



DEPARTMENT OF HEALTH & HUMAN SERVICES

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2/11/97  
3/3/97

Public Health Service

Food and Drug Administration  
1141 Central Parkway  
Cincinnati, OH 45202

February 28, 1997

**WARNING LETTER**  
CIN-WL-97-221

**CERTIFIED MAIL**  
**RETURN RECEIPT REQUESTED**

Durenda M. Holt,  
Operations Manager  
Housecalls  
18 Troy Rd. Shopping Center  
Delaware, OH 43015

Dear Ms. Holt:

During a January 29 - February 3, 1997 inspection of your compressed medical oxygen transfilling facility, located at the above address, our investigator documented serious deviations from the Current Good Manufacturing Practices Regulations (Title 21 Code of Federal Regulations, Part 211). These deviations cause your drug product, Oxygen USP, to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act).

Specific observations made during the Inspection include:

- (1) Failure to withhold each lot of incoming bulk liquid oxygen from use until that lot has been sampled, tested or examined as appropriate and released for use. FDA provides for three different methods by which this can be accomplished. These are described under Liquid to Liquid Filling on page 4 of the attached document Fresh Air "96".
- (2) Failure to assure that each lot of compressed medical oxygen gas manufactured conforms to the appropriate USP specifications for purity prior to shipment in that samples are drawn directly from the manifold and not the final product container.
- (3) Failure to calibrate or document the calibration of your ~~XXXXXXXXXX~~ Oxygen Analyzer at least once each day of use. Calibration records are missing for at least six (6) production dates.

- (4) Failure to properly calibrate the ~~XXXXXXXXXX~~ Oxygen Analyzer in that the Oxygen standard gas used to calibrate (adjust the span) and the Nitrogen used to zero the analyzer are not acceptable standard gases.

Standard gases used must be purchased from a specialty gas manufacturer, since problems may result from many other types of firms selling gases used as a reference standards. The Oxygen standard gas used to adjust the span must be at least 99.0% purity and must include a lot specific Certificate of Analysis which must be maintained on file. While 99.0% is the minimum purity for this standard, we recommend that the oxygen standard used for span adjustment be at least as high as the highest purity tested. The Nitrogen standard gas used to zero the analyzer must be at least 99.9% purity with the purity level documented on a Certificate of Analysis.

- (5) Failure to perform or document inspections of high pressure cylinders in that results are not recorded for odor test, hammer test (not required for aluminum cylinders), fill leak test, pressure and temperature of transfilled cylinders.
- (6) Failure to perform or document inspections of cryogenic home units for condition of external vessel, valve, contents gauge and labeling.
- (7) Failure to establish and maintain adequate written operating procedures in that the current procedures do not explain in adequate detail the requirements for the following:
  - (a) high pressure cylinder tests and inspections for odor test, hammer test (not required for aluminum and fiber wrapped cylinders), and fill leak test
  - (b) inspection during filling of cryogenic home units for external vessel condition, valve inspection, contents gauge and label inspection
  - (c) label control procedures to document the receipt, inspection and acceptance of incoming labels; label access control; and reconciliation of labels used, returned and destroyed.

- (8) Failure to assign unique lot numbers for every manifold sequence of high pressure cylinders filled, and for each filling sequence of cryogenic home vessels filled on site. For liquid oxygen filled onsite into cryogenic home vessels, separate lot/batch numbers are required for each uninterrupted filling sequence filled from a specific Dewar or bulk source lot. If additional vessels are filled from the same source/Dewar the next day, a new lot number should be assigned to those vessels.
- (9) Failure to review and approve production and control records, by responsible personnel, prior to release and shipment of medical gases. This review must be performed at least once each day of production. The review must be performed by a knowledgeable individual other than the person performing the filling. The review should identify any failure in product specifications, testing, or failure to follow established standard operating procedures and current Good Manufacturing Practices.
- (10) Failure to calibrate the production thermometer according to an established written standard operating procedure.
- (11) Failure to perform training in current Good Manufacturing Practices with sufficient frequency to ensure the employees are familiar with the requirements of their job. One operator has not received any training since having received on-the-job training in 1993.

The above described violations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure that you adhere to all current regulations applicable to your operations. Federal agencies are advised of the issuance of all warning letters about drugs so that they may take this information into account when considering the award of contracts.

By copy of this letter, we are advising Health Care Finance Administration (HCFA) that our inspection of your firm revealed significant deviations from the Act. They may elect to defer or discontinue payment for any health care product in violation of state or federal law.

You should take prompt action to correct these violations. Failure to achieve

prompt correction may result in regulatory action without further notice. These include seizure and/or injunction.

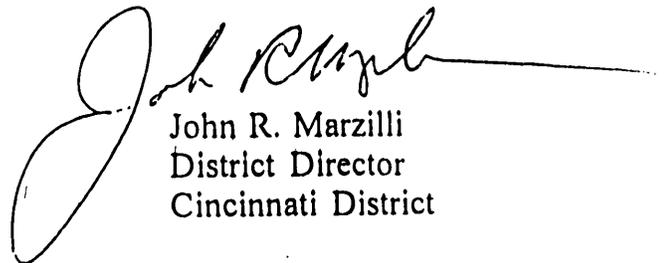
For your information, I have enclosed copies of: (1) the FDA speech "FRESH AIR '96" - A LOOK AT FDA'S MEDICAL GAS REQUIREMENTS", which describes current FDA requirements and policy on medical gases; and (2) "Compressed Medical Gases Guideline", revised February 1989.

Please advise us in writing within fifteen (15) working days of receipt of this letter of the specific actions you are taking to correct these violations. Your response should explain each step you have taken to correct the noted violations, including steps taken to prevent recurrence of similar violations. Include any documentation showing these corrections.

If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be sent to the U.S. Food and Drug Administration, 1141 Central Parkway, Cincinnati, Ohio 45202-1097, to the attention of Charles S. Price, Compliance Officer. Any questions regarding this letter may be directed to Mr. Price at telephone (513) 684-3501.

Sincerely,



John R. Marzilli  
District Director  
Cincinnati District

Enclosure: 1) Speech: Fresh Air "96"  
2) Compressed Medical Gas Guideline