Airgas

Wade Holt
Director of FDA Operations
Airgas, Inc.
618 Gallego Ave.
Ocoee, FL 34761
(407) 905-8812 Fax: (407) 905-8813
http://www.airgas.com
wade.holt@airgas.com

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Docket Management Branch (HFA-305)

U.S. Public Health Service

Food and Drug Administration

5630 Fishers Lane, rm.1061

Rockville, MD 20852

RE: [Docket No. 2003D-0165]

Comments to proposed Guidance – Draft Guidance for Industry on Current Good Manufacturing Practice for Medical Gases - 68 Federal Register 24005, May 6, 2003.

Dear Sir or Madam:

Airgas, Inc. (NYSE: ARG), comprised of 22 wholly owned subsidiary companies, is the largest U.S. distributor of industrial, medical and specialty gases, welding, safety and related products. Its integrated network of nearly 800 locations includes branches, retail stores, gas fill plants, specialty gas labs, production facilities and distribution centers. Airgas also distributes its products and services through an extensive list of dealers and home respiratory care companies, as well as e-Business, catalog and telesales channels.

Airgas fully supports the Agency's efforts to strive for continuous improvement in the Compressed Medical Gas industry. Airgas is a proud member of the Compressed Gas Association and has devoted a substantial amount of time to the development of safety and regulatory standards for the compressed gas industry. We are a leader in embracing new technologies and practices that enhance public safety, both inside and outside of the medical gas arena. However, we feel compelled to respond to the proposed Guidance and to address some of those items that are technically incorrect, contradictory, do not conform to current good industry practice, or offer no benefit to patient safety.

This response identifies a number of items in the proposed Guidance found to be in technical disagreement with standard industry practices. Disagreement is also found with the premise under which the document, as a whole, is proposed, as the proposed Guidance is filled with language of a mandatory nature and completely negates the former guidelines. Guidance documents are required to be a compilation of recommendations provided by the FDA on how to comply with the Current Good Manufacturing Practices during the manufacturing and distribution processes for medical gases. The proposed Guidance document mandates certain practices throughout its contents, which is equivalent to promulgating regulation without the benefit of an economic impact study that would accompany such a proposal.

Our experiences with “Fresh Air”, which evidently formed the basis for the proposed Guidance, leads us to believe that this document will be used both as a training source and field guide for inspectors. We base this on the fact that “Fresh Air” continued to be used as the basis for citations even after the Agency issued the stay to “Fresh Air” on April 27, 2000. This became so problematic that when inspectors showed up at our facilities with a copy of “Fresh Air” in hand, we would provide them with a copy of the above letter.

We believe that the proposed Guidance document fails to recognize and utilize a risk-based approach when making many of the recommendations and mandates listed therein. The compressed gas industry has experienced only a minuscule number of incidents in the last hundred years, in spite of the millions of uses of our products on a daily basis. Airgas has identified more than 40 instances where the proposed Guidance takes a section of the regulations, replaces or inserts the words “medical gases” or some other phrase unique to our industry, and then presents this as if it were a direct quote of the regulations, complete with section number reference. It is inappropriate to propose Guidance and then re-write the regulations to support what is being proposed. The following is an example presented as if it were a direct quotation of §211.25(a); it is not.

> *“Each person engaged in the manufacturing, filling, processing, packing, or holding of a medical gas must have the education, training, and experience, or a combination thereof, to enable that person to perform the assigned functions. Training must be in the particular operations that the employee performs and in current good manufacturing practice regulations as they relate to the employee’s functions. Training in the CGMP regulations must be conducted by qualified individuals on a continuing basis and with sufficient frequency to ensure that employees remain familiar with CGMP requirements applicable to them (§211.25(a)).”*

A false and inaccurate premise of the proposed Guidance is the statement, “*FDA has investigated a number of deaths and injuries resulting from medical gas mix-ups. In all of these incidents, the injuries and deaths could have been prevented if the manufacturer had followed the CGMP and industry standards.”* This statement is absolutely <u>not</u> true. Manufacturers are not responsible for even a majority of the incidents that have resulted in death or injury to medical gas users over the past 25+ years. In most cases, the end-user tampered with or circumvented industry safeguards by deliberate and sometimes elaborate means. Such a statement must not be used to justify a CGMP.

The CDRH Manual for the Good Guidance Practices (GGP) Regulations; Final Guidance for FDA Staff lists provisions for the public to suggest that FDA withdraw a Guidance document if it is no longer relevant or accurate. We believe the proposed Guidance is so technically flawed that it should be withdrawn. We recommend that the FDA continue to use the 1989 Medical Gas Guideline until such time as an accurate and meaningful revision can be completed. We strongly recommend the Agency work with industry in the development of such a revision. Airgas stands ready to assist the Agency, and is willing to commit the time and resources necessary to produce a meaningful and accurate Guidance revision.

To that end, we would respectfully offer a non-exclusive sampling of our specific concerns for your consideration:

1 **Section:** **Statutory and Regulatory Requirements**

Line: 58-62

Statement: Manufacturers of medical gases must follow the requirements in the CGMP regulations to comply with section 501(a)(2)(B). For example, each time a medical gas is filled into another container, finished product testing must be performed in accordance with § 211.165(a).

Issue: See underlined text. As written, the Guidance would require testing in instances where testing is redundant without potential benefit to patient health. There are a number of instances where "medical gas is filled into another container" but testing cannot be performed because there are no provisions for product withdrawal.

Rationale:

- Hospital/healthcare installations are qualified for and dedicated to medical service. These facilities receive USP/NF product with a Certificate of Analysis (COA). The finished product is tested prior to introduction into the supply system. Industry practice is that after initial qualification of a storage tank, subsequent testing is not required after each delivery.
- Product poured into open-faced dewars, (e.g., liquid nitrogen used for removing warts at a dermatology office), is taken from a medical source and is not tested and cannot be tested through conventional means, as there is no vapor withdrawal port.
- The Guidance document describes instances where product transferal does not trigger analytical requirements, such as in the case of homecare units filled from curbside, and should recognize that there are several circumstances where product transferal would not trigger analytical requirements.

Recommendation: Remove the underlined text from the document to prevent confusion in the field. The current guidelines fully address known instances where patient safety could be adversely affected by the failure to test.

2 **Section:** **Statutory and Regulatory Requirements**

Line: 65-75

Statement: A number of injuries and deaths have resulted from mix-ups of medical gases associated with CGMP violations including:

- Mislabeling (in some cases the container had two or more labels)
- Inadequate training, including training of medical gas filling personnel as well as delivery personnel
- Inadequate finished product testing
- Inadequate quality control unit
- Failure to qualify equipment prior to use (e.g., stainless steel hoses, large cryogenic containers)
- Inadequate written procedures for manufacturing, processing, testing

Issue: The number of injuries and deaths associated with CGMP violations attributed to our industry.

Rationale: The majority of these incidents have been attributed to the compressed gas industry when, instead, most of the incidents have been due to the end-user deliberately circumventing safety features already in place.

Recommendation: Remove inaccurate generalizations such as this in the Guidance document.

3 Section: **Organization and Personnel / Responsibilities of the Quality Control Unit**

Line: 113-114

Statement: We recommend that the QCU perform more than a testing function, be independent of the production process, and have both quality assurance and quality control responsibilities.

Line: 120-121

Statement: In a well-structured and well-defined corporate structure, the QCU would be included as a separate unit.

Issue: Independence of the Quality Control Unit.

Rationale: Cross-utilization of staff is an acceptable practice provided employees have been trained in the function of the QCU and that they recognize this is their only responsibility when acting in this capacity. Unlike traditional pharmaceutical industries, the typical medical gas plant has very few employees. If each medical gas plant were not allowed to cross-utilize staff, and had to provide dedicated QCU personnel, a large number of the medical gas filling facilities would be shut down resulting in a significant impact to patient supply and the availability of oxygen in small communities.

Recommendation: Restate to clarify that cross-utilization of staff is acceptable (with appropriate training standards). If the Agency has some new statistics on why this is no longer acceptable, they should be shared with the compressed gas industry.

4 Section: **Buildings and Facilities**

A. Design and Construction

Line: 207-209

Statement: The Agency also recommends the creation of quarantine areas to separate incoming medical gases, high-pressure cylinders, cryogenic containers, manufacturing equipment, rejected containers and closures, and the finished product. No matter how large your operation, we recommend you avoid storing industrial gases and medical gases in close proximity to each other.

Issue: The separation of compressed gas cylinders, manufacturing equipment and rejected containers and closures.

Rationale: The Guidance recommends that areas be created for incoming medical gases, high-pressure cylinders, cryogenic containers, manufacturing equipment, rejected containers and closures, and the finished product be separated. This recommendation does not take into consideration the nuances of the compressed gas industry. The compressed gas industry reuses their containers. These cylinders are delivered and returned on large trucks. These cylinders are picked up at our customers along with industrial gas cylinders. These cylinders are usually unloaded in a staging area to await further separation and qualification. As the Guidance is currently written, it could be construed that this would not be acceptable.

The Guidance goes on to state that "*No matter how large your operation, we recommend you avoid storing industrial gases and medical gases in close proximity to each other*". Cylinders are grouped according to their hazard potential (e.g., oxidizers together, flammables together, etc.). It is not feasible to require that these cylinders not be stored in close proximity to each other, as long as they are clearly separated and identified through signs, physical barriers, delineation markings to floors, etc.

Recommendation: Remove this recommendation from the Guidance document; it is unrelated to patient safety.

5 **Section:** **Buildings and Facilities**

A. Design and Construction

Line: 213-216

Statement: We also recommend that delivery vehicles have well-defined, separate areas for medical gases and industrial gases to prevent mix-ups from occurring. For example, medical and industrial gases could be separated physically in the delivery truck, or a manufacturer could use a unique identifier to distinguish medical gases from industrial gases.

Issue: Defined areas on trucks.

Rationale: The requirement to have separate areas on trucks is not required by law. FedEx, UPS, and the US Postal Service do not have separate areas on their trucks and they transport medical gases. The DOT has specific requirements for segregation and safe loading of hazardous materials, which are followed by industry.

Recommendation: Remove this recommendation from this Guidance.

6 **Section:** **Equipment Cleaning and Maintenance**

Line: 259-260

Statement: We recommend that equipment used in the manufacture of medical gas (e.g., manifolds, pigtails, valve assemblies, hoses and gauges) be cleaned at initial use and if exposed to a contaminant.

Issue: This section could be interpreted that industrial and medical product cannot be manufactured using the same equipment.

Rationale: The Guidance should not preclude a manufacturer from using the same manifold for both medical and industrial gases. Industry practice is to be able to fill medical and industrial cylinders on the same manifold, and has been so for as long as cylinders have been filled. The same product from the same storage tank is used to fill both medical and industrial cylinders. The 1989 Medical Gas Guideline recognized this fact and even allowed for the filling of both medical and industrial gas on the same manifold, at the same time, as long as the industrial cylinders were prepared in the same manner as medical cylinders.

Recommendation: Change or revise the Guidance to be consistent with this rationale and as previously published in the 1989 Guideline.

7 **Section:** Components, Containers and Closures

Line: 379-380

Statement: To avoid the possibility of contamination, we recommend that all high-pressure cylinders and cryogenic containers used for medical gases be dedicated to medical use only.

Issue: There is no justification for dedicated cylinders.

Rationale: As pointed out in the previous item, there is no danger associated with the use of industrial gas cylinders or equipment. The product comes from a medical grade storage tank and is downgraded for industrial use. Medical gas containers can be qualified for alternative applications assuming proper procedures are followed. We also pointed out that industrial gases, and the containers they are filled into, are generally prepared and filled the same way that medical gases are, except for the testing and labeling. This recommendation offers no benefit to patient safety while providing a significant financial hardship for industry.

Recommendation: Remove this requirement.

8 **Section:** **Components, Containers and Closures**

Line: 402-403

Statement: We recommend that cylinders containing liquid be inverted and drained.

Issue: Not all cylinders containing liquid can or should be inverted and drained.

Rationale: We understand that in some cases it may be appropriate to invert and drain a cylinder that may contain a foreign liquid substance. However, there are some cylinders that are specifically intended to contain liquid. To make a broad statement that cylinders containing liquid be inverted and drained will bring much confusion to the field and misinterpretation by inspectors. Moreover, there are many cases where liquefied gas cylinders are not and cannot be inverted and drained, as in the case of cryogenic cylinders. Liquefied gas cylinders such as carbon dioxide and nitrous oxide are only inverted using racks made for this purpose, and only when the actual weight exceeds the cylinder's tare weight markings, after residual product has been removed. Inverting medical gas cylinders can be dangerous and exposes plant personnel to injury.

Recommendation: Clarify the Guidance document, if the intent was to address potential removal of liquefied contaminants, such as water.

9 **Section:** **Components, Containers, and Closures**

A. General Recommendations

3. Dedication of Large Cryogenic Cylinders to Medical Use Only

Line: 472-473

Statement: To avoid the possibility of industrial contaminants, we recommend that large cryogenic containers used to contain medical gases be dedicated to medical service only.

Issue: That we should dedicate large cryogenic cylinders to medical use only.

Rationale: We do not feel that the law requires us to dedicate specific cylinders to medical service only. We believe that as long as the company's SOP makes adequate provision for qualifying the cylinder prior to the introduction and release of a medical gas, and that the existing procedures are followed, that there is no reason to dedicate assets.

Recommendation: Remove this recommendation from the Guidance document and retain the existing procedures.

10 **Section:** **Components, Containers, and Closures**

B. Retesting of Containers

Line: 506-509

Statement: Containers and closures must be retested or reexamined, as appropriate, for identity, strength, quality, and purity and approved or rejected by the QCU in accordance with §211.84 as necessary (e.g., after storage for long periods or after exposure to air, heat or other conditions that might adversely affect the medical gas container or closure) (§211.87).

Issue: Misquote of §211.87.

Rationale: The word "component" has been omitted from this inaccurate reference to the regulation, which substantially changes the intent of the regulation. Components must be tested for identity, strength, quality, and purity after storage for long periods of time before they can be added to the drug product. If a component or excipients have been in storage for a long period of time, it is possible they could have lost their potency.

Compressed gas cylinders cannot be tested for strength, quality, or purity. Pill bottles that are purchased in bulk and sit for long periods of time can conceivably become contaminated and must be examined for the absence of contamination. High-pressure cylinders are equipped with gas-tight valves and do not have the same potential for contamination with dust or moisture as a conventional container closure, i.e., a pill bottle.

Recommendation: Retain the existing regulations.

11 **Section:** **Charge-in of Components**

Line: 568-569

Statement: Each component must be added to the batch by one person and verified by a second person (§211.101(d)).

Issue: Each component must be added to the batch and confirmed by a second person only if the testing protocol does not verify that the proper components were added, and that any improper components were not added.

Rationale: Testing can be an acceptable alternative to visual verification of component addition. Unlike a traditional pharmaceutical, most CMG products, including the most common, oxygen, are not made up of multiple chemicals blended to make a single drug. Even if the drug gas mixture is made up of two or three components, each gas is already being identified through finished product testing or verification of supply gas.

As this statement is written, second person verification would be required even if only one component were used. The final review includes a verification of the analytical results.

Recommendation: Modify reflect acceptability of testing verification or remove the statement altogether.

12 **Section:** **Packaging and Labeling Controls**

Line: 572

Statement: Net content statement indicated on the label in accordance with section 502(b)(2) of the act.

Line: 739-741

Statement: We recommend that the net contents appear on the body label or shoulder label and not on (1) a removable tag, (2) a certificate of analysis, or (3) a small separate sticker.

Issue: Recommendation that the net contents appear on the body label or shoulder label and not on (1) a removable tag, (2) a certificate of analysis, or (3) a small separate sticker.

Rationale: It has been an industry safety practice to indicate the net contents on a separate sticker. We believe that requiring the net contents to appear on the product label could lead to the wrong label being applied to cylinders.

Airgas fills over 40 different styles of oxygen cylinders. Indicating the net contents on the label would require Airgas to have 40 different labels for the same gas product, or one label with 40 different net content marking provisions. This would dramatically increase the possibility of a cylinder going out with the wrong net content markings indicated and would adversely affect patient safety.

Recommendation: Retain the current procedures.

13 Section: **Calculation of Yield**

Line: 628-631

Statement: Actual yields and percentage of theoretical yield must be determined at the conclusion of each appropriate phase of manufacturing, processing, packing, or holding of gases. Such calculations must be performed by one person and independently verified by a second person. FDA recognizes that accurate inventory records and reconciliation of use are difficult to maintain for liquefied gases. Normal losses of gas occur through vaporization, the filling process, and venting and could reach 10 percent or more.

Issue: We do not feel that it is appropriate for this class of product, as the losses are anticipated and occur naturally, and do not represent misuse of a drug product.

Rationale: The use of a theoretical yield and its comparison to a calculated actual yield does not provide any additional process control given the significant losses that occur through vaporization (Normal Evaporation Rate (N.E.R.) of the bulk container) and the product mix (high-pressure cylinder filling, cryogenic container filling). The Agency has previously acknowledged the validity of the industry argument to exempt medical gases from the requirement for calculation of yields and reconciliation.

Recommendation: Please remove this recommendation.

14 Section: **Packaging and Labeling Controls**

A. Materials Examination and Usage

Line: 675-676

Statement: Upon receipt from the printer, labels would be counted to verify the quantity received and would be examined to ensure correctness when compared against the master label.

Issue: Verification of the quantity of labels received from the printer.

Rationale: Cylinder labels are purchased on rolls of 250, 500, or even 1,000 each. The labels must be purchased in bulk in order to be cost efficient. It is not uncommon to order in lots of 10,000 to 100,000 or more. There is no benefit to requiring the firm to roll every label off the roll, count it, and roll it back on the spool. In fact, human error is such that it is not practical to attempt to count labels manually in such huge quantities. Labels are issued in smaller more manageable numbers and reconciled to 100% when they are used. We also do not believe the regulations found in §211.125 require that "roll stock" be reconciled.

Recommendation: Retain the current procedures.

15 Section: **Packaging and Labeling Controls**

C. Packaging and Labeling Operations

Line: 753-755

Statement: We recommend the labeling for large permanently mounted containers, trailers, and rail cars bear a statement consisting of “Name of the Medical Gas, Refrigerated Liquid USP or NF,” such as "Oxygen Refrigerated Liquid USP."

Issue: That permanently mounted containers, trailers, and rail cars bear a medical label.

Rationale: The containers listed above are not “final use” containers and therefore should not be required to be labeled with a medical label. There is no advantage to patient safety from this requirement.

Recommendation: Remove this requirement from the Guidance document.

16 Section: **Expiration Dating**

Line: 780-782

Statement: To ensure that a medical gas meets applicable standards of identity, strength, quality, and purity at the time of use, each container must bear an expiration date determined by appropriate stability testing described in §211.166 (§211.137(a)).

Issue: Industry does not believe that compressed medical gas products degrade over time.

Rationale: The Agency has previously agreed with industry in using enforcement discretion and not requiring an expiration date be applied to compressed medical gases.

Recommendation: Retain the current procedures.

17 Section: **Expiration Dating**

Line: 794-799

Statement: The Agency recommends that high-pressure cylinders stored for long periods of time, such as those provided to patients as a back up to their oxygen concentrator, be monitored to ensure they contain the correct net contents (i.e., pressure). We recommend that companies, especially home care companies and durable medical equipment suppliers, establish and follow a written plan to periodically verify the pressure (i.e., net content) of each high pressure cylinder stored at a patient’s home and that the results be documented.

Issue: It is not practical to expect that medical gas manufacturers, home care companies and durable equipment suppliers can go to every individual’s home that uses medical oxygen to perform and document cylinder content checks.

Rationale: Millions of patients use oxygen in the United States on a daily basis. To require these cylinders be tested at patient's homes would be so cost prohibitive that suppliers would simply get out of the business. Further, one of the most common causes of oxygen-related fires are as a result of adiabatic heat of compression. The most common cause is "dead-heading" high-pressure oxygen against a closed piping system. An oxygen pressure gauge, as this provision would require, represents an example of such a system. This requirement would result in an increased risk of oxygen-enriched fires in patient homes.

Recommendation: Remove this requirement.

18 Section: **Warehousing Procedures**

Line: 820-821

Statement: We recommend medical gas containers be stored under protective covering and not be subject to temperature extremes. Based on this recommendation, storage areas would be clean, dry, well ventilated, and free of combustible materials. Also, all valve assemblies, hoses, and other relevant equipment would be protected from contamination such as insect infestation.

Issue: The proposed Guidance is overly burdensome.

Rationale: The environmental conditions under which cylinders are stored will not affect their identity, quality, and purity.

Recommendation: Remove these recommendations.

19 Section: **Holding and Distribution**

B. Distribution Procedures and Recalls

Line: 837-838

Statement: The Agency recommends that delivery vehicles have well-defined, separate areas for medical gases and industrial gases to prevent mix-ups from occurring.

Issue: Delivery trucks should have well-defined, separate areas for medical gases and industrial gases.

Rationale: It is not practical to expect that delivery vehicles could have separate areas for medical and industrial gases. There are many factors to consider when loading a delivery vehicle. Weight distribution and compatibility of gases are just two major considerations. The Department of Transportation (DOT) regulates vehicle loading. Tens of thousands of deliveries are made everyday without incident. Furthermore, the patient health statistics do not justify this change.

Recommendation: Remove this recommendation from the Guidance document.

20 Section: **Laboratory Controls**

B. Testing and Release for Distribution
b. Testing of an oxygen storage tank used to fill large vehicle-mounted cryogenic containers.

Line: 1014-1016

Statement: If a new shipment of oxygen is combined in a storage tank with a previously received, tested, and approved lot, we recommend that the manufacturer test the combined product and approve it before use.

Issue: The requirement to test and approve the new shipment before use.

Rationale: Industry practice has always been to test and approve a new shipment before release. One of the most common ways to accomplish this approval is to test one cylinder from the first medical manifold filling sequence and use this test to also satisfy the storage tank-testing requirement.

Recommendation: Review this recommendation and bring it into line with current industry safe practice.

21 Section: **Laboratory Controls**

2. Liquid-to-Gas; Filling Large Cryogenic Cylinders

Line: 1061

Statement: Each filled large cryogenic container would be tested prior to release.

Issue: That each large cryogenic container filled would need to be tested.

Rationale: In most cases large cryogenic cylinders are top filled with new liquid being added to the residual product. In this case, we would agree that each cryogenic cylinder filled would need to be tested. However, there are occasions where the liquid cylinders are vented and evacuated prior to fill. In this case, only one cylinder from each uninterrupted filling sequence needs to be tested.

Recommendation: Review this recommendation and recognize the situations where liquid cylinders may be vented and evacuated prior to fill to be more consistent with existing policy.

22 Section: **Laboratory Controls**

2. Liquid-to-Gas; Filling Large Cryogenic Cylinders

Line: 1064

Statement: A valid COA would be provided with each cryogenic container.

Issue: The requirement for a COA with each cryogenic container.

Rationale: We are concerned with the recommendation that a COA (Certificate of Analysis) must be supplied with each cryogenic container. The COA is only used by the receiving firm to relieve themselves from full compendial testing. If the filling firm does not provide a COA, the recipient must perform full testing. This section of the Guidance is for the filling firm, not the receiving firms. Therefore, this recommendation does not apply here. If this is not removed, it could be construed that each liquid cylinder a manufacturer ships would have to be accompanied with a COA, which would significantly increase analytical costs without benefit to public safety.

Recommendation: Remove this statement from the Guidance document.

23 Section: **Stability Testing**

Line: 1138-1156

Statement: There must be a written testing program designed to assess the stability characteristics of medical gases. The result of such stability testing must be used in determining appropriate storage conditions and expiration dates. The written program must be followed and must include:

Reliable, meaningful, and specific test methods.

Testing of the medical gas in the same container-closure system as that in which the medical gas is marketed.

An adequate number of batches of each medical gas must be tested to determine an appropriate expiration date, and a record of such data must be maintained.

The Agency recommends that the testing program take into account the compatibility of the valve assembly, the acceptability of the valve packing and the valve seal used, the type of cylinder, and any other factor that can have an effect on the stability of the medical gas. Each medical gas would be tested for stability in the exact container closure that it is marketed in, such as steel high-pressure cylinders, aluminum high-pressure cylinders, and cryogenic containers.

Issue: Cylinders do not leak their contents at a rate that would cause any significant loss of product over several years.

Rationale: The valve manufacturers state their valves have a leak rate in the range of 10^{-3}. This means that a typical medical gas cylinder will only lose approximately 2 liters of product out of a total volume of 660 liters, or more over a period of 5 years. This is an insignificant volume and is, in fact, not an issue, as most products are used in a relatively short time span.

Recommendation: Use enforcement discretion to determine the need for expiration dating.

24 **Section:** **Storage Tank Installations at Healthcare Facilities**

Line: 1576

Statement: Maintain batch production records.

Issue: This section attempts to address bulk storage tank filling as if it were in a form or "batch" as is associated with cylinder filling operations.

Rationale: In a typical delivery environment, batch production records are not used and are impractical. Only records of deliveries are kept. Batch production records have specific requirements such as *Review and Release Before Use* that is just not feasible in a bulk delivery application. One could not stop the flow of medical gas going into a hospital while a *Review and Release Before Use* step was being conducted.

Recommendation: Remove this recommendation from the Guidance document.

25 **Section:** **Storage Tank Installations at Healthcare Facilities**

Line: 1583-1584

Statement: The supply firm would consider itself responsible for the actions of the third party installer.

Issue: The supply firm is being held responsible for the actions of the third party installer.

Rationale: Many hospitals own their own storage tanks and send out bids for their installation as well as the actual supply of product. These installations may change vendors on an annual basis. It is the owner who should be responsible for the installation, whether installed by themselves or a third party.

Recommendation: Remove this statement from the Guidance document.

26 **Section:** **Medical Gas Mix-ups**

Line: 1589-1591

Statement: FDA has investigated a number of deaths and injuries resulting from medical gas mix-ups. In all of these incidents, the injuries and deaths could have been prevented if the manufacturer had followed the CGMP and industry standards.

Issue: The statement that "In all of these incidents, the injuries and deaths could have been prevented if the manufacturer had followed the CGMP and industry standards" is inflammatory, misleading, and has no basis in fact.

Rationale: Manufacturers are not responsible for all of the incidents that have resulted in death or injury to medical gas users. To the contrary, in most cases the end-user tampered with or circumvented safeguards by deliberate and sometimes elaborate means.

Recommendation: Remove this statement from the Guidance document.

27	**Section:**	**Carbon Dioxide and Helium Manufacturers and Wholesale Distributors**
	Line:	1669-1670
	Statement:	The Agency recommends that all tankers or trailers used for the delivery of carbon dioxide be dedicated to medical use only.
	Issue:	As long as the trailer is properly qualified, there is no need to dedicate assets. All tankers and trailers can be qualified for alternative applications assuming proper procedures are followed.
	Rationale:	Dedicated trailers do not add any benefit to public safety.
	Recommendation:	That the Agency remove this recommendation.

Conclusion:

Airgas stands ready to work with the Agency to produce a meaningful and accurate Guidance document. Please let me know if you have any specific questions or concerns. I may be reached at my office at (407) 905-8812, or via email at wade.holt@airgas.com.

Sincerely,