



DEPARTMENT OF HEALTH & HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

M2245N

PHILADELPHIA DISTRICT

WARNING LETTER

900 U.S. Customhouse
2nd and Chestnut Streets
Philadelphia, PA 19106

Telephone: 215-597-4390

99-PHI-05

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

November 16, 1998

John Paul Jones III, President
Air Products and Chemicals, Inc.
7201 Hamilton Boulevard
Allentown, PA 18195-1501

Dear Mr. Jones:

From October 21 through October 28, 1998, Food and Drug Administration (FDA) Investigator David J. Hafner conducted an inspection of your facility located at 3250 Hempland Road, Lancaster, PA, with regard to your medical oxygen manufacturing operation. Our inspection determined that your firm manufactures medical oxygen by an air-liquefaction process. Our inspection also determined that your firm uses the [REDACTED] System to control and document the filling of medical oxygen into tractor trailers for distribution. The [REDACTED] System also controls and documents purity testing during the filling operation. At the conclusion of this inspection, a Form FDA-483 (copy attached), List of Inspectional Observations, was issued to and discussed with Roger A. Cramlet, Site Manager. The inspection revealed that drug products manufactured at your facility are adulterated under Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) in that the methods used in or the facilities or controls used for their manufacture, processing, packing, or holding do not conform to Current Good Manufacturing Practice (CGMP) regulations as described in Title 21 Code of Federal Regulations Part 211, as follows:

1. Failure to validate the [REDACTED] System to assure that drug products meet applicable standards of identity, strength, quality, and purity at the time of use. For example:

a) There is no assurance that all purity test results are recorded by the [REDACTED] System.

On 6/2/98 a purity recheck was conducted on trailer #515248 with a result of 99.89% as identified on the trailer product integrity notice. This test result does not appear on the [REDACTED] generated production record or on the COA on file.

On 9/4/98 a purity recheck was required for trailer #515247 as identified on the trailer product integrity notice. The [REDACTED] generated production record has only one purity test result recorded. There is no documentation for the results of the purity recheck.

b) The [REDACTED] System provides no documentation to identify the reason for a purity recheck.

On 3/4/98 a purity recheck was conducted on trailer #515223. The reason for this recheck could not be determined.

c) The [REDACTED] System does not record and maintain all test results related to a particular trailer fill, when multiple purity testing is conducted. There is no audit capability to review the frequency and types of alarms triggered by the system.

2. The [REDACTED] System production record does not always identify manual entry of production data into the system when the system is not fully operational.

The filling and purity testing of trailer #515246 on 10/8/98 is not identified on the [REDACTED] production record as data manually entered. Written records containing data generated when the [REDACTED] system is not fully functional, are not retained after that data is manually entered into the system.

3. Records are not maintained to document times when the [REDACTED] System is not fully operational. Records are not maintained. Corrective action taken and/or review by qualified personnel is not documented prior to returning the [REDACTED] system to service.

4. There is no review of medical oxygen, USP, production

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records prior to release. Initial review of production record is performed by production personnel subsequent to shipment of product.

The above is not intended to be an all-inclusive list of violations which may exist at your firm. As top management, it is your responsibility to ensure that all requirements of the CGMP regulations are being met as well as all other requirements of the Act at all of your facilities and air separation plants. You should take prompt action to correct the above violations and that you establish procedures whereby such violations do not recur. Failure to do so may result in regulatory action without further notice such as seizure and/or injunction.

Federal agencies are advised of the issuance of all warning letters about drugs and devices so that they may take this information into account when considering the award of contracts.

Please advise this office in writing within fifteen (15) days of the steps you have taken to bring your firm into compliance with the law. Your response should include each step that has been taken or will be taken to correct the violations and prevent their recurrence. If corrective actions cannot be completed within 15 working days, state the reason for the delay and the time within which the correction will be completed. Your reply should be directed to the Food and Drug Administration, James C. Illuminati, Compliance Officer, at the address above.

Sincerely,

Marguerite E. Eagan
Marguerite E. Eagan
Acting District Director
Philadelphia District Office

jci

cc: Pennsylvania Department of Health
Health & Welfare Building
7th and Forster Streets
P.O. Box 90
Harrisburg, PA 17120
Attn: Robert E. Bastian, Director
Division of Primary Care and Home Health Services