DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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-03

November 6, 2002

Mr. John J. Cunningham
President
Wyandotte Welding Supply, Inc.
Lab Gases Division
2025 Eureka Avenue
Wyandotte, MI 48192

Dear Mr. Cunningham:

An inspection of your medical oxygen manufacturing firm was conducted on August 8-15, 2002 by Investigators Deanna Lampley and Jennifer A. Kemp. At the conclusion of the inspection, a FORM FDA-483, List of Inspectional Observations (copy attached) was issued to you.

The Oxygen USP sold by your firm is misbranded within the meaning of Section 502(b)(2) 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 and the cryogenic vessels of oxygen are misbranded in that they lack indication of the net contents.

2. The cryogenic vessels of liquid oxygen are misbranded in that the labels lack the established name of the product, "Oxygen Refrigerated Liquid USP."

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. Your Quality Assurance Unit failed to perform their functions and responsibilities as required in 21 C.F.R. § 211.22. The failure is demonstrated by the number and type of inspectional observations made during this inspection.

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. Your quality control unit has failed to review all drug product production and control records 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 3.**

4. Your firm has failed to consistently document the performance of an analysis of every finished batch of Oxygen USP, as required by 21 C.F.R. § 211.165, prior to release for distribution. For example, **see FDA-483 observation 2.**

5. Your firm has failed to consistently document the calibration of the [redacted] Oxygen analyzer instrument as required by 21 C.F.R. § 211.160(b)(4). For example, **see FDA-483 observations 1 and 7.**

6. Your firm has failed to maintain on file the analytical method validation data for the [redacted]xygen analyzer instrument, as required by 21 C.F.R. § 211.165(e). Although this deficiency was not listed on the FDA-483, our Investigators reported that you presented no additional information in support of validation of the instrument.

7. You have failed to consistently 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 4** reported that lot numbers represented incorrect fill dates.

8. 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 the failure to remove the obsolete lot number/expiration date stickers prior to application of a fresh sticker for the current batch.

9. The expiration dates observed on the recent filling records appear to be set at four years from the fill date. This date is not supported by appropriate stability testing as required by 21 C.F.R. § 211.137. **FDA-483 observation 4** notes the expiration date is not 5 years from the fill date, even though your USP LABEL SAMPLES instructions specify to use a five (5) year date.

10. You have failed to follow the instructions in your written procedure, USP LABEL SAMPLES, to include the cylinder volume on the labeling as required by 21 C.F.R. § 211.130(b). **FDA-483 observation 4** notes that cylinder volumes are not on the lot number stickers.

11. Your Quality Control Unit failed to approve **(sign and date)** the three handwritten pages of notes titled, How to Fill Liquid Tanks as required by 21 C.F.R. § 211.100(a). **See FDA-483 observation 9.** These notes were presented as representing the "manufacturer's instructions" named in the one-half page procedure, FILLING USP LIQUID CYLINDERS

included in your document entitled USP OXYGEN CYLINDER FILLING STANDARD. The three handwritten pages:

a. Do not provide for specific pre-fill inspection of the cryogenic vessels as required by 21 C.F.R. § 211.84(d)(3).

b. Do not refer to any form or any other type of document on which to record completion of the filling operation as required by 21 C.F.R. § 211.100(b).

12. 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 observations 10 and 11.**

13. You have failed to document performance of the annual calibration of the vacuum gauge as called for in your USP Equipment Calibration procedure, as required by 21 C.F.R. § 211.68(a). For example, see **FDA-483 observation 5.**

14. The last calibration of the [redacted] performed on February 18, 2000, failed to comply with your established written procedure, Calibration Checklist Form 4.9-2 , that also requires an annual calibration. This is a violation of 21 C.F.R. § 211.68(a). **See FDA-483 observation** 6.

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.

Informational section

1. Although you failed to follow your written procedure to include the contents of your containers on the small grocery-store sticker labels along with the lot numbers, the FDA believes that you should indicate the contents in the space provided on the formal cylinder shoulder labels. They are a permanent label less likely to become separated from the container.

2. Your cylinder and cryogenic vessel labels must be revised prior to February 19, 2003 to bear the statement, "Rx Only". This must replace the existing statement "Caution: Federal Law Prohibits Dispensing Without Prescription." Enclosed are sample labels.

3. Concerning adulteration violation number nine (9) above, the Food and Drug Administration currently recognizes the use of a five (5) year expiration date as an industry practice, and is reviewing the data of a petition from the [redacted] requesting exemption of medical gases from 21 C.F.R. § 211.137. In the meantime, a five (5) year expiration date may be used, but any other expiration dating period, whether [redacted] must be supported by your own stability studies.

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

Enclosures
FDA-483
Model Labels