(c) *Record retention period.* You must maintain all records and documentation referenced in this part for a period of at least 1 year from the date of final release, including conditional final release, of a PET drug product.

PART 213—CURRENT GOOD MANUFACTURING PRACTICE FOR MEDICAL GASES (Eff. 12-18-25)

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AUTHORITY: 21 U.S.C. 321, 351, 352, 353, 355, 360b, 360ddd, 360ddd–1, 371, 374.

SOURCE: 89 FR 51770, June 18, 2024, unless otherwise noted.

EFFECTIVE DATE NOTE: At 89 FR 51770, June 18, 2024, part 213 was added, effective Dec. 18, 2025.

Subpart A—General Provisions

§ 213.1 Scope.

The regulations in this part contain the minimum current good manufacturing practice for preparation of medical gases for administration to humans or animals.

§ 213.3 Definitions.

(a) The definitions and interpretations contained in section 201 of the Federal Food, Drug, and Cosmetic Act shall be applicable to such terms when used in this part.

(b) The following definitions of terms apply to this part:

(1) *Acceptance criteria* means the product specifications and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level, with an associated sampling plan, that are necessary for making a decision to accept or reject a lot or batch (or any other convenient subgroups of manufactured units).

(2) *Batch* means a specific quantity of a medical gas or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.

(3) *Commingling or commingled* refers to the act of combining one lot of designated medical gas or component with another lot or lots of the same designated medical gas or component.

(4) *Component* means any ingredient intended for use in the manufacture of a medical gas, including those that may not appear in such gas. It does not include an incoming designated medical gas.

(5) *Designated medical gas* means a drug that is manufactured or stored in a liquefied, nonliquefied, or cryogenic state; is administered as a gas; and is defined in section 575(1) of the Federal Food, Drug, and Cosmetic Act.

(6) *FDA* means the Food and Drug Administration.

(7) *In-process material* means any material fabricated, compounded, blended, or derived by chemical reaction that is produced for, and used in, the preparation of the medical gas.

(8) *Incoming designated medical gas* means a designated medical gas received from one source that, after receipt, is commingled with the same gas from another source, used in a medically appropriate combination of designated medical gases or in the production of another medical gas, or further distributed.

(9) *Lot* means a batch, or a specific identified portion of a batch, having uniform character and quality within specified limits; or, in the case of a medical gas produced by continuous process, it is a specific identified amount produced in a unit of time or quantity in a manner that assures its having uniform character and quality within specified limits.

(10) *Lot number, control number, or batch number* means any distinctive combination of letters, numbers, or symbols, or any combination of them, from which the complete history of the manufacture, processing, packing, holding, and distribution of a batch or lot of medical gas or other material can be determined.

(11) *Manufacture, processing, packing, or holding of medical gases* includes packaging and labeling operations, testing, and quality control.

(12) *Medical gas* has the meaning given the term in section 575(2) of the Federal Food, Drug, and Cosmetic Act.

(13) *Original manufacturer* means the person that initially produces a designated medical gas by chemical reaction, physical separation, compression of atmospheric air, purification (*e.g.*, re-processing an industrial gas into a medical gas), or other means.

(14) *Quality unit* means any person or persons designated with the authority and responsibility for overall quality management and other responsibilities as defined in § 213.22.

(15) *Strength* means:

(i) The concentration of the medical gas (for example, weight/weight, weight/volume, or unit dose/volume basis); and/or

(ii) The potency, that is, the therapeutic activity of the medical gas as indicated by appropriate laboratory tests or by adequately developed and controlled clinical data (expressed, for example, in terms of units by reference to a standard).

Subpart B—Organization and Personnel

§ 213.22 Responsibilities of quality unit.

(a) There shall be a quality unit that shall have the responsibility and authority to approve or reject all components, medical gas containers and closures, in-process materials, packaging material, labeling, and medical gases, and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated. The quality unit shall be responsible for approving or rejecting medical gases manufactured, processed, packed,

or held under contract by another company.

(b) Adequate laboratory facilities for the testing and approval (or rejection) of components, medical gas containers and closures, packaging materials, in-process materials, and medical gases shall be available to the quality unit.

(c) The quality unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the medical gas.

(d) The responsibilities and procedures applicable to the quality unit shall be in writing; such written procedures shall be followed.

(e) Quality unit personnel may perform other functions provided appropriate written controls are in place to ensure any other functions are performed separately from quality unit responsibilities and such other functions do not interfere with the quality unit's responsibilities or subordinate the quality unit's responsibilities to any other unit.

§ 213.25 Personnel qualifications and responsibilities.

(a) Each person engaged in the manufacture, processing, packing, or holding of a medical gas shall have education, training, and experience, or any combination thereof, to enable that person to perform the assigned functions. Training shall be in the particular operations that the employee performs and in current good manufacturing practice (including the current good manufacturing practice regulations in this chapter and written procedures required by these regulations) as they relate to the employee's functions. Training in current good manufacturing practice shall be conducted by qualified individuals on a continuing basis and with sufficient frequency to assure that employees remain familiar with current good manufacturing practice requirements applicable to them. Written documentation shall be maintained demonstrating the completion of employee training, and shall include the date of the training, the type of the training, and the results of any completion criteria, such as test results.

(b) There shall be an adequate number of qualified personnel to perform the manufacture, processing, packing, or holding of each medical gas.

(c) Only authorized personnel shall enter those areas of the buildings and facilities designated as limited-access areas.

§ 213.34 Consultants.

Consultants advising on the manufacture, processing, packing, or holding of medical gases shall have sufficient education, training, and experience, or any combination thereof, to advise on the subject for which they are retained. Records shall be maintained stating the name, address, and qualifications of any consultants and the type of service they provide.

Subpart C—Buildings and Facilities

§ 213.42 Design and construction features.

(a)(1) Any buildings and facilities used in the manufacture, processing, packing, or holding of a medical gas shall be of adequate design, including having adequate space, for the orderly placement of equipment and materials to prevent mix-ups between:

(i) Components;

(ii) Incoming designated medical gases;

(iii) Medical gas containers and closures;

(iv) Labeling;

(v) In-process materials; or

(vi) Medical gases.

(2) Such buildings and facilities shall also allow for adequate cleaning, maintenance, and proper operations.

(b)(1) Operations shall be performed within specifically defined areas of adequate size. There shall be separate or defined areas or such other control systems for the firm's operations as are necessary to prevent contamination or mix-ups during the course of the following procedures:

(i) Receipt, identification, storage, and withholding from use of components, incoming designated medical gases, medical gas containers and closures, and labeling, pending the appropriate sampling, testing, or examination by the quality unit before release for manufacturing or packaging;

(ii) Holding rejected components, incoming designated medical gases, medical gas containers and closures, and labeling before disposition;

(iii) Storage of released components, incoming designated medical gases, medical gas containers and closures, and labeling;

(iv) Storage of in-process materials;

(v) Manufacturing and processing operations;

(vi) Packaging and labeling operations;

(vii) Quarantine storage before release of medical gases;

(viii) Storage of medical gases after release; and

(ix) Control and laboratory operations.

(2) The flow of components, incoming designated medical gases, medical gas containers and closures, labeling, in-process materials, and medical gases through the buildings and facilities shall be designed to prevent contamination and mix-ups.

(c) Any building or facility used in the manufacture, processing, packing, or holding of a medical gas shall be maintained in a clean condition so as to assure the safety, identity, strength, quality, and purity of the medical gas. Written procedures applicable to the maintenance and cleaning of buildings and facilities shall be established and followed.

Subpart D—Equipment

§ 213.63 Equipment design, size, and location.

Equipment used in the manufacture, processing, packing, or holding of a medical gas shall be of appropriate design and adequate size, and be suitably located to facilitate operations for its intended use and any necessary cleaning and maintenance.

§ 213.65 Equipment construction.

(a) Equipment shall be constructed so that surfaces that contact components, in-process materials, or medical gases shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the medical gas beyond the official or other established requirements.

(b) Any substances required for operation, such as lubricants or coolants, shall not come into contact with components, containers, closures, in-process materials, or medical gases so as to alter the safety, identity, strength, quality, or purity of the medical gas beyond the official or other established requirements.

§ 213.67 Equipment maintenance and cleaning.

(a) Written procedures shall be established, maintained, and followed for adequate cleaning and maintenance of equipment used in the manufacture, processing, packing, or holding of medical gases. These procedures shall include, but are not necessarily limited to, the following:

(1) Assignment of responsibility for cleaning and maintaining equipment;

(2) Maintenance and cleaning schedules, including, where appropriate, sanitizing schedules;

(3) A description in sufficient detail of the methods, equipment, and materials used in cleaning and maintenance operations, and the methods of disassembling and reassembling equipment as necessary to assure proper cleaning and maintenance;

(4) Removal or obliteration of previous batch identification;

(5) Protection of clean equipment from contamination prior to use; and

(6) Inspection of equipment for cleanliness immediately before use.

(b) The procedures described in paragraph (a) of this section shall not alter the safety, identity, strength, quality, or purity of the medical gas beyond the established requirements.

(c) Records shall be kept of cleaning, maintenance, and inspection as specified in §§ 213.180 and 213.182.

§ 213.68 Automatic, mechanical, and electronic equipment.

(a) Automatic, mechanical, and electronic equipment used in the manufacture, processing, packing, and holding of medical gases shall be routinely calibrated, inspected, and checked according to a written program designed to ensure proper performance. Written procedures and records of calibration, inspections, and checks shall be maintained.

(b) Computerized systems that record, store, or use data shall be appropriately validated.

(c) A backup file of data entered into the computer system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes.

(d) Appropriate change control shall be used whenever modifications are made to computer systems to assure that any changes do not adversely affect data integrity or product quality. Records of such modifications shall be maintained.

Subpart E—Control of Incoming Designated Medical Gas, Components, and Medical Gas Containers and Closures

§ 213.80 General requirements.

(a) There shall be written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components, incoming designated medical gases, and medical gas containers and closures; such written procedures shall be followed.

(b) Components, incoming designated medical gases, and medical gas containers and closures shall at all times be handled and stored in a manner to prevent contamination and mix-ups.

(c) Lots of incoming designated medical gases or components, whether used directly as supply or commingled with an existing supply, shall be assigned a unique identification number.

§ 213.82 Receipt and storage of incoming designated medical gases.

(a)(1) Upon receipt of each shipment of each incoming designated medical gas, the firm shall either perform full compendial testing on the gas and record the results or verify and record that a signed certificate of analysis from the supplier accompanies each different designated medical gas in a shipment. The certificate of analysis shall include the following:

(i) Supplier's name;

(ii) Name of the incoming designated medical gas;

(iii) Lot number or other unique identification number;

(iv) Actual analytical result obtained for strength, as well as the results of other tests performed;

(v) Identification of the test method(s) used for analysis;

(vi) New drug application and/or new animal drug application number of the incoming designated medical gas; and

(vii) Supplier representative's signature and the date of signature.

(2) If the incoming designated medical gas is obtained from a supplier other than the original manufacturer, the shipment shall also include complete information from the original manufacturer's certificate of analysis. The firm shall establish and maintain a program to ensure the reliability of the supplier's capabilities through appropriate assessment and testing procedures.

(b) An identity test shall be performed upon receipt of the incoming designated medical gas.

§ 213.84 Testing and approval or rejection of components, containers, and closures.

(a) Components, containers, and closures (including valves) shall be examined for conformance with appropriate written procedures and specifications, and approved or rejected, prior to the manufacturing or filling process. In lieu of such examination by the firm, a statement of verification that the component, container, or closure meets specifications may be accepted from the supplier, provided that the firm establishes and maintains a program to ensure the reliability of the supplier's capabilities through appropriate assessment and testing provisions. Any rejected items shall be handled in accordance with § 213.89.

(b) Firms shall take appropriate actions to protect against container and closure leaks, which shall include performing leak tests on containers and closures at the time of fill and after fill but prior to release.

(c) Each component shall be sampled, tested, and approved or rejected as appropriate prior to use. This requirement can be met by performing testing

for conformance with written specifications or by an identity test on the component accompanied by an acceptable certificate of analysis from the supplier, provided that the firm establishes and maintains a program to ensure the reliability of the supplier's capabilities through appropriate assessment and testing procedures.

§ 213.89 Rejected components, incoming designated medical gases, and medical gas containers and closures.

Rejected components, incoming designated medical gases, and medical gas containers and closures shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which they are unsuitable and shall be documented and assessed.

§ 213.94 Medical gas containers and closures.

(a) Medical gas containers and closures shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the gas beyond the official or established requirements.

(b) Container closure systems shall provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the medical gas.

(c) Medical gas containers and closures shall be clean to assure that they are suitable for their intended use.

(d) Standards or specifications, methods of testing, and, where indicated, methods of cleaning shall be written and followed for medical gas containers and closures.

(e) Medical gas containers and closures must meet the following requirements—

(1) *Gas-specific use outlet connections.* Portable cryogenic medical gas containers that are not manufactured with permanent gas use outlet connections (*e.g.*, those that have been silver-brazed) must have gas-specific use outlet connections that are attached to the valve body so that they cannot be readily removed or replaced (without making the valve inoperable and preventing the containers' use) except by the manufacturer. For the purposes of this paragraph (e)(1), the term *manufacturer* includes any individual or firm that fills high-pressure medical gas cylinders or cryogenic medical gas containers. For the purposes of this section, a *portable cryogenic medical gas container* is one that is capable of being transported and is intended to be attached to a medical gas supply system within a hospital, healthcare entity, nursing home, other facility, or home healthcare setting, or is used to fill small cryogenic gas containers for use by individual patients. The term excludes cryogenic containers that are not designed to be connected to a medical gas supply system, *e.g.*, tank trucks, trailers, rail cars, or small cryogenic gas containers for use by individual patients (including portable liquid oxygen units as defined at § 868.5655 of this chapter).

(2) *Gauges for certain medical gas containers.* Portable cryogenic medical gas containers as described in paragraph (e)(1) of this section and small cryogenic gas containers for use by individual patients (including portable liquid oxygen units as defined at § 868.5655 of this chapter) must have a working gauge sufficient to assist the user in determining whether the container contains an adequate supply of medical gas for continued use.

(3) *Label and coloring requirements.* The labeling specified at § 201.328(a) of this chapter must be affixed to the container in a manner that does not interfere with other labeling. Each such label as well as materials used for coloring medical gas containers must be reasonably resistant to fading, durable when exposed to atmospheric conditions, and not readily soluble in water.

Subpart F—Production and Process Controls

§ 213.100 Written procedures; deviations.

(a) There shall be written procedures for production and process controls designed to assure that medical gases have the identity, strength, quality, and purity they purport or are represented to possess. Such procedures shall include all requirements in this subpart. These written procedures, including any changes, shall be drafted,

reviewed, and approved by the appropriate organizational units and reviewed and approved by the quality unit.

(b) Written production and process control procedures shall be followed in the execution of the various production and process control functions and shall be documented at the time of performance. Any deviation from the written procedures shall be recorded and justified.

§ 213.101 Charge-in of components and incoming designated medical gases.

Written production and control procedures shall include the following, which are designed to assure that the medical gases produced have the identity, strength, quality, and purity they purport or are represented to possess:

(a) Except when a monograph or formulary specifies a range, the batch shall be formulated with the intent to provide 100 percent of the labeled or established amount of each medical gas. When a monograph or formulary specifies a range for the contents of a medical gas, the batch shall be formulated with the intent to provide an amount of the medical gas within such specified range.

(b) Components and incoming designated medical gases added to in-process supply or final product containers shall be weighed or measured as appropriate. In-process and final product containers shall identify the name of the component or designated medical gas or the name and percentage of each component or designated medical gas if they contain multiple components or designated medical gases, and the unique lot number assigned.

§ 213.110 Sampling and testing of in-process materials.

(a) In-process materials shall be tested for identity, strength, quality, and purity as appropriate, and approved or rejected by the quality unit during the production process.

(b) To assure batch uniformity and integrity of drug products, written procedures shall be established and followed that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch. Such control procedures shall be established to monitor the output and to validate the performance of those manufacturing processes.

(c) Rejected in-process materials shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which they are unsuitable.

Subpart G—Packaging and Labeling Control

§ 213.122 Materials examination and usage criteria.

(a) There shall be written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, examination, and/or testing of labeling and packaging materials; such written procedures shall be followed. Labeling and packaging materials shall be representatively sampled, and examined or tested upon receipt and before use in packaging or labeling of a medical gas.

(b) Any labeling or packaging materials meeting appropriate written specifications may be approved and released for use. Any labeling or packaging materials that do not meet such specifications shall be rejected to prevent their use in operations for which they are unsuitable.

(c) Records shall be maintained for each shipment received of each different labeling and packaging material indicating receipt, examination, and whether accepted or rejected.

(d) Labels and other labeling materials for each different medical gas, strength, or quantity of contents shall be stored with suitable identification to avoid mix-ups. Access to the label storage area shall be limited to authorized personnel.

(e) Labels, labeling, and other packaging materials that are obsolete, outdated, or that do not meet applicable requirements shall be destroyed.

(f) Packaging and labeling operations shall include one of the following special control procedures:

(1) Dedication of labeling and packaging lines to each different strength of each different medical gas;

(2) Use of appropriate electronic or electromechanical equipment to conduct a 100-percent examination for correct labeling during or after completion of finishing operations; or

(3) Use of visual inspection to conduct a 100-percent examination for correct labeling during or after completion of labeling operations for hand-applied labeling. Such examination shall be performed by one person and independently verified by a second person.

(g) Printing devices on, or associated with, manufacturing lines used to imprint labeling upon the unit label or case shall be monitored to assure that all imprinting conforms to the print specified in the batch production record.

(h) Labels may be reused if they are legible, properly affixed to the container, and otherwise meet all applicable requirements.

§ 213.125 Labeling issuance.

(a) Labeling and packaging operations must be controlled to prevent labeling and product mix-ups. Procedures shall be written and followed describing in sufficient detail the control procedures employed for the issuance of labeling.

(b) Procedures shall be used to reconcile the quantities of labeling issued, used, and returned, and shall require evaluation of discrepancies found between the quantity of medical gas and the quantity of labeling issued when such discrepancies are outside narrow preset limits based on historical operating data. Such discrepancies shall be investigated in accordance with §213.192. Labeling reconciliation is waived for cut or roll labeling if a 100-percent examination for correct labeling is performed in accordance with §213.122(f)(2). Labeling reconciliation is also waived for 360° wraparound labels on portable cryogenic medical gas containers.

(c) All excess lot number stickers or decals bearing lot or control numbers shall be discarded.

(d) Bulk or transport containers (as defined in §201.161(c)(3) of this chapter) are exempt from this section.

§ 213.130 Packaging and labeling operations.

There shall be written procedures designed to assure that correct labels, labeling, and packaging materials are used for medical gases; such written procedures shall be followed. These procedures shall incorporate the following features:

(a) Prevention of mix-ups by physical or spatial separation from operations on other products.

(b) Identification and handling of filled containers of medical gas that are set aside and held in unlabeled condition for future labeling operations to preclude mislabeling of individual containers, lots, or portions of lots. Identification need not be applied to each individual container but shall be sufficient to determine name, strength, quantity of contents, and lot or control number of each container.

(c) Identification of the medical gas with a lot or control number that permits determination of the history of the manufacture and control of the batch. The lot or control number of the medical gas may be identified by use of a separate identification sticker or decal.

(d) Examination of packaging and labeling materials for suitability and correctness before packaging operations, and documentation of such examination in the batch production record. Product labels, including 360° wraparound labels, can be reused provided they meet all applicable labeling requirements, all information on the label is legible, and the label is in good condition.

(e) Inspection of the packaging and labeling facilities immediately before use to assure that all medical gases have been removed from previous operations. Inspection shall also be made to assure that packaging and labeling materials not suitable for subsequent operations have been removed. Results of inspection shall be documented in the batch production records.

(f) Bulk or transport containers (as defined in §201.161(c)(3) of this chapter) are exempt from this section provided they are identified with the name of

the product contained therein and accompanied by documentation identifying the product as meeting applicable compendial standards.

Subpart H—Holding and Distribution

§ 213.150 Warehousing and distribution procedures.

(a) Written procedures shall be established, and followed, describing the distribution of medical gases and including a system by which the distribution of each lot can be readily determined to facilitate its recall if necessary.

(b) Written procedures shall be established, and followed, describing the warehousing of medical gases, including quarantine of such gases before release by the quality unit.

Subpart I—Laboratory Controls

§ 213.160 General requirements.

(a) The establishment of any specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms required by this subpart, including any change in such specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms, shall be drafted by the appropriate organizational unit and reviewed and approved by the quality unit. The requirements in this subpart shall be followed and shall be documented at the time of performance. Any deviation from the written specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms shall be recorded and justified.

(b) Laboratory controls shall include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, medical gas containers and closures, in-process materials, labeling, and medical gases conform to appropriate standards of identity, strength, quality, and purity. Laboratory controls shall include:

(1) Determination of conformity to applicable written specifications for the acceptance of each lot within each shipment of components, medical gas containers and closures, and labeling used in the manufacture, processing, packing, or holding of a medical gas. The specifications shall include a description of the sampling and testing procedures used. Samples shall be representative and adequately identified. Such procedures shall also require appropriate retesting of any component, container, or closure that is subject to deterioration.

(2) Determination of conformance to written specifications and a description of sampling and testing procedures for in-process materials. Such samples shall be representative and properly identified.

(3) Determination of conformance to written descriptions of sampling procedures and appropriate specifications for medical gases. Such samples shall be representative and properly identified.

(4) The calibration or verification of calibration for instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with an established written program containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in the event accuracy and/or precision limits are not met. Instruments, apparatus, gauges, and recording devices not meeting established specifications shall not be used.

§ 213.165 Testing and release for distribution.

(a) For each batch of medical gas, there shall be appropriate laboratory determination of satisfactory conformance to final specifications for the medical gas, including the identity and strength, prior to release.

(b) Any sampling and testing plans shall be described in written procedures that shall include the method of sampling, the number of units per batch to be tested, and acceptance criteria. Such written procedures shall be followed.

(c) The accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm shall be established and documented. Such validation and documentation may be accomplished in accordance with § 213.194(a)(2). The suitability of all

testing methods shall be verified under actual conditions of use.

(d) Medical gases failing to meet established standards or specifications and any other relevant quality criteria shall be rejected.

(e) This section does not apply to the filling of a designated medical gas or medically appropriate combination of designated medical gases via liquid to liquid into a container at a delivery site.

§ 213.166 Stability testing and expiration dating for medical gases marketed under applications submitted under section 505 or section 512 of the Federal Food, Drug, and Cosmetic Act.

(a) For medical gases marketed under applications submitted under section 505 or section 512 of the Federal Food, Drug, and Cosmetic Act, any stability testing performed and any expiration date established shall be in accordance with paragraph (b) of this section, subject to the conditions established in their approved applications, if any.

(b) To assure that the medical gas described in paragraph (a) of this section meets applicable standards of identity, strength, quality, and purity at the time of use:

(1) The stability testing program shall be designed to assess the stability characteristics of the medical gas and its container closure system. The results of stability testing shall be used in determining appropriate storage conditions and any expiration date included on the label. The stability program shall include the appropriate sample size, test intervals, container closure systems, and storage conditions for samples retained for testing.

(2) Any expiration dates included on the label shall appear in accordance with the requirements of § 201.17 of this chapter.

(3) Stability shall be evaluated periodically to ensure that the medical gas continues to meet the standards for identity, strength, quality, and purity stated on the labeling to support the expiration date.

Subpart J—Records

§ 213.180 General requirements.

(a) *Record availability.* All records required under this part, or copies of such records, shall be readily available for authorized inspection during the retention period at the establishment where the activities described in such records occurred and are subject to copying as part of such inspection. Records that can be immediately retrieved from another location by computer or other electronic means shall be considered as meeting the requirements of this paragraph (a).

(b) *Record requirements.* All records must be legible, stored to prevent deterioration or loss, and original or accurate reproductions of the original records.

(c) *Record retention period.* Except where otherwise provided, all records required to be maintained in compliance with this part must be maintained for a period of at least 3 years after the distribution of the batch of medical gas.

(d) *Maintenance of written records.* Written records required by this part shall be maintained 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. Written procedures shall be established and followed for such evaluations and shall include provisions for:

(1) A review of a representative number of batches, whether approved or rejected, and, where applicable, records associated with the batch; and

(2) A review of complaints, recalls, returned or salvaged medical gases, and investigations conducted under § 213.192 for each gas.

(e) *Written procedure requirements.* A firm shall establish and follow written procedures to assure that responsible officials of the firm are notified in writing of any recalls, reports of inspectional observations by FDA, regulatory actions related to good manufacturing practices brought by FDA, or investigations resulting from adverse event complaints.

§ 213.182 Equipment cleaning and use log.

A written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use shall be included in individual equipment logs that show the date, time, product, and lot number of each batch processed. If equipment is dedicated to manufacture of one product, then individual equipment logs are not required, provided that lots or batches of such product follow in numerical order and are manufactured in numerical sequence. In cases where dedicated equipment is employed, the records of cleaning, maintenance, and use shall be part of the batch record. The persons performing and double-checking the cleaning and maintenance (or, if the cleaning and maintenance is performed using automated equipment under § 213.68, just the person verifying the cleaning and maintenance done by the automated equipment) shall date and sign or initial the log indicating that the work was performed. Entries in the log shall be in chronological order.

§ 213.184 Records for components, medical gas containers and closures, and labeling.

Records for components, medical gas containers and closures, and labeling shall include the following:

(a) The results of any test or examination performed (including those performed as required by § 213.84 or § 213.122) and the conclusions derived therefrom.

(b) Documentation of the examination and review of labels and labeling for conformity with established specifications in accordance with §§ 213.122 and 213.130.

(c) The disposition of rejected components, medical gas containers and closures, and labeling.

§ 213.186 Master production and control records.

(a) To assure uniformity from batch to batch, master production and control records for each medical gas shall be prepared, dated, and signed. The preparation of master production and control records shall be described in a written procedure and such written procedure shall be followed.

(b) Master production and control records shall include:

(1) The name and strength of the medical gas;

(2) A complete list of components and any incoming designated medical gases used in manufacturing designated by names or codes sufficiently specific to indicate any special quality characteristic;

(3) A description of the medical gas containers and closures, packaging materials, and labels; and

(4) Complete manufacturing and control instructions, sampling and testing procedures, specifications, special notations, and precautions to be followed.

§ 213.189 Batch production and control records.

(a) Batch production and control records shall be prepared for each batch of medical gas produced.

(b) These records shall include documentation that each significant step in the manufacture, processing, packing, or holding of the medical gas produced was accomplished, including:

(1) Dates of each significant step, including in-process and laboratory tests as applicable;

(2) A description of the container for the medical gas, including the number and size of the containers filled as applicable;

(3) Specific identification of each component and its source or in-process material used as applicable;

(4) Measures of components used in the course of processing as applicable;

(5) Testing results, including any in-process test results and finished product test results;

(6) Dated signature or initials of the persons performing and directly supervising or checking each significant step in the operation;

(7) Inspection of the packaging and labeling area before and after use;

(8) Complete labeling control records, including specimens or copies of all labeling used and label application and reconciliation records as appropriate; and

(9) Any investigation made according to § 213.192.

§ 213.192 Production record review.

(a) Manufacturing production and control records, including those for packaging and labeling, shall be reviewed and approved by the quality unit to determine compliance with all established, approved written procedures before a batch is released or distributed. The quality unit must review production records to determine whether errors or unexplained discrepancies have occurred prior to batch release. If errors or unexplained discrepancies have occurred, or a batch or any component of the batch fails to meet any of its specifications, the firm must thoroughly investigate and take appropriate corrective actions. A written record of the investigation shall be made and shall include the conclusions and followup.

(b) For production and control records of filling at a delivery site, quality unit review as described in paragraph (a) of this section shall be within one business day after fill.

§ 213.194 Laboratory records.

(a) Laboratory records related to the manufacture of a medical gas must include complete data derived from all tests necessary to assure compliance with established specifications and standards, including examinations and assays, as follows:

(1) A description of the sample, the batch or lot number to be tested, the date the sample was taken, and the date the sample was tested.

(2) The method used in the testing of the sample, the result of the test, how the results compare with established standards of identity, strength, quality, and purity for the component, container, closure, in-process materials (as applicable), and medical gas tested, a record of any calculations performed in connection with each test and any calculated results, and the unit of measurement of the result for each test. It is not necessary to provide the actual calculation where the result is evident through use of simple addition and subtraction.

(3) Where applicable, any graphs, charts, and spectra from laboratory instrumentation, properly identified to show the specific component, in-process material, or medical gas for each lot tested.

(4) The initials or signature of the person performing the test and the initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards.

(b) Complete records shall be maintained of any modification of an established method employed in testing. Such records shall include the reason for the modification and data to verify that the modification produced results that are at least as accurate and reliable for the material being tested as the established method.

(c) Complete records shall be maintained of any testing and standardization of laboratory reference standards, reagents, and standard solutions.

(d) Complete records shall be maintained of the periodic calibration or verification of calibration of laboratory instruments, apparatus, gauges, and recording devices required by § 213.160(b)(4).

(e) Complete records shall be maintained of all stability testing performed in accordance with § 213.166.

§ 213.196 Distribution records.

Distribution records shall contain the name of the medical gas, lot or batch number, name and address of the consignee, and date and quantity shipped. For medically appropriate combinations of designated medical gases, the distribution record shall include the percentage of each gas.

§ 213.198 Complaint files.

(a) Written procedures shall be established and followed for the receipt and handling of all written or oral complaints concerning a medical gas. These procedures must include quality unit review of any complaint involving the possible failure of a medical gas to meet any of its specifications and provisions for determining the need for an investigation in accordance with § 213.192 as well as determining whether the complaint represents an event that is required to be reported to FDA under part 230 of this chapter. Any complaint involving a possible leak of a container or closure must be reviewed, evaluated,

and investigated in accordance with §213.192.

(b) A written record of each complaint regarding a medical gas must be maintained. The record must include the name of the gas, the lot or batch number, the name of the complainant, the date the complaint was received, the nature of the complaint, and the response to the complaint. It must also include the findings of any investigation and followup. Where an investigation is not conducted, the written record shall include the reason that an investigation was found not to be necessary and the name of the responsible person making such a determination.

(c) Complaint files shall be maintained in a manner such that they are readily available for inspection by the firm or by FDA during an inspection. Complaint files shall be maintained for at least 1 year after the date the complaint was received or for at least 3 years after distribution of the medical gas, whichever is longer.

Subpart K—Returned and Salvaged Medical Gases

§213.204 Returned medical gases.

Returned medical gases shall be identified as such and held. If the conditions under which such returned gases have been held, stored, or shipped before or during their return, or if the condition of the gas, its container, carton, or labeling, as a result of storage or shipping, casts doubt on the safety, identity, strength, quality, or purity of the gas, the returned gas shall be destroyed unless examination, testing, or other investigations prove the gas meets appropriate standards of safety, identity, strength, quality, or purity. Records of returned medical gases shall be maintained and shall include the name, lot number (or control number or batch number), reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned gas. If the reason for a medical gas being returned implicates associated batches, an appropriate investigation shall be conducted in accordance with the requirements of §213.192. Procedures for the holding, testing, and use of returned medical gases shall be in writing and shall be followed. This section is not applicable to the routine refilling of cryogenic medical gas containers in the normal course of business unless the cryogenic medical gas container was returned due to a quality issue.

§213.208 Salvaging of medical gases.

Medical gases in containers that have been subjected to improper storage conditions may be salvaged unless their containers have been subjected to adverse conditions that impact the identity, strength, quality, and purity of the gas or integrity of the container closure. Whenever there is a question whether medical gases have been subjected to such conditions, salvaging operations may be conducted only if there is evidence from laboratory tests that such gases meet all applicable standards of identity, strength, quality, and purity, and the integrity of the container closure system is not compromised. Procedures for the holding, testing, and use of salvaged medical gases shall be in writing and shall be followed.

PART 216—HUMAN DRUG COMPOUNDING

Subpart A—General Provisions [Reserved]

Subpart B—Compounded Drug Products

Sec.

AUTHORITY: 21 U.S.C. 351, 352, 353a, 353b, 355, and 371.

SOURCE: 64 FR 10944, Mar. 8, 1999, unless otherwise noted.

Subpart A—General Provisions [Reserved]