DEPARTMENT OF HEALTH AND HUMAN SERVICES

Refer to FEI: 3003807546

Food and Drug Administration
Baltimore District Office
Central Region
6000 Metro Drive, Suite 101
Baltimore, MD 21215
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03-BLT-16

June 9, 2003

WARNING LETTER

VIA CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. David P. Drennen, President
Nicholas Pharmacy, Inc.
421 Main Street
Summersville, West Virginia 26651

Dear Mr. Drennen:

The Food and Drug Administration (FDA) inspected your medical oxygen gas transfilling facility located at the above cited address on March 20 and 21, 2003. Medical gases are drug products as defined by Section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act). Our inspection found significant deviations from the Current Good Manufacturing Practice (CGMP) regulations for drug products, set forth in Title 21, Code of Federal Regulations, (21 CFR), Parts 210 and 211. These deviations cause your product, medical oxygen 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 the manufacturing, processing, packing, storage or holding of your product are not in conformance with CGMP regulations. In addition, cylinders of Oxygen U.S.P. manufactured by your firm are misbranded within the meaning of Section 502(f)(1) of the Act in that they fail to bear drug labels with adequate directions for use.

The deviations observed during the inspection include the following:

1. Failure to assay each batch of drug product produced to determine satisfactory conformance to final specifications for the drug product, Oxygen U.S.P., including identity and purity prior to release as required by 21 CFR 211.165. For example, no assay was performed on lot numbers 010903, 011303, and 011703. Although batch records for lot numbers 021703 and 021803 document the filling operations for a total of 99 size E cylinders, no pre-fill, fill, and post-fill tests, including assay tests were completed. In addition, finished product odor tests are not done as required by the Oxygen USP monograph.

2. Failure to establish proper laboratory controls in that there is no documentation to show that the [redacted] Oxygen Analyzer used to test Oxygen U.S.P. for purity has been calibrated at suitable intervals as required by 21 CFR 211.160(b)(4). For example there are no calibration records for this instrument.

3. Failure to establish and implement scientifically sound and appropriate procedures designed to assure that your drug product conforms to appropriate standards of identity, strength, quality, and purity as required by 21 CFR 211.160 (a) and (b). For example, your firm failed to establish written procedures for the sampling and testing of each lot of incoming and outgoing compressed medical oxygen cylinders.

4. Failure to establish a Quality Control Unit (QCU) that has the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products and the authority to review production records to assure that no errors have occurred as required by 21 CFR 211.22 (a). Failure to have written procedures defining the responsibilities of the QCU unit as required by 21 CFR 211.22 (d). In addition, your production and control records (e.g., batch records) are not reviewed by a QCU as required by 21 CFR 211.192.

5. Failure to establish adequate written procedures for production and process control designed to assure that the drug product, Oxygen U.S.P., has the identity, strength, quality, and purity it purports or is represented to possess as required by 21 CFR 211.100 (a). For example, the procedure titled "Oxygen Transfill Policy & Procedure" currently used by your firm does not contain specific step-by-step instructions for each of the pre-fill, fill and post-fill steps.

6. Failure to prepare complete master (batch) production and control records for your drug product, Oxygen U.S.P., to assure uniformity from batch to batch as required by 21 CFR 211.186. For example, batch records for lot numbers 022603, 043002, 041702, 010903, 013003, 011703, 011703, and 021803 do not include defined steps for documenting cylinders' fill and post-fill operations such as temperature, heat-touch check, and pressure and odor tests.

7. Failure to routinely calibrate mechanical equipment used in the transfilling of Oxygen U.S.P. or keep written records of calibration checks according to a written program designed to assure proper performance as required by 21 CFR 211.68 (a). For example, there was no documentation to show that your vacuum and pressure gauges for the oxygen manifold system have been calibrated, nor was there documentation for the calibration of the thermometer used during the fill operation of the medical oxygen.

8. Failure to establish written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, examination, and/or testing of labeling as required by 21 CFR 211.122 (a). Failure to establish written procedures designed to assure that correct labels and labeling are used for drug products as required by 21 CFR 211.130. For example, several cylinders bore illegible or mutilated labels or lacked required labeling such as product identification and the air liquefaction statement.

9. Failure to document the initials or signature of the person who performs each test (pre-fill, fill, and post-fill/assay) and the date(s) the test were performed and the initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards as required by 21 CFR 211.194 (a)

(7) and (8), respectively. For example, batch records for lot numbers 022603, 043002, 041702, 010903, 013003, 011703, 021703, and 021803 do not document dates, initials, or signatures regarding who performed the test(s) and on what date(s) or who performed reviews of original records for accuracy.

10. Failure to maintain complete data derived from all tests necessary to assure compliance with established specifications and standards, including oxygen assays and as required by 21 CFR 211.194(a)(6). For example, production records from 3/20/02 to 3/20/03 do not include the actual numeric values obtained with the oxygen analyzer. Instead, a check mark or dash was recorded.

11. Failure to maintain complete records of the testing and standardization of reference standards and the periodic calibration of instruments as required by 21 CFR 211.194(c) and (d). For example, there are no certificates of analysis (COA's) for the reference standards (Nitrogen "Zero gas" cylinder or the Oxygen "Span gas" cylinder) used to calibrate the lower and upper limits of the firm's [redacted] Oxygen Analyzer.

12. Failure to establish written procedures describing a system by which the distribution of each lot of drug product filled by your firm can be readily determined to facilitate its recall if necessary as required by 21 CFR 211.150 (b).

13. Failure to have written procedures describing the handling of all written and oral complaints regarding your drug product as required by 21 CFR 211.198 (a).

You can find guidance and information regarding regulations for drug products through FDA's internet page for the regulated industry at http://www.fda.gov/oc/industry/.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the CGMP regulations. 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.

You should take prompt action to correct these violations, and you should establish procedures whereby such violations do not recur. Failure to do so may result in regulatory action without further notice. Possible actions include, but are not limited to, seizure and/or injunction.

Your firm must also take prompt action to register with FDA as a drug manufacturer and file a drug listing form for the Oxygen U.S.P. Failure to do constitutes violations under sections 510(c) and 510(j) of the Act. We acknowledge the steps your firm has already taken towards corrective action in this area.

You should notify this office in writing, within (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violation(s), including an explanation of each step taken to prevent recurrence of similar violations. 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 directed to the Food and Drug Administration, Attention: Jose R. Hernandez, Compliance Officer, 10710 Midlothian Turnpike, suite 424, Richmond, Virginia 23235. If you have questions regarding any issue in this letter, please contact Mr. Hernandez at (804) 379-1627, extension 15.

Sincerely,

Lee Bowers,
Director, Baltimore District