DEPARTMENT OF HEALTH AND HUMAN SERVICE

949960
Public Health Service

Food and Drug Administration
Kansas City District
Southwest Region
11630 West 80th Street
Lenexa, Kansas 66214-3340

Telephone: (913) 752-2100

September 21, 2004

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER
Ref. KAN 2004-18

Kimberly A. Russell
President and CEO
Mary Greeley Medical Center
1111 Duff Avenue
Ames, IA 50010

Dear Ms. Russell:

During an inspection of your blood bank, Mary Greeley Medical Center, between April 27 through June 10, 2004, FDA investigators from this office documented numerous deviations from the current Good Manufacturing Practice (cGMP) regulations, Title 21, Code of Federal Regulations (CFR), Parts 211 and 606. These deviations cause your products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) [21 U.S.C. 351(a)(2)(B)]. The deviations included the following:

1) Your establishment distributed blood components that were collected from a donor with a previous record of a reactive screening test for evidence of infection due to a designated communicable disease agent. [21 CFR 610.40(h)] For Example:
a) Unit number [redacted], collected on 3-20-02, was found to be reactive by a screening test for HIV antigen. The results of supplemental testing for the donation were indeterminate. Unit number [redacted], collected on 2-11-03, was also found to be reactive by a screening test for HIV antigen. The results of supplemental testing for the donation were again indeterminate. On 1-28-04, unit [redacted] was collected from the same donor. The red blood cell component was transfused to a patient on 2-17-04, and the Frozen Recovered Plasma was shipped for further manufacture on 3-1-04.
b) Unit number [redacted] collected on 11-20-03, was found to be reactive by a screening test for HIV-1/2 antibody. The results of supplemental testing for the donation were indeterminate. On 5-24-04, unit [redacted] was collected from the same donor. The platelet component was transfused to a patient on 5-29-04.

2) Your establishment failed to conduct training in cGMP as it relates to the employees' functions. [21 CFR 211.25(a)] Specifically, there is no documented evidence that your

facility conducted cGMP training for blood bank employees.

3) Your establishment failed to follow written production and process control procedures in the execution of various production and process control functions. [21 CFR 211.100(b)] For Example:
a) Your Donor History Record (Form ID 970214, revised 2-25-04), found to be in use during the inspection, indicated that the establishment was to inquire about the donor's use of Avodart in the 4 weeks prior to donation. However, your SOP, "Deferral Information to Donor History Card Questions," revised 4/04, requires a 6 month deferral for Avodart. Therefore, your establishment was unable to follow the SOP.
b) Your SOP, "Donor Screening Procedure," effective 10/1986, required that personnel "make a check of both arms" in preparation for blood donation "and make sure they are free of skin disease at the phlebotomy site and signs of addiction or scars of self-injected drugs." During FDA's inspection, your establishment was not performing this arm check until the deviation was brought to the attention of the Blood Bank Supervisor on the morning of 5-3-04.
c) Your SOP, "Donor Reactions: Prevention and Treatment," effective 10/1988, required that personnel fill out a donor reaction form that was reviewed and signed by a pathologist in case of a donor reaction. Yet your establishment was not using donor reaction forms to document adverse donor reactions, and there is no evidence that donor reaction information was being reviewed by a pathologist.
d) Because your biologics license does not include irradiated blood products, your SOP, "Request for Irradiated Blood Products," effective 12/1985, required obliteration of the FDA license number on irradiated blood products prior to release for distribution. On three occasions during the current inspection, our investigator(s) observed at least eleven red cell products that had been irradiated by your firm and were released for distribution without obliteration of the FDA license number.
e) Your SOP, "Donor Screening Procedure," effective 10/1986, required that personnel: [r]eview each question on the front of the history card. Any answer that is 'questionable' (answered YES when NO would have been appropriate) must be investigated and approved. Write the line number, a brief explanation, and whether it is OK for the donation to occur, in the comments section on the back of the history card. Refer to the donor qualification manual in the donor screening area for guidelines. Your establishment violated this procedure in several instances, including the following:
    i) The donor of unit number [redacted] which was collected on 2-11-04, answered "Yes" to question 10 on the Donor History Record, "Have you ever had seizures, convulsions, or fainting spells?" Fainting spells was indicated, but your establishment failed to perform any documented investigation of this response. The donor was accepted for donation.

ii) Unit number [redacted] was collected on 4-16-03, from a donor who answered "Yes" to question 12 on the Donor History Record, "In the past 12 months, have you been given rabies shots?" The information provided is "vaccine - summer of '02". Your establishment failed to perform any documented investigation of this response, however, the donor was accepted for donation.

iii) On 1-16-04, a donor answered "Yes" to question 3 - "Have you for any reason been deferred or refused as a blood donor or told not to donate blood?" Your establishment failed to perform any documented investigation of this response, and the donor's deferral status could not be determined.

iv) On 1-21-04 a donor answered "Yes" to question 55 - "Were you born in, have you lived in, or have you traveled to any African country since 1977?" Your establishment failed to perform any documented investigation of this response to determine deferral status.

v) On 1-7-04, a donor answered "Yes" to question 40, "In the past 4 weeks, have you had any shots or vaccines?" Your establishment failed to perform any documented investigation of this response, and deferral status could not be determined.

4) Your establishment failed to maintain processing, storage and distribution records including all relevant dates, times and distribution and disposition as appropriate of blood and blood products. [21 CFR 606.160(b)] For Example:
a) Your establishment's component preparation records do not include all relevant information including date of component preparation, time and date frozen products were placed in the freezer, and time and date platelets were placed on rotation. [21 CFR 606.160(b)(2)(ii)]
b) Units [redacted] collected on 6-3-03, [redacted] collected on 9-17-02, and [redacted] collected on 1-9-04 were all partially transfused; however there is no record of their return to the blood bank or of their destruction. [21 CFR 606.160(b)(3)(i)]

5. Your establishment failed to maintain records concurrently with the performance of each significant step in the collection, processing, compatibility testing, storage, and distribution of each unit of blood and blood components so that all steps can be clearly traced. [21 CFR 606.160(a)(1)]. For Example:
a) During a review of donor histories on 5-13-04, FDA investigators observed that a draw start time of 1050 (10:50 a.m.) had been recorded on the Donor History Record for whole blood unit [redacted] but no stop time was recorded. When this omission was brought to the attention of the Blood Bank Supervisor at approximately 1415 (2:15 p.m.), the Donor History Record was taken to the phlebotomist. The phlebotomist wrote in a time of 1057 (10:57 a.m.) with no further documentation or explanation on the Donor History Record. This correction was not dated and initialed by the

phlebotomist per your SOP, "Correcting Errors Recorded On Worksheets," effective 5/90.

b) On 2-2-04, your establishment collected autologous whole blood unit [redacted] from a donor. All test results, including HCV NAT, were recorded as non-reactive on 2-4-04. However, HCV NAT testing records for unit [redacted] document receipt of these tests on 2-5-04, not 2-4-04.

6. Your establishment failed to notify, as soon as possible, the Director, Office of Compliance and Biologics Quality (OCBQ), Center for Biologics Evaluation and Research (CBER), when a complication of blood collection or transfusion was confirmed to be fatal. [21 CFR 606.170(b)] Specifically, on 6-21-03, a patient was transfused with two units of Packed Red Blood Cells (PRBC), unit numbers [redacted] and [redacted]. Transfusion of the first unit, number [redacted], began at 5:00 P.M. on 6-21-03 and ended at 7:50 P.M. on 6-21-03. Transfusion of the second unit, number [redacted], began at 9:00 P.M. on 6-21-03 and was stopped prematurely at 9:15 because the patient was complaining of lower back pain. The patient expired at approximately 6:38 A.M. on 6-22-03. Your establishment investigated this incident and examined the units of PRBC. During this investigation, unit [redacted] was found to be hemolyzed. Your establishment failed to notify CBER when the complication was confirmed to be fatal.

7. Your establishment failed to obtain CBER's prior approval for a change in the production process that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. [21 CFR 601.12(b)] Specifically, your establishment has implemented procedures for donor qualification that allow distribution of products that have been collected for allogeneic use from donors who are taking medications determined to be potentially teratogenic in recipients. The procedures in place during FDA's inspection were implemented by your firm without submission to or approval from CBER prior to distribution of such products.

The deviations identified above are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure that your establishment is in compliance with all requirements of the federal regulations. You should take prompt measures to correct these deviations. Failure to correct these deviations promptly may result in administrative and/or regulatory action without further notice. Such action includes license suspension and/or revocation, seizure, and/or injunction.

We acknowledge receipt of your response dated July 19, 2004, which proposes corrective actions to the Inspectional Observations noted on the Form FDA-483, issued on June 10, 2004. We offer the following comments:

- Our review finds your response to Observation 1 & 2 incomplete in that you failed to provide documentation to demonstrate that SOP's and donor collection criteria have been appropriately revised and employees have been trained and competency assessed on the revised procedures. Your response was also inadequate in that:
  - You did not provide any details or time frames outlining the specific steps you plan to take to implement, and validate a blood bank information system.
  - You did not provide any details or time frames outlining the specific steps you plan to take to implement a training plan within your facility.
  - You did not include any actions you plan to take relating to BPD reporting [21 CFR 606.171], initiation of retrospective reviews to determine the number of unsuitable units that were distributed, and consignee notification.

- Our review finds your response to Observation 3a appears to be adequate.

- Our review finds your response to Observations 3(b-e), 4 & 5 incomplete in that you failed to provide documentation to demonstrate that SOP's, forms, and your Donor History Card have been appropriately revised and employees have been trained and competency assessed on the revised procedures. In addition, your response did not provide any details or time frames other than "later this summer" outlining the specific procedures you plan to implement to ensure the disposition of blood and blood products is traceable through final incineration.

- Our review finds your response to Observation 6 incomplete in that you failed to address your lack of initial reporting of a transfusion complication that was confirmed to be fatal to the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research. Per 21 CFR 606.170(b), "When a complication of blood collection or transfusion is confirmed to be fatal, the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research shall be notified by telephone, facsimile, express mail, or electronically transmitted mail as soon as possible."

- Our review finds your response to Observation 7 appears to be adequate.

- Our review finds your response to Observation 8 through 11 incomplete in that you failed to provide documentation to demonstrate that SOP's have been appropriately

revised, and employees have been trained and competency assessed on the revised procedures.

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 deviations and to prevent their recurrence. Your response should include copies of updated written procedures and verification of personnel training. 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. Your reply should be sent to Nadine Nanko Johnson, Compliance Officer, at the above address.

Sincerely,

Charles W. Sedgwick
District Director
Kansas City District

cc: Jean Colacecchi, Acting Director of Public Health
Iowa State Department Of Public Health
Lucas State Office Building
Des Moines, IA 50319-0075