DEPARTMENT OF HEALTH & HUMAN SERVICES

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Food and Drug Administration
Detroit District
1560 East Jefferson Avenue
Detroit, MI 48207-3179
Telephone 313-226-6260

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER
2003-DT-04

December 3, 2002

Mr. John J. Laga
President
Classic Medical, Inc.
22919 Industrial Drive East
St. Clair Shores, MI 48080

Dear Mr. Laga:

An inspection of your medical oxygen manufacturing firm was conducted on September 23-27, 2002 by Investigator Jennifer A. Kemp. At the conclusion of the inspection, a FORM FDA-483, List of Inspectional Observations (copy attached) was issued to Mr. Henry E. Litz, Distribution Manager.

The Oxygen USP sold by your firm is misbranded within the meaning of Section 502(b)(1) and (c) of the Federal Food, Drug, and Cosmetic Act (the Act), and it is adulterated within the meaning of Section 501(a)(2)(B) of the Act.

Misbranding violations:

1. The compressed gas cylinders of oxygen USP are misbranded if they do not bear the name and place of business of the firm responsible for having filled the cylinders as required by Section 502(b)(1) of the Act. **You have refilled and distributed cylinders bearing the name and address of a different firm. For example, FDA-483 observation #8, reported on [redacted] "E" size cylinders bearing multiple lot number stickers, one from a different firm. The FDA Investigator also noted that some of those cylinders had the original label applied by your supplier, rather than your own firm label.**

2. The cylinders of compressed oxygen gas USP are misbranded if they lack any name of the product and all other labeling as required by Section 502(c) of the Act. **You refilled and held for distribution cylinders that failed to bear the required Compressed Oxygen U.S.P. label. See FDA-483 observation # 7.** The new cylinder labels obtained on 10-10-02, as supplied with the response letter are also not in full compliance. See comment #4 on page 4 of this letter.

Adulteration violations:

The Oxygen USP is adulterated based on the inspectional evidence which revealed serious deviations from the Current Good Manufacturing Practices for Finished Pharmaceuticals, Title 21, Code of Federal Regulations, (C.F.R.) Part 211, as follows:

1. You fail to have a Quality Assurance Unit as required in 21 C.F.R. § 211.22. For example, **see FDA-483 observation 13.**

2. You have failed to assure that each person engaged to perform or to supervise the manufacture, processing, packing, or holding of the drug product, has the training and experience to enable them to perform their assigned functions, as required by 21 C.F.R. § 211.25. Your failure to have a staff trained to perform their assigned functions is demonstrated by the number and types of inspectional observations made during this inspection.

3. You lack written procedures for production operations, except for lot number determination, as required in 21 C.F.R. § 211.100. For example, **see FDA-483 observation 11.**

4. You failed to formally approve (sign and date) the INSTRUCTIONS ON LOT NUMBERING FOR OXYGEN REFILLING procedure as required by 21 C.F.R. § 211.100. For example, **see FDA-483 observation 12.**

5. You have failed to assure that a review of all drug product production and control records is performed to determine compliance with established written procedures **before** each batch is released or rejected, as required by 21 C.F.R. § 211.192. For example, **see FDA-483 observation 4.**

6. You have failed to perform an analysis of every finished batch of Oxygen USP, prior to release for distribution, as required by 21 C.F.R. § 211.165. For example, **see FDA-483 observation 2.**

7. Your firm has failed to consistently document the calibration of the [redacted] analyzer instrument as required by 21 C.F.R. § 211.160(b)(4). For example, **see FDA-483 observation 3(c) and 5(a).**

8. You have failed to label your Oxygen USP with a lot or batch number that accurately reflects the history of the manufacture and control of the batch, as required by 21 C.F.R. § 211.130(c). For example, **FDA-483 observation 1** reported that multiple filling sequences of medical oxygen are assigned the same lot number.

9. You have failed to assure that all labeling materials not suitable for subsequent operations have been removed during the empty cylinder preparation process, as required by 21 C.F.R. § 211.130(e). For example, **FDA-483 observation 8** reported multiple lot code number stickers were affixed to [redacted] of [redacted] size "E" cylinders, one from your supplier and one for your firm's filling operations.

10. You have failed to consistently maintain complete batch production records that document performance of each required step in the pre-fill, filling, testing, and labeling process as required by 21 C.F.R. § 211.188. For example, **see FDA-483 observation 3.**

11. You have failed to document the calibration of the vacuum gauge, pressure gauge, and thermometer as required by 21 C.F.R. § 211.68(a). For example, **see FDA-483 observation 5.**

The above is not intended to be an all-inclusive list of deviations which may exist at your firm. It is your responsibility to ensure that your firm is in full compliance with the Act and regulations promulgated thereunder. Other 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.

We request that you take prompt action to correct these deviations. Failure to make prompt corrections may result in regulatory action without further notice, such as seizure and/or injunction.

We acknowledge receipt of an October 29, 2002 letter from Mr. Henry Litz, Distribution Manager, written in response to the inspectional observations. The corrective actions described in his letter indicate that several of the above listed violations have been or are being corrected. We are concerned that some of the corrections have been designed and implemented without performing a thorough evaluation of all your production and records systems, and they may not address all the requirements of the Act and the regulations. For example:

1. The response to observations 11-13 is not acceptable.
   The response states the written procedures are not expected to be finished and in place until January 2003, and the existence of a Quality Control Unit (QAU) is left as a "point of consideration in the written procedure program." The regulations require that a Quality Assurance Unit be established and be responsible for review and approval of all written procedures. A small firm such as yours may designate a single individual with these responsibilities. You should review the section covering RESPONSIBILITY OF QUALITY CONTROL UNIT in the guidance document [redacted] that was provided to Mr. Litz, by Investigator Kemp, during the inspection.

2. The response to observation number 4 is not acceptable.
   It states, "Batch records are verified by second employee and signed daily." Although it is common practice in the medical gas industry to record the filling of multiple batches on a single daily or weekly page, it is necessary that every batch be completed and documented including the review of all the steps by a second responsible individual who must sign and date the release **before the batch can be released and distributed.** Therefore, a daily signature somewhere on the page is not adequate to address each specific batch release.

3. The response to observation number 8 does not fully address the problem.
   We noted multiple lot number stickers on some cylinders. The situation during the inspection was the result of filling cylinders owned by another firm so your people had left that firm's labeling intact. Our concern is the failure to remove the outdated lot number stickers. They must be removed every time as part of the pre-filling check of the empty cylinders.

4. The response to observation number 7 includes a sample of a new USP label with the "Rx Only" statement. This new label is not acceptable as follows:
   a. The label includes the statement, "CAUTON: Federal law prohibits dispensing without a prescription" followed by "Rx Only." Section 503(b)(4) of the Act requires that the label bear, at a minimum, the symbol, "Rx Only." Under Section 502(c) of the Act, the "Rx Only" symbol must be prominently displayed and should not be buried in other statements on the label. We recommend that you delete the statement, "CAUTION: Federal law prohibits dispensing without a prescription," as that statement is no longer required, and that you place the "Rx Only" symbol immediately after the statement, "For all other medical applications." Also, as noted in paragraph (c) of this comment, you should enlarge the label so that the "Rx Only" symbol can be easily read and understood under customary conditions of use.
   b. The established name of the product is "Oxygen Compressed USP." Your sample label incorrectly lists "OXYGEN COMPRESSED" on the left end and "OXYGEN* U.S.P." in the top center.
   c. Your label is too small. Under Section 502(c) of the Act and 21 C.F.R. 201.15, any word or statement required under the Act must be prominently placed on the label with such conspicuousness that it is likely to be read and understood by the ordinary individual under customary conditions of use. You should enlarge the label so that the information contained on the label is easily readable by the unaided eye.

   Attached is a copy of a sample label for use in designing your labels.

5. Finally, we have noted your firm has failed to maintain on file the analytical method validation data for the [redacted] oxygen analyzer instrument, as required by 21 C.F.R. § 211.165(e). This was not discussed with Mr. Litz during the inspection nor was it listed on the FDA-483. You should contact the manufacturer of the instrument and request a copy of their validation data for your records.

Please notify this office in writing, within fifteen (15) working days of your receipt of this letter, of the specific steps you have taken to correct the noted deviations and to prevent their recurrence. If corrective action cannot be completed within 15 working days, please state the reason for the delay, and the time in which the corrections will be completed.

Your response should be directed to this office to the attention of Mr. Melvin O. Robinson, Compliance Officer (313) 226-6260, Extension 178

Sincerely yours,

Joann M. Givens
District Director
Detroit District