



DEPARTMENT OF HEALTH AND HUMAN SERVICE

Refer to: CFN 1116019

Public Health Service

Food and Drug Administration
Baltimore District Office
900 Madison Avenue
Baltimore, MD 21201-2199
Telephone: (410) 962-3396
FAX: (410) 962-2219

HFI-35

M3104

September 2, 1999

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Patrick F. Murphy
Chief Executive Officer
AGA Gas, Incorporated
6055 Rockside Woods Boulevard
Cleveland, Ohio 44101

Dear Mr. Murphy:

A Food and Drug Administration (FDA) inspection was conducted on August 23-25, 1999 at your medical gas manufacturing facility located at #1 AGA Plaza, Washington, West Virginia. Medical gases are drug products as defined by Section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act).

During our inspection, deviations from the Current Good Manufacturing Practice (GMP) requirements (Title 21, Code of Federal Regulations (CFR), Part 211) were observed. These deviations cause your medical gases 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, their manufacturing, processing, packing, storage, or holding, are not in conformance with GMP regulations.

The deviations included the following:

- Failure to ensure that equipment used in the manufacture and holding of Oxygen, U.S.P. and Nitrogen N.F. is adequate and suitable for its intended use. For example, no installation, operational, or performance qualifications of equipment were completed or documented.
- Failure to document and/or test each bulk lot of Oxygen, U.S.P. for identity and purity. For example, each individual batch of drug product (bulk tanks) is not always tested prior to release.
- Failure to always document calibration of instruments used in the manufacture and testing of Oxygen U.S.P. in accordance with the instrument manufacturer's instructions and/or approved procedures.
- Failure to ensure validation of test methods used in the testing of Nitrogen N.F. have the accuracy, sensitivity, specificity, and reproducibility to meet established specifications.

- Failure to ensure that written production and process control procedures are followed in the performance of the production record review process. For example, individuals not specified in SOP 51W-001 (i.e., non-AGA employees) as having responsibility for quality control/assurance functions were involved in the production record review and sign-off for finished products.
- Failure to investigate in-process drug products that fail to meet specifications. The investigation, if done, is not documented.
- Failure to establish and maintain complete production and process control procedures. For example, procedures do not address completion of the "Operator's Daily Log."
- Failure to maintain complete batch production and control records. For example, exact analytical results were not always recorded and review of batch production records by the quality control unit was not always documented.

At the conclusion of the inspection, Mr. Daniel S. Wharmby, Plant Manager, was presented with a written list of inspectional observations (FDA-483) which was discussed with him. A copy of the FDA-483 is enclosed for your reference. Your firm's response letter to the FDA-483 dated August 27, 1999 was received and will be made part of our official files.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to all requirements of the Act and regulations at your facilities. The specific violations noted in this letter and in the FDA-483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If you determine the causes to be systems problems, you must promptly initiate permanent corrective action.

Federal agencies are advised of the issuance of all Warning Letters concerning drug products so that they may take this information into account when awarding contracts. By copy of this letter, we are advising the Health Care Financing Administration (HCFA) that our inspection revealed significant deviations from the Act. They may elect to defer or discontinue payment for any health care product in violation of state or federal law.

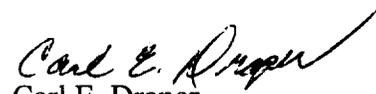
You should take prompt action to correct these deviations. Failure to do so may result in regulatory action without further notice. These actions include, but are not limited to, seizure and/or injunction.

Please 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 violations and to prevent their recurrence. 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.

Mr. Patrick F. Murphy
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Your reply should be sent to the Food and Drug Administration, Northern Virginia Resident Post, 101 West Broad Street, Suite 400, Falls Church, Virginia 22046, to the attention of Gerald W. Miller, Compliance Officer. Mr. Miller can be reached at (703) 235-8440, extension 504.

Sincerely,



Carl E. Draper
Acting Director, Baltimore District

Enclosure

cc: Mr. Daniel S. Wharmby
Plant Manager
AGA Gas, Inc.
#1 AGA Plaza
Washington, West Virginia 26181

Mr. Dennis Carroll
Associate Regional Administrator
Health Care Finance Administration
Room 3100
3535 Market Street
Philadelphia, PA 19101 (purged)