

CGA M-15—2018

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

THIRD EDITION

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Work Item 24-003
Medical Gases Committee

THIRD EDITION: 2018
SECOND EDITION: 2017
FIRST EDITION: 2014

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Introduction

This standard reflects the Compressed Gas Association's (CGA) consensus position for how the Federal Food and Drug Administration's (FDA) 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 standard is consistent with established and long standing industry practice yielding safe and efficacious designated medical gases and consistent with the Congressional intent in the *Food and Drug Administration Safety and Innovation Act's* (FDASIA) identifying the need for revisions to 21 CFR [1, 2].¹

For 21 CFR Part 201 only those subparts and sections where CGA has submitted proposed modifications to the FDA for designated medical gases and combinations thereof are included below. For 21 CFR Parts 205, 210, and 211, all subparts and sections are reproduced in this standard in their entirety with CGA's proposed modifications for designated medical gases and combinations thereof.

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

Title 21—Food and Drugs, Chapter I—Food and Drug Administration, Department of Health and Human Services Subchapter C—Drugs: General

Part 201 Labeling

NOTE—Only includes those subparts and sections with proposed changes for designated medical gases and combinations thereof.

Subpart A—General Labeling Provisions

§ 201.1 Drugs; name and place of business of manufacturer, packer, or distributor.

- (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.
- (b) As used in this section, and for purposes of section 502 (a) and (b)(1) of the act, the manufacturer of a drug product is the person who performs all of the following operations that are required to produce the product: (1) Mixing, (2) granulating, (3) milling, (4) molding, (5) lyophilizing, (6) tableting, (7) encapsulating, (8) coating, (9) sterilizing, and (10) filling sterile, aerosol, or gaseous drugs into dispensing containers, and (11) filling designated medical gases or combinations thereof into containers by any of the following processes: (a) liquid to liquid, (b) liquid to gas, or (c) gas to gas.
- (c) If no person performs all of the applicable operations listed in paragraph (b) of this section, no person may be represented as manufacturer except as follows:
 - (1) If the person performs more than one half of the applicable operations listed in paragraph (b) of this section and acknowledges the contribution of other persons who have performed the remaining applicable operations by stating on the product label that "Certain manufacturing operations have been performed by other firms."; or
 - (2) If the person performs at least one applicable operation listed in paragraph (b) of this section and identifies by appropriate designation all other persons who have performed the remaining applicable operations, e.g., "Made by (Person A), Filled by (Person B), Sterilized by (Person C)"; or

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

- (3) If the person performs at least one applicable operation listed in paragraph (b) of this section and the person is listed along with all other persons who have performed the remaining applicable operations as "joint manufacturers." A list of joint manufacturers shall be qualified by the phrase "Jointly Manufactured By -----," and the names of all of the manufacturers shall be printed together in the same type size and style; or
- (4) If the person performs all applicable operations listed in paragraph (b) of this section except for those operations listed in paragraph (d) of this section. For purposes of this paragraph, person, when it identifies a corporation, includes a parent, subsidiary, or affiliate company where the related companies are under common ownership and control.
- (d) The Food and Drug Administration finds that it is the common practice in the drug industry to contract out the performance of certain manufacturing operations listed in paragraph (b) of this section. These operations include: (1) Soft-gelatin encapsulating, (2) aerosol filling, (3) sterilizing by irradiation, (4) lyophilizing, ~~and~~ (5) ethylene oxide sterilization, and (6) designated medical gas filling or combinations of designated medical gas filling.
- (e) A person performs an operation listed in paragraph (b) of this section only if the operation is performed, including the performance of the appropriate in-process quality control operations, except laboratory testing of samples taken during processing, as follows:
 - (1) By individuals, a majority of whom are employees of the person and, throughout the performance of the operation, are subject to the person's direction and control;
 - (2) On premises that are continuously owned or leased by the person and subject to the person's direction and control; and
 - (3) On equipment that is continuously owned or leased by the person. As used in this paragraph, person, when it identifies a corporation, includes a parent, subsidiary, or affiliate company where the related companies are under common ownership and control.
- (f) The name of the person represented as manufacturer under paragraph (b) or (c) of this section must be the same as either (1) the name of the establishment (as defined in §207.3(b) of this chapter) under which that person is registered at the time the labeled product is produced or (2) the registered establishment name of a parent, subsidiary, or affiliate company where the related companies are under common ownership and control. In addition, the name shall meet the requirements of paragraph (g) of this section.
- (g) The requirement for declaration of the name of the manufacturer, packer, or distributor shall be deemed to be satisfied, in the case of a corporate person, only by the actual corporate name, except that the corporate name may be the name of a parent, subsidiary, or affiliate company where the related companies are under common ownership and control. The corporate name may be preceded or followed by the name of the particular division of the corporation. "Company," "Incorporated," etc., may be abbreviated or omitted and "The" may be omitted. In the case of an individual, partnership, or association, the name under which the business is conducted shall be used.
- (h)
 - (1) Except as provided in this section, no person other than the manufacturer, packer, or distributor may be identified on the label of a drug or drug product.
 - (2) The appearance on a drug product label of a person's name without qualification is a representation that the named person is the sole manufacturer of the product. That representation is false and misleading, and the drug product is misbranded under section 502(a) of the act, if the person is not the manufacturer of the product in accordance with this section. Permanent stamped markings on containers or closures for designated medical gas or combination thereof that are required by an agency other than FDA are not considered labeling for the purposes of this part.
 - (3) If the names of two or more persons appear on the label of a drug or drug product, the label may identify which of the persons is to be contacted for further information about the product.

- (4) If a trademark appears on the drug or drug product label or appears as a mark directly on the drug product (e.g., tablet or capsule), the label may identify the holder or licensee of the trademark. The label may also state whether the person identified holds the trademark or is licensee of the trademark.
- (5) If the distributor is named on the label, the name shall be qualified by one of the following phrases: "Manufactured for -----", "Distributed by -----", "Manufactured by ----- for -----", "Manufactured for -----by -----", "Distributor: -----", "Marketed by -----". The qualifying phrases may be abbreviated.
- (6) If the packer is identified on the label, the name shall be qualified by the phrase "Packed by -----" or "Packaged by -----". The qualifying phrases may be abbreviated.
- (7) If the owner of a container filled with a designated medical gas or combination thereof is distributing supplier-filled and labeled product, the name and address of the container owner may appear on a separate label from the product label to designate to whom the empty container should be returned to provided the name on the separate label is qualified by the phrase "Property of -----". The firm adding this separate label shall not be considered a "relabeler" for purposes of registration and listing under § 207 of this part.
- (i) The statement of the place of business shall include the street address, city, State, and ZIP Code. For a foreign manufacturer, the statement of the place of business shall include the street address, city, country, and any applicable mailing code. The street address may be omitted if it is shown in a current city directory or telephone directory. The requirement for inclusion of the ZIP Code shall apply to consumer commodity labels developed or revised after July 1, 1969. In the case of non-consumer packages, the ZIP Code shall appear either on the label or the labeling (including the invoice).
- (j) If a person manufactures, packs, or distributes a drug or drug product at a place other than the person's principal place of business, the label may state the principal place of business in lieu of the actual place where such drug or drug product was manufactured or packed or is to be distributed, unless such statement would be misleading.
- (k) Paragraphs (b), (c), (d), (e), and (f) of this section, do not apply to the labeling of drug components.
- (l) A drug product is misbranded under section 502(a) of the act if its labeling identifies a person as manufacturer, packer, or distributor, and that identification does not meet the requirements of this section.
- (m) This section does not apply to biological drug products that are subject to the requirements of section 351 of the Public Health Service Act, 42 U.S.C. 262.

[45 FR 25775, Apr. 15, 1980; 45 FR 72118, Oct. 31, 1980, as amended at 48 FR 37620, Aug. 19, 1983; 81 FR 60212, Aug. 31, 2016]

§ 201.10 Drugs; statement of ingredients.

- (a) The ingredient information required by section 502(e) of the Federal Food, Drug, and Cosmetic Act shall appear together, without any intervening written, printed, or graphic matter, except the proprietary names of ingredients, which may be included with the listing of established names, and such statements that are specifically required for certain ingredients by the act or regulations in this chapter.
- (b) The term ingredient applies to any substance in the drug, whether added to the formulation as a single substance or in admixture with other substances.
- (c) The labeling of a drug may be misleading by reason (among other reasons) of:
 - (1) The order in which the names of the ingredients present in the drug appear in the labeling, or the relative prominence otherwise given such names.
 - (2) Failure to reveal the proportion of, or other fact with respect to, an ingredient present in such drug, when such proportion or other fact is material in the light of the representation that such ingredient is present in such drug.

- (3) The employment of a fanciful proprietary name for a drug or ingredient in such a manner as to imply that the drug or ingredient has some unique effectiveness or composition when, in fact, the drug or ingredient is a common substance, the limitations of which are readily recognized when the drug or ingredient is listed by its established name.
 - (4) The featuring in the labeling of inert or inactive ingredients in a manner that creates an impression of value greater than their true functional role in the formulation.
 - (5) Designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient.
- (d) (1) If the drug is in tablet or capsule form or other unit dosage form, any statement of the quantity of an ingredient contained therein shall express the quantity of such ingredient in each such unit. If the drug is not in unit dosage form, any statement of the quantity of an ingredient contained therein shall express the amount of such ingredient in a specified unit of weight or measure of the drug, or the percentage of such ingredient in such drug. Such statements shall be in terms that are informative to licensed practitioners, in the case of a prescription drug, and to the layman, in the case of a nonprescription drug.
- (2) A statement of the percentage of an ingredient in a drug shall, if the term percent is used without qualification, mean percent weight-in-weight, if the ingredient and the drug are both solids, or if the ingredient is a liquid and the drug is a solid; percent weight in volume at 68 [deg]F. (20 [deg]C.), if the ingredient is a solid and the drug is a liquid; and percent volume in volume at 68 [deg]F. (20 [deg]C.), if both the ingredient and the drug are liquids, except that alcohol shall be stated in terms of percent volume of absolute alcohol at 60 [deg]F. (15.56 [deg]C.), if all ingredients are designated medical gases the statement of percentage shall be in accordance with 201.161 (f).
- (e) A derivative or preparation of a substance named in section 502(e) of the act is an article derived or prepared from such substance by any method, including actual or theoretical chemical action.
- (f) If an ingredient is a derivative or preparation of a substance specifically named in section 502(e) of the act and the established name of such ingredient does not indicate that it is a derivative or preparation of the parent substance named in section 502(e) of the act, the labeling shall, in conjunction with the listing of the established name of such ingredient, declare that such article is a derivative or preparation of such parent substance.
- (g) (1) If the label or labeling of a prescription drug bears a proprietary name or designation for the drug or any ingredient thereof, the established name, if such there be, corresponding to such proprietary name or designation shall accompany such proprietary name or designation each time it is featured on the label or in the labeling for the drug; but, except as provided in this subparagraph, the established name need not be used with the proprietary name or designation in the running text of the label or labeling. On any label or page of labeling in which the proprietary name or designation is not featured but is used in the running text, the established name shall be used at least once in the running text in association with such proprietary name or designation and in the same type size used in such running text: Provided, however, That if the proprietary name or designation is used in the running text in larger size type, the established name shall be used at least once in association with, and in type at least half as large as the type used for, the most prominent presentation of the proprietary name or designation in such running text. If any labeling includes a column with running text containing detailed information as to composition, prescribing, side effects, or contraindications and the proprietary name or designation is used in such column but is not featured above or below the column, the established name shall be used at least once in such column of running text in association with such proprietary name or designation and in the same type size used in such column of running text: Provided, however, That if the proprietary name or designation is used in such column of running text in larger size type, the established name shall be used at least once in association with, and in type at least half as large as the type used for, the most prominent presentation of the proprietary name or designation in such column of running text. Where the established name is required to accompany or to be used in association with the proprietary name or designation, the established name shall be placed in direct conjunction with the proprietary name or designation, and the relationship between the proprietary name or designation and the established name

shall be made clear by use of a phrase such as “brand of” preceding the established name, by brackets surrounding the established name, or by other suitable means.

- (2) The established name shall be printed in letters that are at least half as large as the letters comprising the proprietary name or designation with which it is joined, and the established name shall have a prominence commensurate with the prominence with which such proprietary name or designation appears, taking into account all pertinent factors, including typography, layout, contrast, and other printing features.
- (h) (1) In the case of a prescription drug containing two or more active ingredients, if the label bears a proprietary name or designation for such mixture and there is no established name corresponding to such proprietary name or designation, the quantitative ingredient information required on the label by section 502(e) of the act shall be placed in direct conjunction with the most prominent display of the proprietary name or designation. The prominence of the quantitative ingredient information shall bear a reasonable relationship to the prominence of the proprietary name.
- (2) If the drug is packaged in a container too small to bear the quantitative ingredient information on the main display panel, the quantitative ingredient information required by section 502(e) of the act may appear elsewhere on the label, even though the proprietary name or designation appears on the main display panel of the label; but side- or back-panel placement shall in this case be so arranged and printed as to provide size and prominence of display reasonably related to the size and prominence of the front-panel display.
- (i) A drug packaged in a container too small or otherwise unable to accommodate a label with sufficient space to bear the information required for compliance with section 502(e)(1) (A)(ii) and (B) of the act shall be exempt from compliance with those clauses: Provided, That:
 - (1) The label bears:
 - (i) The proprietary name of the drug;
 - (ii) The established name, if such there be, of the drug;
 - (iii) An identifying lot or control number; and
 - (iv) The name of the manufacturer, packer, or distributor of the drug; and
 - (2) All the information required to appear on the label by the act and the regulations in this chapter appears on the carton or other outer container or wrapper if such carton, outer container, or wrapper has sufficient space to bear such information, or such complete label information appears on a leaflet with the package.

[40 FR 13998, Mar. 27, 1975, as amended at 67 FR 4906, Feb. 1, 2002]

§ 201.18 Drugs; significance of control numbers.

The lot number on the label of a drug should be capable of yielding the complete manufacturing history of the package. An incorrect lot number may be regarded as causing the article to be misbranded. See 201.161 (d) for lot numbers on containers of designated medical gas or combinations thereof.

Subpart B—Labeling Requirements for Prescription Drugs and/or Insulin

§ 201.51 Declaration of net quantity of contents.

- (a) The label of a prescription or insulin-containing drug in package form shall bear a declaration of the net quantity of contents. This shall be expressed in the terms of weight, measure, numerical count, or a combination of numerical count and weight or measure. The statement of quantity of drugs in tablet, capsule, ampule, or other unit dosage form shall be expressed in terms of numerical count; the statement of quantity for drugs in other dosage forms shall be in terms of weight if the drug is solid, semi-solid, or viscous, or in terms of fluid measure if the drug is liquid. When the drug quantity statement is in terms of the numerical count of the drug units, it shall be augmented to give the weight or measure of the drug units or the quantity

of each active ingredient in each drug unit or, when quantity does not accurately reflect drug potency, a statement of the drug potency.

- (b) Statements of weight of the contents shall in the case of prescription drugs be expressed in terms of avoirdupois pound, ounce, and grain or of kilogram, gram, and subdivisions thereof. A statement of liquid measure of the contents shall in the case of prescription drugs be expressed in terms of the U.S. gallon of 231 cubic inches and quart, pint, fluid-ounce, and fluid-dram subdivisions thereof, or of the liter and milliliter, or cubic centimeter, and shall express the volume at 68 [deg]F. (20 [deg]C.). A statement of the liquid measure of the contents in the case of insulin-containing drugs shall be expressed in terms of the liter and milliliter, or cubic centimeter, and shall express the volume at 68 [deg]F. (20 [deg]C.).
- (c) The declaration shall contain only such fractions as are generally used in expressing the quantity of the drug. A common fraction shall be reduced to its lowest terms; a decimal fraction shall not be carried out to more than three places, except in the case of a statement of the quantity of an active ingredient in a unit of a drug.
- (d) The declaration shall appear as a distinct item on the label and, in the case of large volume parenterals, may be embossed on the glass.
- (e) The declaration shall accurately reveal the quantity of drug in the package exclusive of wrappers and other material packed therewith.
- (f) A statement of the quantity of a prescription or insulin-containing drug in terms of weight or measure applicable to such drug, under the provisions of paragraph (a) of this section, shall express with prominence and conspicuousness the number of the largest whole unit, as specified in paragraph (b) of this section, that are contained in the package. Any remainder shall be expressed in terms of common or decimal fractions of such unit or in terms of the next smaller whole unit and common or decimal fractions thereof.
- (g) The declaration of net quantity of contents shall express an accurate statement of the quantity of contents of the package. Reasonable variations caused by loss or gain of moisture during the course of good distribution practice or by unavoidable deviations in good manufacturing practice will be recognized. Variations from stated quantity of contents shall not be unreasonably large. In the case of a liquid drug in ampules or vials, intended for injection, the declaration shall be considered to express the minimum quantity and the variation above the stated measure shall comply with the excess volume prescribed by the National Formulary or the U.S. Pharmacopeia for filling of ampules. In the case of a solid drug in ampules or vials, the declaration shall be considered to express the accurate net weight. Variations shall comply with the limitations provided in the U.S. Pharmacopeia or the National Formulary.
- (h) A drug shall be exempt from compliance with the net quantity declaration required by this section if it is an ointment labeled "sample", "physician's sample", or a substantially similar statement and the contents of the package do not exceed 8 grams.
- (i) Designated medical gases or combinations thereof are exempt from this section and shall comply with 201.161 (f).

§ 201.56 Requirements on content and format of labeling for human prescription drug and biological products.

- (a) General requirements. Prescription drug labeling described in §201.100(d) must meet the following general requirements:
 - (1) The labeling must contain a summary of the essential scientific information needed for the safe and effective use of the drug.
 - (2) The labeling must be informative and accurate and neither promotional in tone nor false or misleading in any particular. In accordance with Sec. §314.70 and 601.12 of this chapter, the labeling must be updated when new information becomes available that causes the labeling to become inaccurate, false, or misleading.
 - (3) The labeling must be based whenever possible on data derived from human experience. No implied claims or suggestions of drug use may be made if there is inadequate evidence of safety or a lack of

substantial evidence of effectiveness. Conclusions based on animal data but necessary for safe and effective use of the drug in humans must be identified as such and included with human data in the appropriate section of the labeling.

- (b) Categories of prescription drugs subject to the labeling content and format requirements in Sec. §201.56(d) and 201.57.
 - (1) The following categories of prescription drug products are subject to the labeling requirements in paragraph (d) of this section and §201.57 in accordance with the implementation schedule in paragraph (c) of this section:
 - (i) Prescription drug products for which a new drug application (NDA), biologics license application (BLA), or efficacy supplement was approved by the Food and Drug Administration (FDA) between June 30, 2001 and June 30, 2006;
 - (ii) Prescription drug products for which an NDA, BLA, or efficacy supplement is pending on June 30, 2006; or
 - (iii) Prescription drug products for which an NDA, BLA, or efficacy supplement is submitted anytime on or after June 30, 2006.
 - (2) Prescription drug products not described in paragraph (b)(1) of this section are subject to the labeling requirements in paragraph (e) of this section and §201.80.
- (c) Schedule for implementing the labeling content and format requirements in Sec. §201.56(d) and 201.57. For products described in paragraph (b)(1) of this section, labeling conforming to the requirements in paragraph (d) of this section and §201.57 must be submitted according to the following schedule:
 - (1) For products for which an NDA, BLA, or efficacy supplement is submitted for approval on or after June 30, 2006, proposed conforming labeling must be submitted as part of the application.
 - (2) For products for which an NDA, BLA, or efficacy supplement is pending on June 30, 2006, or that has been approved any time from June 30, 2005, up to and including June 30, 2006, a supplement with proposed conforming labeling must be submitted no later than June 30, 2009.
 - (3) For products for which an NDA, BLA, or efficacy supplement has been approved anytime from June 30, 2004, up to and including June 29, 2005, a supplement with proposed conforming labeling must be submitted no later than June 30, 2010.
 - (4) For products for which an NDA, BLA, or efficacy supplement has been approved anytime from June 30, 2003, up to and including June 29, 2004, a supplement with proposed conforming labeling must be submitted no later than June 30, 2011.
 - (5) For products for which an NDA, BLA, or efficacy supplement has been approved anytime from June 30, 2002, up to and including June 29, 2003, a supplement with proposed conforming labeling must be submitted no later than June 30, 2012.
 - (6) For products for which an NDA, BLA, or efficacy supplement has been approved anytime from June 30, 2001, up to and including June 29, 2002, a supplement with proposed conforming labeling must be submitted no later than June 30, 2013.
- (d) Labeling requirements for new and more recently approved prescription drug products. This paragraph applies only to prescription drug products described in paragraph (b)(1) of this section and must be implemented according to the schedule specified in paragraph (c) of this section.

- (1) Prescription drug labeling described in §201.100(d) must contain the specific information required under §201.57(a), (b), and (c) under the following headings and subheadings and in the following order:

Highlights of Prescribing Information

Product Names, Other Required Information

Boxed Warning

Recent Major Changes

Indications and Usage

Dosage and Administration

Dosage Forms and Strengths

Contraindications

Warnings and Precautions

Adverse Reactions

Drug Interactions

Use in Specific Populations

Full Prescribing Information: Contents

Full Prescribing Information

Boxed Warning

1 Indications and Usage

2 Dosage and Administration

3 Dosage Forms and Strengths

4 Contraindications

5 Warnings and Precautions

6 Adverse Reactions

7 Drug Interactions

8 Use in Specific Populations

8.1 Pregnancy

8.2 Labor and delivery

8.3 Nursing mothers

8.4 Pediatric use

8.5 Geriatric use

9 Drug Abuse and Dependence

9.1 Controlled substance

9.2 Abuse

9.3 Dependence

10 Overdosage

11 Description

12 Clinical Pharmacology

12.1 Mechanism of action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

13 Nonclinical Toxicology

13.1 Carcinogenesis, mutagenesis, impairment of fertility

13.2 Animal toxicology and/or pharmacology

14 Clinical Studies

15 References

16 How Supplied/Storage and Handling

17 Patient Counseling Information

- (2) Additional nonstandard subheadings that are used to enhance labeling organization, presentation, or ease of use (e.g., for individual warnings or precautions, or for each drug interaction) must be assigned a decimal number that corresponds to their placement in labeling. The decimal numbers must be consistent with the standardized identifying numbers listed in paragraph (d)(1) of this section (e.g., subheadings added to the “Warnings and Precautions” section must be numbered 5.1, 5.2, and so on).
- (3) Any reference in Highlights to information appearing in the full prescribing information must be accompanied by the identifying number (in parentheses) corresponding to the location of the information in the full prescribing information.

- (4) Omit clearly inapplicable sections, subsections, or specific information. If sections or subsections required under paragraph (d)(1) of this section are omitted from the full prescribing information, the heading “Full Prescribing Information: Contents” must be followed by an asterisk and the following statement must appear at the end of Contents: “* Sections or subsections omitted from the full prescribing information are not listed.”
- (5) Any risk information that is required under §201.57(c)(9)(iv) is considered “appropriate pediatric contraindications, warnings, or precautions” within the meaning of section 505A(l)(2) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355A(l)(2)), whether such information appears in the “Contraindications,” “Warnings and Precautions,” or “Use in Specific Populations” section of labeling.
- (e) Labeling requirements for older prescription drug products other than designated medical gases or combinations thereof that are labeled in accordance with the requirements of 201.161. This paragraph applies only to approved prescription drug products not described in paragraph (b)(1) of this section.
- (1) Prescription drug labeling described in §201.100(d) must contain the specific information required under §201.80 under the following section headings and in the following order:
- Description
 - Clinical Pharmacology
 - Indications and Usage
 - Contraindications
 - Warnings
 - Precautions
 - Adverse Reactions
 - Drug Abuse and Dependence
 - Overdosage
 - Dosage and Administration
 - How Supplied
- (2) The labeling may contain the following additional section headings if appropriate and if in compliance with §201.80(l) and (m):
- Animal Pharmacology and/or Animal Toxicology
 - Clinical Studies
 - References
- (3) Omit clearly inapplicable sections, subsections, or specific information.
- (4) The labeling may contain a “Product Title” section preceding the “Description” section and containing only the information required by §201.80(a)(1)(i), (a)(1)(ii), (a)(1)(iii), and (a)(1)(iv) and §201.100(e). The information required by §201.80(a)(1)(i) through (a)(1)(iv) must appear in the “Description” section of the labeling, whether or not it also appears in a “Product Title.”
- (5) The labeling must contain the date of the most recent revision of the labeling, identified as such, placed prominently immediately after the last section of the labeling.
- (6) The requirement in §201.80(f)(2) to reprint any FDA-approved patient labeling at the end of prescription drug labeling or accompany the prescription drug labeling must be implemented no later than June 30, 2007.

[71 FR 3986, Jan. 24, 2006, as amended at 79 FR 72101, Dec. 4, 2014]

Subpart D—Exemptions from Adequate Directions for Use**§ 201.100 Prescription drugs for human use.**

A drug subject to the requirements of section 503(b)(1) of the act shall be exempt from section 502(f)(1) if all the following conditions are met:

(a) The drug is:

- (1) (i) In the possession of a person (or his agents or employees) regularly and lawfully engaged in the manufacture, transportation, storage, or wholesale distribution of prescription drugs; or
 - (ii) In the possession of a retail, hospital, or clinic pharmacy, or a public health agency, regularly and lawfully engaged in dispensing prescription drugs; or
 - (iii) In the possession of a practitioner licensed by law to administer or prescribe such drugs; or
 - (iv) A designated medical gas in the possession of a person who is cleaning or purging medical gas containers, including medical gas pipelines; and
- (2) It is to be dispensed in accordance with section 503(b)

(b) Other than designated medical gases or combinations thereof in compliance with 201.161, The label of the drug bears:

- (1) The statement “Rx only” and
- (2) The recommended or usual dosage and
- (3) The route of administration, if it is not for oral use; and
- (4) The quantity or proportion of each active ingredient, as well as the information required by section 502 (d) and (e); and
- (5) If it is for other than oral use, the names of all inactive ingredients, except that:
 - (i) Flavorings and perfumes may be designated as such without naming their components.
 - (ii) Color additives may be designated as coloring without naming specific color components unless the naming of such components is required by a color additive regulation prescribed in subchapter A of this chapter.
 - (iii) Trace amounts of harmless substances added solely for individual product identification need not be named. If it is intended for administration by parenteral injection, the quantity or proportion of all inactive ingredients, except that ingredients added to adjust the pH or to make the drug isotonic may be declared by name and a statement of their effect; and if the vehicle is water for injection it need not be named.
- (6) An identifying lot or control number from which it is possible to determine the complete manufacturing history of the package of the drug.
- (7) A statement directed to the pharmacist specifying the type of container to be used in dispensing the drug product to maintain its identity, strength, quality, and purity. Where there are standards and test procedures for determining that the container meets the requirements for specified types of containers as defined in an official compendium, such terms may be used. For example, “Dispense in tight, light-resistant container as defined in the National Formulary”. Where standards and test procedures for determining the types of containers to be used in dispensing the drug product are not included in an

official compendium, the specific container or types of containers known to be adequate to maintain the identity, strength, quality, and purity of the drug products shall be described. For example, "Dispense in containers which (statement of specifications which clearly enable the dispensing pharmacist to select an adequate container)": Provided, however, That in the case of containers too small or otherwise unable to accommodate a label with sufficient space to bear all such information, but which are packaged within an outer container from which they are removed for dispensing or use, the information required by paragraph (b) (2), (3), (5), and (7) of this section may be contained in other labeling on or within the package from which it is to be dispensed; the information referred to in paragraph (b)(1) of this section may be placed on such outer container only; and the information required by paragraph (b)(6) of this section may be on the crimp of the dispensing tube. The information required by this paragraph (b)(7) is not required for prescription drug products packaged in unit-dose, unit-of-use, or other packaging format in which the manufacturer's original package is designed and intended to be dispensed to patients without repackaging.

- (c) (1) Labeling on or within the package from which the drug is to be dispensed bears adequate information for its use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and precautions under which practitioners licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended, including all purposes for which it is advertised or represented; and
- (2) If the article is subject to section 505 of the act, the labeling bearing such information is the labeling authorized by the approved new drug application or required as a condition for the certification or the exemption from certification requirements applicable to preparations of insulin or antibiotic drugs.
- (d) Any labeling, as defined in section 201(m) of the act, whether or not it is on or within a package from which the drug is to be dispensed, distributed by or on behalf of the manufacturer, packer, or distributor of the drug, that furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for the use of the drug (other than dose information required by paragraph (b)(2) of this section and §201.105(b)(2) contains:
 - (1) Adequate information for such use, including indications, effects, dosages, routes, methods, and frequency and duration of administration and any relevant warnings, hazards, contraindications, side effects, and precautions, under which practitioners licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended, including all conditions for which it is advertised or represented; and if the article is subject to section 505 of the act, the parts of the labeling providing such information are the same in language and emphasis as labeling approved or permitted, under the provisions of section 505, and any other parts of the labeling are consistent with and not contrary to such approved or permitted labeling; and
 - (2) The same information concerning the ingredients of the drug as appears on the label and labeling on or within the package from which the drug is to be dispensed.
 - (3) The information required, and in the format specified, by Sec. §201.56, 201.57, and 201.80.
- (e) All labeling described in paragraph (d) of this section bears conspicuously the name and place of business of the manufacturer, packer, or distributor, as required for the label of the drug under §201.1.
- (f) Reminder labeling which calls attention to the name of the drug product but does not include indications or dosage recommendations for use of the drug product is exempted from the provisions of paragraph (d) of this section. This reminder labeling shall contain only the proprietary name of the drug product, if any; the established name of the drug product, if any; the established name of each active ingredient in the drug product; and, optionally, information relating to quantitative ingredient statements, dosage form, quantity of package contents, price, the name and address of the manufacturer, packer, or distributor or other written, printed, or graphic matter containing no representation or suggestion relating to the drug product.
 - If the Commissioner finds that there is evidence of significant incidence of fatalities or serious injury associated with the use of a particular prescription drug, he may withdraw this exemption by so notifying the manufacturer, packer, or distributor of the drug by letter.

- Reminder labeling, other than price lists and catalogs solely intended to convey price information including, but not limited to, those subject to the requirements of §200.200 of this chapter, is not permitted for a prescription drug product whose labeling contains a boxed warning relating to a serious hazard associated with the use of the drug product.
- Reminder labeling which is intended to provide consumers with information concerning the price charged for a prescription for a particular drug product shall meet all of the conditions contained in §200.200 of this chapter.
- Reminder labeling, other than that subject to the requirements of §200.200 of this chapter, is not permitted for a drug for which an announcement has been published pursuant to a review of the labeling claims for the drug by the National Academy of Sciences/National Research Council (NAS/NRC), Drug Efficacy Study Group, and for which no claim has been evaluated as higher than “possibly effective.”
- If the Commissioner finds the circumstances are such that reminder labeling may be misleading to prescribers of drugs subject to NAS/NRC evaluation, such reminder labeling will not be allowed and the manufacturer, packer, or distributor will be notified either in the publication of the conclusions on the effectiveness of the drug or by letter.

[40 FR 13998, Mar. 27, 1975, as amended at 40 FR 58799, Dec. 18, 1975; 42 FR 15674, Mar. 22, 1977; 43 FR 37989, Aug. 25, 1978; 44 FR 20659, Apr. 6, 1979; 44 FR 37467, June 26, 1979; 45 FR 25777, Apr. 15, 1980; 63 FR 26698, May 13, 1998; 64 FR 400, Jan. 5, 1999; 67 FR 4906, Feb. 1, 2002; 71 FR 3996, Jan. 24, 2006]

§ 201.105 Veterinary drugs.

A drug subject to the requirements of section 503(f)(1) of the act shall be exempt from section 502(f)(1) of the act if all the following conditions are met, or if it is a designated medical gas or combination thereof that it is in compliance with 201.161:

(a) The drug is:

- (1) (i) In the possession of a person (or his agents or employees) regularly and lawfully engaged in the manufacture, transportation, storage, or wholesale distribution of drugs that are to be used only by or on the prescription or other order of a licensed veterinarian; or
 - (ii) In the possession of a retail, hospital, or clinic pharmacy, or other person authorized under State law to dispense veterinary prescription drugs, who is regularly and lawfully engaged in dispensing drugs that are to be used only by or on the prescription or other order of a licensed veterinarian; or
 - (iii) In the possession of a licensed veterinarian for use in the course of his professional practice; and
- (2) To be dispensed in accordance with section 503(f) of the act.

(b) The label of the drug bears:

- (1) The statement “Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian”; and
- (2) The recommended or usual dosage; and
- (3) The route of administration, if it is not for oral use; and
- (4) The quantity or proportion of each active ingredient as well as the information required by section 502(e) of the act; and
- (5) If it is for other than oral use, the names of all inactive ingredients, except that:
 - (i) Flavorings and perfumes may be designated as such without naming their components.
 - (ii) Color additives may be designated as coloring without naming specific color components unless the naming of such components is required by a color additive regulation prescribed in subchapter A of this chapter.

- (iii) Trace amounts of harmless substances added solely for individual product identification need not be named. If it is intended for administration by parenteral injection, the quantity or proportion of all inactive ingredients, except that ingredients added to adjust the pH or to make the drug isotonic may be declared by name and a statement of their effect; and if the vehicle is water for injection, it need not be named.
- (6) An identifying lot or control number from which it is possible to determine the complete manufacturing history of the package of the drug; Provided, however, That in the case of containers too small or otherwise unable to accommodate a label with sufficient space to bear all such information, but which are packaged within an outer container from which they are removed for dispensing or use, the information required by paragraphs (b) (2), (3), and (5) of this section may be contained in other labeling on or within the package from which it is to be so dispensed, and the information referred to in paragraph (b)(1) of this section may be placed on such outer container only, and the information required by paragraph (b)(6) of this section may be on the crimp of the dispensing tube.
- (c) (1) Labeling on or within the package from which the drug is to be dispensed bears adequate information for its use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and precautions under which veterinarians licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended, including all purposes for which it is advertised or represented; and
- (2) If the article is subject to section 512 or 572 of the act, the labeling bearing such information is the labeling authorized by the approved new animal drug application or contained in the index listing: Provided, however, That the information required by paragraph (c)(1) of this section may be omitted from the dispensing package if, but only if, the article is a drug for which directions, hazards, warnings, and use information are commonly known to veterinarians licensed by law to administer the drug. Upon written request, stating reasonable grounds therefore, the Commissioner will offer an opinion on a proposal to omit such information from the dispensing package under this proviso.
- (d) Any labeling, as defined in section 201(m) of the act, whether or not it is on or within a package from which the drug is to be dispensed, distributed by or on behalf of the manufacturer, packer, or distributor of the drug, that furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for the use of the drug (other than dose information required by paragraph (b)(2) of this section and §201.100(b)(2)) contains:
 - (1) Adequate information for such use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, and any relevant warnings, hazards, contraindications, side effects, and precautions, and including information relevant to compliance with the new animal drug provisions of the act, under which veterinarians licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended, including all conditions for which it is advertised or represented; and if the article is subject to section 512 or 572 of the act, the parts of the labeling providing such information are the same in language and emphasis as labeling approved, permitted, or indexed under the provisions of section 512 or 572, and any other parts of the labeling are consistent with and not contrary to such approved, permitted, or indexed labeling; and
 - (2) The same information concerning the ingredients of the drug as appears on the label and labeling on or within the package from which the drug is to be dispensed; Provided, however, That the information required by paragraphs (d)(1) and (2) of this section is not required on the so-called reminder-piece labeling which calls attention to the name of the drug but does not include indications or dosage recommendations for use of the drug.
- (e) All labeling, except labels and cartons, bearing information for use of the drug also bears the date of the issuance or the date of the latest revision of such labeling.
- (f) A prescription drug intended for both human and veterinary use shall comply with paragraphs (e) and (f) of this section and §201.100.

[40 FR 13998, Mar. 27, 1975, as amended at 42 FR 15674, Mar. 22, 1977; 57 FR 54300, Nov. 18, 1992; 72 FR 69119, Dec. 6, 2007]