DEPARTMENT OF HEALTH & HUMAN SERVICES

EB 8/3/99 M2811

Food and Drug Administration
Kansas City District Office
11630 West 80th Street
P.O. Box 15905
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Telephone: (913) 752-2100

Certified/Return Receipt Requested

August 2, 1999

WARNING LETTER

Charles C. Canterberry, President
Linweld, Inc.
1225 "L" Street
Lincoln, NE 68501

KAN #99-023

Dear Mr. Canterberry:

Inspections were made of your medical gas transfilling operations located at 4900 No. 4th Avenue, Sioux Falls, South Dakota, 3930 North 10th Street, Gering, Nebraska, and 100 Madison Street, Topeka, Kansas. These inspections were conducted on December 2, 3 and 8, 1998, December 4 and 7, 1998, and February 11 and 12, 1999, respectively, by Food and Drug Administration (FDA) Investigators from FDA's Minneapolis District office and this office. The investigators documented deviations from the Current Good Manufacturing Practice (CGMP) Regulations (Title 21, Code of Federal Regulations, Parts 210 and 211). These deviations cause the medical gases transfilled at these locations to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act).

Significant deviations include, but may not be limited to the following:

- Failure to maintain a computer system with validated program capabilities for operating a medical gas facility [21 CFR 211.68]. Examples include:

    - No testing of the system after installation at the operating site. Operating sites are part of the overall system and lack of their qualification means the system validation was incomplete.

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- The validation protocol is incomplete for information needed to effectively operate a medical gas facility. For example, the protocol: (1) does not call for testing the system under worse case (e.g., full capacity) conditions; (2) lacks testing provisions to show correct functioning of the software; (3) mentions without explanation or supportive documentation, "historic experience" with terminals, but doesn't specifically identify the terminals; and (4) lacks change control procedures. In addition, protocol execution on 8/93 predates protocol approval (5/94) and requirements approval (9/93).

It is necessary for you to take action on this matter now. Please let this office know in writing within fifteen (15) working days from the date you received this letter if the January 7 and March 10 letters will suffice as your response to this letter, or you may expand on those letters with additional information concerning corrections being made. 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. We request a meeting with you to discuss your corrective action plan. Please contact Mr. Clarence R. Pendleton, Compliance Officer, telephone number (913) 752-2103 to schedule a date for this meeting.

You should know that these serious violations of the law may result in FDA taking regulatory action without further notice to you. These actions include, but are not limited to, seizure and/or obtaining a court injunction against further marketing of your medical gasses. Also, other Federal agencies are informed about the Warning Letters we issue, such as this one, so that they may consider this information when awarding government contracts.

We have received and reviewed letters dated January 7, and March 10, 1999, from Mr. Thomas L. Hilger, Director of Quality/Regulatory Affairs, which responded to the Form FDA 483 observations made at the Gering, Nebraska and Topeka, Kansas facilities. We find these responses to be generally unacceptable. For example, in the March 10 letter, you:

(1) fail to recognize the basic need to include each location within the validation of the overall computer system; and
(2) acknowledge that your system, by design, does not record results that are out of specification. Only parameters that are within specifications may be recorded.

In the January 7, 1999 letter you requested specific guidance and advice from FDA as to how to go about validating your computer system. Much has been written and discussed about this subject within the pharmaceutical industry itself over the course of many years. You may wish to research that body of knowledge and, as necessary, seek technical assistance.

In addition, we request further details regarding steps your firm is taking to bring your electronic CGMP production records into conformance with the requirements of 21 CFR, Part 11; Electronic Records; Electronic Signatures. Part 11 establishes requirements to ensure that electronic records and electronic signatures are trustworthy, reliable and generally equivalent substitutes for paper records and traditional handwritten signatures. Electronic records and electronic signatures may be used to meet record and signature requirements of 21 CFR Parts 210 and 211 when part 11 requirements are met. Our inspection disclosed numerous and significant deviations from part 11. Examples include:

- The system does not generate an audit trail, and there is no way to determine if values have been changed on batch production records. This is important because an audit trail can be the only evidence that an electronic record has been altered. We note, for instance, that your system only records the last value entered by an operator and that values, such as Oxygen potency levels that my have been entered earlier and that may indicate potentially serious quality problems, are not recorded. The system prompts an operator when equipment detects that an Oxygen potency value is non-conforming, and permits the operator to record a value that is within specification, but does not record the original out of specification value.

- No written procedures that would hold individuals accountable for actions taken under their electronic signatures. It is vital that employees accord their electronic signatures the same legal weight and solemnity as their traditional handwritten signatures. Absent such written and unambiguous policies, employees may be more apt to make mistakes, under the erroneous assumption that they will be held to a lower level of accountability than they might otherwise expect when they execute traditional handwritten signatures.

- No documentation or testing of the system's ability to discern invalid or altered records. This is significant because electronic records by their nature may be easily altered in a manner that is difficult or impossible to detect. If an employee were to alter an electronic batch record in an unauthorized manner, your system would not be able to detect such change.

- No documentation to show if the system has the ability to generate accurate and complete copies of records in electronic form; copies of electronic records cannot be generated at these sites. It is vital for FDA to be able to audit electronic production records by, among other things, reviewing electronic copies of your electronic records. It is therefore a serious matter that your system cannot generate such on-site electronic copies.

- No safeguards to prevent unauthorized use of electronic signatures that are based on identification codes/passwords when an employee who has logged onto a terminal leaves the terminal without logging off. This is serious because another employee or individual could impersonate the individual who has already been logged on, and thereby easily falsify an electronic record. The resulting batch production record, for instance, would not be an accurate and reliable indication of the lot's history. Moreover, in such an environment it would be fairly easy for the genuine logged on employee to disavow a signature as false, and thereby seek to avoid responsibility for actions under his/her signature (on the basis that it is fairly easy for someone else to apply his/her electronic signature.)

The untrustworthy nature of the electronic production records would make it difficult to reliably reconstruct the full history of a lot's production in the event problems had to be investigated and solved.

We note that your electronic recordkeeping system is centralized and that all your facilities use the same procedures. This leads us to conclude that these deficiencies may be replicated throughout your organization. FDA has, on several occasions informed your company of part 11 requirements in an effort to facilitate your voluntary compliance with the regulation. For example, we advised your management of part 11: (1) during our October 1997 inspection of your Gering, Nebraska facility; and (2) by letter to you dated December 3, 1997 from Ms. Shirley J. Berryman of our Kansas City office. We are prepared to discuss part 11 issues with you further at the above referenced meeting.

This letter is not intended to be an all-inclusive list of deficiencies at the inspected facilities. At the conclusion of each inspection Form FDA 483 was issued to Mr. Ted R. Schaaf, Area Manager, Earl F. Goracke, Branch Manager, and Mr. Garry Burnham, Branch Manager. The FDA 483 is a list of the investigator's observations of GMP deviations noted during the inspections. You have multiple sites performing the same operations as the inspected sites. It is your responsibility to ensure adherence to each requirement of the Act and regulations, at each medical gas facility that you operate.

Your reply should be sent to Clarence R. Pendleton, Compliance Officer, at the above address.

Sincerely,

W. Michael Rogers
District Director
Kansas City District

cc: Ted R. Schaaf, Area Manager
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