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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

San Francisco District
1431 Harbor Bay Parkway
Alameda, California 94502-7070
Telephone: 510-337-6700

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Our Reference: 2952355

June 2, 1997

Nancy A. Mendoza, President
Respiratory Health Care Specialists, Inc.
805 Pohukaina Street
Honolulu, Hawaii 96813

WARNING LETTER

Dear Ms. Mendoza.

An inspection of your medical oxygen manufacturing facility was conducted by Food and Drug Administration (FDA) Investigator Kenneth M. Okihara on April 29 through May 7, 1997. The inspection revealed serious violations of the Federal Food Drug and Cosmetic Act (Act) as follows:

VIOLATION

BRIEF DESCRIPTION

501(a)(2)(B)

Your drug product, Oxygen, USP, is adulterated in that the controls used for the manufacture, processing, packing or holding of this product are not in conformance with the current Good Manufacturing Practice (GMP) regulations, parts 210 and 211 (21 CFR 210 and 211). as follows:

1. Failure to assay incoming liquid oxygen for identity prior to filling cryogenic home vessels at your facility [21 CFR 211.165(a)]. Specifically, each vertical gas liquid (VGL) container is received from the supplier with a valid certificate of analysis (COA). However, since

the analysis is not witnessed, each VGL must be tested for identity. Additionally, periodic analysis should be performed by your firm to verify the reliability of the supplier's analysis and a sample of a new batch should be tested annually by a third party for compliance with United States Pharmacopeia (USP) specifications.

2. Failure to assay one filled medical oxygen gas cylinder from each filling sequence for conformance with USP specifications [21 CFR 165(a)]. Specifically, one cylinder from each manifold filling sequence should be tested for identity and strength. No test results were recorded on the following Compressed Oxygen Cylinder Batch Logs of lot numbers: 030497A, 030597B, 010697, 030797B, 010797, 041197B, C and D, 011397, 011497, 011597, 041597B, 041697A, 011797, 021997B, 022197A and B, 012297, 042297, 012496, 032497B, 012797A and B, and 012997B.
3. Failure to vent and evacuate each cylinder prior to filling with medical oxygen gas [21 CFR 211.84(d)(5)]. Specifically, each cylinder, prior to being filled with a medical gas, should be vented to atmospheric pressure and evacuated to a vacuum of twenty-five inches of mercury at sea level. These steps were recorded as not being done by the word "NO" entered in the "Vent" and "Vac." columns of the Compressed Oxygen Cylinder Batch Logs of lot numbers: 010297, 010697, 010797, 010897, 011097, 021097A and B, 011397, 031397A, 011497, 011597, 011797, 021997A, 012197, 022197A, 012297, 012496, 022697A, 012797A and B, 022797A, 012997B, and 013197A.
4. Failure to review laboratory and production records for accuracy, completeness, and compliance with established standards prior to release for distribution [21 CFR 211.92 and 21 CFR 211.194(a)(8)]. The following lot numbers of the Compressed Oxygen Cylinder Batch Logs were not initialed or signed by the reviewer: 020497A, B and C; 031097A and B; 021797A; 042197A; 042297; and 022597A.
5. Failure to assign a different lot number for each batch or manifold filling sequence [21 CFR 211.130(c)]. The medical gas filling manifold has twenty outlets. However, more than twenty cylinders had the same lot number on the Compressed Oxygen Cylinder Batch Lot as follows: 010897 on sixty cylinders, 011097 on thirty-two cylinders, 011397 on thirty-two cylinders, 031397A on thirty cylinders, 011597 on thirty cylinders, 011797 on fifty-four cylinders, 012197 on thirty-

three cylinders, 012496 on twenty-six cylinders and 013197A on twenty-eight cylinders.

6. Failure to perform adequate prefill checks on each compressed medical oxygen gas cylinder prior to filling [21 CFR 211.84(d)(3)].
7. Failure to include complete information on each batch production record [21 CFR 211.188], and failure to reconcile the quantities of labeling issued, used and returned on each batch production record [21 CFR 211.125(c)].
8. Failure to establish detailed written procedures for all medical liquid and gas operations [21 CFR 211.100(a & b)].
9. Failure to quarantine each finished drug product prior to release [21 CFR 211.142].
10. Failure to calibrate vacuum and pressure gauges and thermometers at suitable intervals [21 CFR 211(b)(4)].
11. Failure to document the execution of the various production and control functions at the time of performance [21 CFR 211.100(b)].

503(b)(4)

1. Your drug product, Oxygen, USP, is misbranded in that it is regarded as a prescription drug and its labeling fails to bear the statement, "Caution: Federal Law prohibits the dispensing without a prescription", or the modified caution statement, "For emergency use only when administered by properly trained personnel for oxygen deficiency and resuscitation. For all other medical applications, Caution: Federal law prohibits dispensing without prescription" [21 CFR 201.100(b)(1), 21 CFR 211.122, 21 CFR 211.125, and 21 CFR 211.130].

The above identification of violations should not be construed to be an all inclusive list of deficiencies at your facility. It is your responsibility to ensure that your facility is in complete compliance with all requirements of the Act.

Adulterated and misbranded drugs may be seized under authority of the Act, Section 304. The introduction or delivery for introduction into interstate commerce of any adulterated or misbranded drug is prohibited by the Act, under Section 301(a).

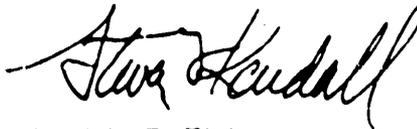
Nancy A. Mendoza
Honolulu, Hawaii

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A copy of the Form FDA 483 Inspectional Observations was presented to you at the conclusion of the inspection. A copy of 21 CFR Part 211 was also furnished to you during the inspection. These are enclosed along with FDA's Compressed Medical Gases Guideline and a copy of a speech by Mr. Duane Sylvia of FDA's Office of Compliance, Division of Manufacturing and Product Quality, Center for Drug Evaluation and Research. His speech contains useful information on how to comply with the requirements of 21 CFR Parts 210 & 211.

Please notify this office in writing within 15 working days of receipt of this letter of the specific steps you have taken to prevent the recurrence of similar violations. Failure to promptly correct these deviations may result in enforcement action being initiated without further notice. If corrective action cannot be completed within 15 days, state the reason for the delay and the time needed to complete the corrections. Please submit your response to the Drug Team Leader, Food & Drug Administration, 1431 Harbor Bay Parkway, Alameda, CA 94502-7070.

Sincerely,



for
Patricia C. Ziobro
District Director
San Francisco District

Enclosures: FDA-483
21 CFR Parts 201.100, 210 & 211
Speech by Mr. Duane Sylvia
Compressed Medical Gases Guideline;