



Food and Drug Administration
Denver District Office
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February 1, 2001

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Kenneth K. Preuss
President
Respiratory Services, Inc.
15701 East 1st Avenue, #101
Aurora, Colorado 80011

Ref. # DEN- 01-17

Dear Mr. Preuss:

During an inspection of your firm, Respiratory Services, Inc., 15701 East 1st Avenue, #101, Aurora, Colorado, on September 6 through September 12, 2000 Consumer Safety Officers Theresa B. Madison and Karen G. Hirshfield determined that your firm transfills high pressure gas cylinders and liquid Medical Oxygen U.S.P. to patient home cryogenic units. Medical Oxygen is a drug product as defined by section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above stated inspection revealed that your gas and liquid Oxygen, U.S.P., is adulterated under section 501(a)(2)(B) of the Act in that the controls used for the manufacturing, processing, packing, or holding of this product are not in conformance with current good manufacturing practice regulations (GMPs) under Title 21, Code of Federal Regulations, parts 210 and 211 (21 CFR 210 and 211). Deviations noted during the inspection include, but are not limited to the following:

1. Failure to test each lot of incoming liquid oxygen for identity and strength prior to filling large cryogenic units, or in lieu of such testing, failure to maintain a report or certificate of analysis from the supplier of the incoming liquid oxygen, to assure that the component conforms with written specifications, as required by 21 CFR 211.84(d)(2). For example, there were no Certificates of Analysis for several lots ([X X X X X X] and [X X X]) of liquid Oxygen distributed to patients. Our investigators also noted several Certificates of Analysis received by your firm failed to have the strength of the Oxygen USP recorded.
2. Failure to properly calibrate instruments, as required by 21 CFR 211.160 (b)(4). For example, your firm does not have the high purity Oxygen standard required to calibrate the

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Servomex Oxygen Analyzer used for the assay of Oxygen U.S.P. Our investigators noted that your firm is using "Medical Grade" Oxygen to calibrate the oxygen analyzer, instead of a certified, calibration gas, as stated in the manual. Also, your firm failed to document the calibration of the oxygen analyzer prior to the manufacturing and release of the high pressure Oxygen USP.

3. Failure to determine satisfactory conformance to final specifications, including identity and strength, as required by 21 CFR 211.165(a). For example, your firm does not always assay a filled cylinder from each manifold filling sequence for identity and purity.
4. Failure to test containers for conformance with all appropriate written procedures, as required by 21 CFR 211.84(d) (3). For example, your firm does not always perform pre-fill, fill and post-fill checks on high-pressure Oxygen USP cylinders.
5. Failure to establish written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they are represented to possess, as required by 21 CFR 211.100(a). Your firm has no written specifications for the acceptance or rejection of transfilled compressed Oxygen U.S.P.
6. Failure to establish a quality control function with the responsibility to approve or reject all components, drug product containers, labeling, and drug products, and the authority to review all records to assure that no errors have occurred, as required by 21 CFR 211.22(a). For example, batch numbers and assay percentages are not always documented on your Daily Log as required by your firm's written procedures. Also, discrepancies were noted between the manufacturing date and the lot number sticker on the Oxygen Transfill Batch Production Records.
7. Failure to assure that each person engaged in the packing or holding of a drug product has the education, training, and experience to enable that person to perform the assigned functions, as required by 21 CFR 211.25(a). For example, your firm failed to have documentation showing that your drivers who witness the analytical testing procedures have received training on the calibration and operation of your supplier's oxygen analyzer.

The above identification of violations is not intended to be an all inclusive list of deficiencies at your facility. As President, it is your responsibility to assure adherence with all requirements of the Act and Good Manufacturing Regulations.

These deviations may be indicative of corporate wide non-compliance. We recommend that you conduct internal audits at all your medical gas facilities and appropriate action taken to assure that similar violations are not occurring at other locations.

By copy of this letter, we are advising the Health Care Financing Administration (HCFA) that our inspection of your firm revealed significant deviations from the Food, Drug and Cosmetic 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 deviations. Failure to promptly correct these deviations may result in regulatory action, including seizure or injunction, without further notice.

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Federal agencies are advised of the issuance of all warning letters so that they may take this information into account when considering the award of contracts.

We are in receipt of your December 19, 2000, response to the FDA-483. Regarding your response, we have the following comments: With respect to the calibration of your oxygen analyzers, your procedure states to use a "pure source of oxygen of at least ~~99%~~." Please be aware that you must follow the manufacturer's specifications for each analyzer and assure that ~~99%~~ is, in fact, the required concentration by the manufacturers. You have not outlined the specific steps each driver receives during training, therefore, it is not possible to assess the adequacy of the "Driver Training" procedures proposed. Regarding the "Quality Control Unit" procedure, you do not include the frequency of the review by your Quality Control Unit. The procedure mentions a "yearly review" but it is unclear what this entails. Many of the deficiencies noted during our inspection would have been detected had you conducted daily reviews of your records. Therefore, it is important that your operations and records are continually reviewed by your Quality Control Unit. Finally, you included copies of the "Daily Log," "Cylinder Log," "Servomex Calibration Log" and "Quality Improvement Form" with your response. These forms do not have a place for sign-off to indicate they have been reviewed. Per the "Quality Control Unit Procedure" included in your response, you state that, "...branch managers or their designate shall be responsible to review all delivery logs, certificates of analysis, distribution forms and any other paperwork necessary to assure compliance with FDA standards..." and that "All reviewed documents will be initialed and dated by QCU personnel."

Please advise this office in writing, within fifteen (15) working days after receipt of this letter, of any additional actions you have taken to correct the violations. Your response should include: (1) each step that has or will be taken to completely correct the current violations and prevent the recurrence of similar violations; (2) the time when correction will be completed; (3) any reason why the corrective action is not completed within the response time and (4) any documentation necessary to indicate correction has been achieved. Your response should be directed to Ms. Regina A. Barrell, Compliance Officer, at the above address.

Sincerely,



Thomas A. Allison
District Director

cc: Mr. Adam Trujillo, Regional Administrator
Health Care Financing Administration, DHHS Region VIII
1600 Broadway, Suite 700
Denver, Colorado 80202-4967

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