



DEPARTMENT OF HEALTH AND HUMAN SERVICE

Public Health Service

HFI-35(PURGE)

MD7901

CFN: 1125350

Food and Drug Administration
Baltimore District Office
900 Madison Avenue
Baltimore, MD 21201-2199
Telephone: (410) 962-3461 x122
FAX: (410) 962-2219

June 15, 1999

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Barry A. Kuhne, President
Signature Healthcare, Inc.
8 Bocster Court
Phoenix, Maryland 21131

Dear Mr. Kuhne:

A Food and Drug Administration (FDA) inspection was conducted May 25 - 26, 1999 at your facility in Reisterstown, Maryland. The inspection determined that you manufacture Liquid Oxygen, U.S.P., a drug product as defined by Section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act).

During our inspection, deviations from the Current Good Manufacturing Practice (GMP) regulations (Title 21, Code of Federal Regulations (CFR), Part 211) were observed. These deviations cause your medical gas to be adulterated within the meaning of Section 501(a)(2)(B) of the Act, in that the methods used in, or the facilities or controls used for, manufacturing, processing, packing, storage, or holding, are not in conformance with the GMP regulations.

The deviations included the following:

1. Failure to test or examine incoming liquid oxygen for conformity to all appropriate specifications for purity, strength, and quality.
2. Failure to determine that each batch of transfilled Liquid Oxygen, U.S.P. conforms to final specifications prior to release.
3. Failure to test or examine home cryogenic vessels for conformity to all appropriate written procedures.
4. Failure to prepare batch production and control records for each batch of Liquid Oxygen, U.S.P. that is transfilled.

5. Failure to have a quality control unit responsible for approving or rejecting all incoming Liquid Oxygen, U.S.P., home cryogenic units, labeling, and transfilled home cryogenic units; reviewing production records for errors; and investigating when errors occur.
6. Failure of any quality control unit to review Liquid Oxygen, U.S.P. production and control records to determine compliance with all established, approved written procedures before a batch is released or distributed.
7. Failure to establish and follow written procedures for all operations, including, but not limited to, a quality control unit, pre-fill operations, analytical testing, distribution, and recall complaint handling, designed to assure that the Liquid Oxygen, U.S.P. has the identity, strength, quality, and purity it is represented to possess.
8. Failure to document the training of all individuals engaged in the manufacture, processing, and packing of Liquid Oxygen, U.S.P.
9. Failure to identify transfilled Liquid Oxygen, U.S.P. vessels with a lot or control number that permits determination of the history of the manufacture and control of each batch.
10. Failure to have a separate or defined area or other control procedure to prevent mix-ups during the quarantine storage of Liquid Oxygen, U.S.P.

We acknowledge a response to the investigator's observations listed on FDA Form 483 from Mr. Michael J. Mayfield, Vice President of Operations, dated June 4, 1999. He states that you promptly ceased transfilling operations and arranged to have your home cryogenic units filled by [REDACTED] and included the necessary safeguards to assure that the Liquid Oxygen, U.S.P. has the identity, strength, quality, and purity it is represented to possess. This action, if properly implemented, appears to adequately address the aforementioned violations.

However, in his response, Mr. Mayfield states that it was your intention to resume transfilling of Liquid Oxygen, U.S.P. by August 26, 1999. Therefore, please notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you will take to correct the noted violations and to prevent their recurrence after you resume transfilling. Also, please notify this office in writing when you are again transfilling Liquid Oxygen, U.S.P. at your facility. Additionally, Mr. Mayfield's response is silent in reference to the actions you have taken regarding Liquid Oxygen, U.S.P. distributed by your firm prior to the FDA inspection.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to all requirements of the Act and regulations.

The specific violations noted in this letter and on the FDA-483 issued to and discussed with Mr. Mayfield at the closeout of the inspection, may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If you determine the causes to be systems problems, you must promptly initiate permanent corrective action.

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Federal agencies are advised of the issuance of all Warning Letters concerning drug products so that they may take this information into account when awarding contracts. By copy of this letter, we are advising the Health Care Financing Administration (HCFA) that our inspection 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 deviations. Failure to do so may result in regulatory action without further notice. These actions include, but are not limited to, seizure and/or injunction.

Your replies should be sent to the Food and Drug Administration, Baltimore District, 900 Madison Avenue, Baltimore, Maryland 21201, to the attention of Thomas C. Knott, Compliance Officer. Mr. Knott can be reached at (410) 962-3461, extension 122.

Sincerely,



Elaine Knowles Cole
Director, Baltimore District

cc: Mr. Michael J. Mayfield
Vice President, Operations
Signature Healthcare, Inc.
234 Business Center Drive
Reisterstown, Maryland 21136

Maryland Board of Pharmacy
4201 Patterson Avenue
Baltimore, Maryland 21215-2299