



1/14/98/22/48
REW

D1052 B

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Food and Drug Administration
7200 Lake Ellenor Drive
Orlando, FL 32809

WARNING LETTER

FLA-98-14

December 16, 1997

Mr. G. William Sievert
Chief Executive Officer
Manatee Respiratory Services
4301 32nd Street West, Suite C18
Bradenton, Florida 34205

Dear Mr. Sievert:

Inspection of your medical gas filling operation on November 12, 13, 19, and 25, 1997, by FDA Investigator Nicolas Rivera, revealed serious violations of the Federal Food, Drug, and Cosmetic Act (the Act). The investigator documented significant deviations from the Current Good Manufacturing Practice (CGMP) Regulations for drugs [Title 21, Code of Federal Regulations, Parts 210 and 211 (21 CFR 210 and 211)] in conjunction with the testing and release for distribution of compressed medical oxygen causing the products to be adulterated within the meaning of Section 501(a)(2)(B) of the Act.

Inspection revealed that there is no assurance that your medical oxygen products meet applicable standards of identity, strength, quality and purity in that you have failed to test each component lot of bulk compressed oxygen to determine conformance with appropriate specifications prior to use, or in lieu of testing, receive a valid certificate of analysis from your supplier and conduct an identity test. Refilled cylinders of compressed medical Oxygen USP are not being tested for purity and identity prior to release for distribution.

Written procedures are not established for all production and process controls designed to assure that your medical oxygen products have the identity, strength, quality, and purity they are represented to possess. For example, no written procedures are established for calibration and maintenance of equipment, labeling, distribution, handling of complaints, product recall, or employee training. No documentation is available to show that personnel have been adequately trained.

Mr. G. William Sievert
Page 2
December 16, 1997

Batch production and control records are incomplete and fail to document that each significant step in the manufacturing operation was accomplished, such as all required pre and post fill cylinder inspections and tests. Records are not maintained documenting calibration and maintenance of the oxygen analyzer used by your firm. The analyzer is not being calibrated properly as specified by the manufacturer. For example, no certified nitrogen of known purity is available to "zero" the analyzer. A review of batch records from November 2, 1997 to November 12, 1997, disclosed that the purity test results recorded on the records remained constant at 99%. The analyzer used provides readings past a decimal point which are not recorded on the batch records. No documentation is available to show that batch records are reviewed and approved by a supervisor prior to release of the batch for distribution.

Review of labeling used on cylinders of compressed medical oxygen filled by your firm reveals the products to be misbranded within the meaning of Section 502(b)(1) of the Act in that the labels fail to bear the place of business of your firm.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that all medical gas products you repack and distribute are in compliance with the Act and the requirements of the CGMP regulations. You should take prompt action to correct these violations. Failure to correct these violations may result in regulatory action, including seizure and/or injunction, without further notice.

Federal Agencies are advised routinely of the issuance of all warning letters issued so that they may take this information into account when considering the award of contracts. Additionally, pending applications for Agency approval (NDA, ANDA, SNDA, etc.) or export approval requests may not be approved.

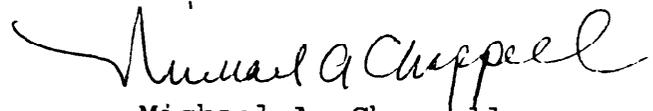
In order to facilitate the Food and Drug Administration (FDA) in making a determination that such corrections have been made and thereby enabling FDA to withdraw its advisory to other Federal agencies concerning the award of government contracts, and to resume review of any pending applications, we request that you notify this office when corrective actions are completed and you believe your facility is in compliance with the CGMP regulations so that a verification inspection can be scheduled.

We request that you notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct these violations. If corrections cannot be completed within 15 working days, state the reason for the delay and the time frame within which corrections will be completed.

Mr. G. William Sievert
Page 3
December 16, 1997

Your reply should be directed to Jimmy E. Walthall, Compliance Officer, U.S. Food and Drug Administration, 7200 Lake Ellenor Drive, Suite 120, Orlando, Florida 32809, telephone (407) 648-6823, extension 263.

Sincerely,

A handwritten signature in cursive script that reads "Michael A. Chappell". The signature is written in black ink and is positioned above the typed name.

Michael A. Chappell
Acting Director
Florida District