition to significant modification of § 201.161 to include labeling requirements for additional designated medical gases or combinations thereof, other requirements within this part require modification. We are proposing to codify in § 201.1(b) the historic FDA position that medical gas container filling operations is manufacturing (identified as "subsequent manufacturers" as opposed to "original manufacturers" in other discussions with FDA). This also has implications with other sections of this part and other parts of 21 CFR. In addition to deeming designated medical gases approved drugs, FDASIA also permits the combination of designated gases to be manufactured requiring a change to labeling requirements for combinations. Given medical gas containers are refilled without relabeling and their type and size vary significantly, various requirements must be modified to reflect this uniqueness. To minimize the effect on existing regulations, we have exempted medical gases from several sections of Part 201 and have included the appropriate requirements in § 201.161.

Proposed Changes to 21 CFR § 201

§ 201.1(b) Drugs; name and place of business of manufacturer, packer, or distributor

Current regulation

(a) A drug or drug product (as defined in §320.1 of this chapter) in finished package form is misbranded under section 502 (a) and (b)(1) of the act if its label does not bear conspicuously the name and place of business of the manufacturer, packer, or distributor. This paragraph does not apply to any drug or drug product dispensed in accordance with section 503(b)(1) of the act.