



OCT 17 1997

CERTIFIED - RETURN RECEIPT REQUESTED

Mr. Craig H. Petrik
Responsible Head
Biosera, Inc.
c/o McGlone & Rasmussen
2030 Maine Street, Suite 1630
Irvine, California 92714

Dear Mr. Petrik:

The Food and Drug Administration's (FDA or the agency) Denver and Los Angeles District Offices conducted inspections of Biosera, Inc.'s (Biosera), Denver, Colorado facility on June 23, 1997 through August 11, 1997; San Diego, California facility on June 23, 1997 through July 11, 1997; and Orange, California facility June 23, 1997 through September 3, 1997. The inspections revealed serious deviations from Subchapter C, Part 211, and Subchapter F, Parts 600-680, Title 21, Code of Federal Regulations (CFR), and the standards in your licenses. At the conclusion of the inspections three lists of observations (Form FDA 483) were issued.

The Commissioner has determined that the deviations identified during the inspections represent grounds for revocation of your licenses and because of their serious nature, constitute a danger to health. Therefore, as you were notified by telephone, the establishment and product licenses held by Biosera, Inc., are suspended pursuant to 21 CFR 601.6(a). Deficiencies noted include, but are not limited to the following:

1. Failure to maintain accurate records concurrently with the performance of each significant step in the collection, processing, storage, and distribution of blood and blood components so that all steps can be clearly traced [21 CFR 600.12, 21 CFR 606.160, 21 CFR 606.165, and 21 CFR 211.180] in that:
 - a. The manufacturing records for red blood cells for immunization reveal discrepancies in lots SC242 and SC262. These lots represent two units of Whole Blood that were collected, glycerolized, aliquoted in glass vials, and frozen in 1992 and 1993 respectively. Processing records for these lots were collected by FDA in 1994 and a complete physical inventory was performed at that time. Processing records collected during the current inspections reveal that the records have been changed, in that additional vials were added to both of these lots;

- (b)(4)
- b. The records incorrectly show that at least [redacted] vials of red blood cells for immunization that are listed in the records as being in inventory are not actually present in the current inventory. The disposition of these vials is unknown;
 - c. At least [redacted] vials of red blood cells for immunization were observed in the current inventory; however, the processing records incorrectly show that these [redacted] vials were deglycerolized either for immunization or titration testing;
 - d. The records incorrectly show that [redacted] vials of red blood cells for immunization were manufactured for lot SC2010; however, the physical inventory revealed [redacted] extra vials labeled [redacted];
 - e. There are two lots of red blood cells for immunization identified in the inventory as SC2012. The corresponding records reveal that one lot was designated SC2012A [redacted] and the other SC2012B [redacted] however, vials examined in the physical inventory from both lots are labeled SC2012 without designation as "A" or "B". The records indicate that lot SC2012A was collected from an individual whose blood type is O positive, and lot SC2012B was collected from an individual whose blood type is B positive;
 - f. In at least four instances, the final disposition information contained in the disposition logs does not correspond to the recipients' immunization records;
 - g. All records associated with Source Plasma donor [redacted] who tested repeatedly reactive for anti-HIV- 1/2, Western blot indeterminate, in September 1995 (unit 02023), were unavailable at the firm and are "considered lost" by the firm;
 - h. The firm routinely receives units of Whole Blood from other collection facilities, but does not keep records documenting the receipt of such units;
 - i. There are no records documenting the routine shipment of vials or syringes of red blood cells for immunizations to other Biosera locations.
- (b)(4)
2. Failure to adequately determine the suitability of donors [21 CFR 640.3 and 21 CFR 640.63] in that:
- a. Whole Blood donors are not interviewed about AIDS high risk behavior at each donation; rather, the questions are asked only during the initial screening and at the yearly medical examination [21 CFR 640.63(c)(9)]. The Whole Blood donors are asked "Answers to AIDS questionnaire neg?" at each donation. Further, in at least one instance the screening records reflect that an individual answered "NO" to the

question "Answers to AIDS questionnaire neg?", but was accepted for Whole Blood donation on May 22, 1997;

- b. For at least two Source Plasma donors, a sample of blood was not drawn on the day of the first medical examination or plasmapheresis, whichever came first, for serum protein electrophoresis to determine immunoglobulin composition [21 CFR 640.65(b)(1)(i)]; and
 - c. The accumulated laboratory data for two Source Plasma donors, including the serum protein electrophoresis pattern, were not reviewed within 21 days of the sample collection to determine whether the donor could continue donating [21 CFR 640.65(b)(2)(i)].
3. Failure to have the selection and scheduling of the injection of the antigen performed by a qualified licensed physician [21 CFR 640.66], in that the selection and scheduling of the red blood cell antigen for immunization is performed by the responsible head and not a licensed physician employed by Biosera, Inc..
4. Failure to maintain and follow adequate standard operating procedures (SOP) for all steps to be followed in the collection, processing, storage and distribution of blood and blood components [21 CFR 606.100 and 21 CFR 211.100], in that:
 - a. Source Plasma, unit 02908, which tested non-reactive for anti-HCV, was collected on January 23, 1997, from donor [*mm*] who had previously tested repeatedly reactive for anti-HCV on four separate occasions. Source Plasma unit 02908 was distributed in May 1997 for further manufacture of injectable products [21 CFR 606.100(c)];
 - b. Monthly antibody identifications are not performed on all donors immunized with red blood cells as required by Biosera, Inc.'s SOPs;
 - c. The whole blood number is not always recorded on the donor immunization form; however, Biosera, Inc.'s SOP states that the donor immunization form should include lot number, whole blood number, and vial number of the antigen.
5. Failure to report important proposed changes in manufacturing methods to the agency prior to implementation [21 CFR 601.12], in that, red blood cells for immunization are routinely stored and shipped in plastic syringes from the Orange, California location to the other two licensed locations. Biosera, however, has neither reported this important change

to, nor received notification of acceptance from the Director, Center for Biologics Evaluation and Research.

6. Failure to maintain adequate records of reports of complaints of adverse reactions regarding each unit of blood or blood product arising as a result of blood collection or transfusion [21 CFR 606.170], in that the donor records do not always contain documentation of donor reactions. For example, two donor reactions were documented only as "Donor Sick" with no report of the investigation, including conclusions or follow up. Additionally, adverse reaction forms were not completed, as required by established written procedures.

7. Failure to observe, standardize and calibrate equipment used in the collection, processing, storage, and distribution of blood and blood components [21 CFR 606.60], in that:
 - a. There is no documentation of annual maintenance of the Autopheresis-C automated plasma collection equipment since installation;
 - b. There is no documentation of error messages for the automated plasma collection equipment;
 - c. Periodic standardization and calibration is not performed on donor weight scales, blood pressure cuffs, or pipettes used in serological testing;
 - d. Internal thermometers used to verify temperatures of the firm's freezers and refrigerators used to store Source Plasma are not checked against a national standard;
 - e. Containers used to ship Source Plasma have not been validated to assure proper temperature would be maintained during shipment; and
 - f. There is no documentation of periodic standardization and calibration of the microhematocrit centrifuge and the serofuge used to perform serological testing.

In addition, FDA obtained official samples of red blood cells for immunization from your inventory during the inspection of the Orange, California facility. Our analysis revealed vials of red blood cells for immunization that were falsely labeled with incorrect donor information. For example, among other findings, one vial from one lot of red blood cells for immunization incorrectly labeled as blood group O, was in fact, blood group B.

As described above, the recent inspections indicate serious and extensive noncompliance with product standards designed to assure the continued safety, purity, potency, and effectiveness of the products manufactured, as well as with donor protection standards intended to assure a continuous

and healthy donor population. These deficiencies represent a comprehensive failure of your firm to maintain control over critical aspects of its manufacturing process, as well as to exercise control over the establishment in all matters relating to compliance and to assure that personnel are adequately trained and supervised and have a thorough understanding of the procedures they perform, as required by 21 CFR 600.10(a) and (b), and 21 CFR 211.25. In addition, FDA has determined that your firm's red blood cells for immunization are misbranded within the meaning of sections 502(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) [21 U.S.C. 352(a)] and section 351 (b) of the Public Health Service Act (PHS Act) [42 U.S.C. 262(b)]. The serious nature and extent of the deficiencies observed at Biosera, Inc., leads the agency to conclude that they are the consequence of a careless disregard for the applicable regulations and standards in your license.

Accordingly, the Commissioner finds that under 21 CFR 601.5(b)(3) and (b)(4) grounds exist for revocation of the establishment and product licenses held by Biosera, Inc., and that by reason thereof, a danger to health exists. This letter confirms the telephone conversation in which notice was given that, pursuant to 21 CFR 601.6(a), all establishment and product licenses encompassed by U.S. license number 1059 issued to Biosera, Inc., have been suspended, as of the time and date indicated below. Instructions were given at that time not to collect or ship Source Plasma or red blood cells for immunization.

Pursuant to 21 CFR 601.6(a), you are required to: 1) notify the selling agents and distributors to whom products subject to licensure have been delivered within the past 60 days of your suspension; and 2) furnish to the Office of Compliance, Center for Biologics Evaluation and Research, complete records of such deliveries and notice of suspension. You are also requested to submit a detailed inventory of all products currently in storage.

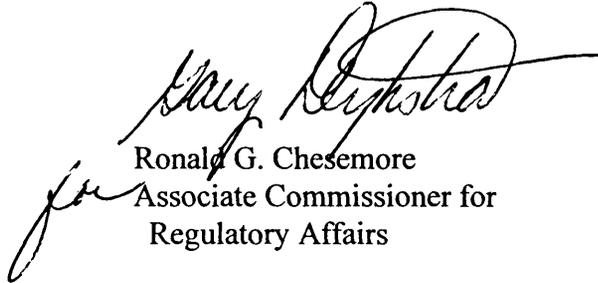
These submissions should be sent to Mr. James C. Simmons, Director, Office of Compliance, HFM-600, Center for Biologics Evaluation and Research, Suite 200N, 1401 Rockville Pike, Rockville, Maryland 20852-1448. Mr. Simmons may be reached at (301) 827-6190. In addition, a copy of all submissions relating to this suspension should be sent to the FDA's Denver District Office, to the attention of Mr. Gary Dean, District Director, P.O. Box 25087, 6th and Kipling Streets, Denver, CO 80225-0087.

You are advised that Biosera, Inc., no longer holds unsuspended and unrevoked licenses for Source Plasma, and that unless and until otherwise notified, any interstate shipment for sale, barter or exchange of Source Plasma and red blood cells for immunization is a violation of section 351(a) of the Public Health Service Act [42 U.S.C. 262(a)], for which criminal penalties may be imposed. Additionally, any shipments of products, including red blood cells for immunization and Source Plasma, manufactured under the conditions found during the most recent inspection or during suspension of the license constitute violations of the FD&C Act, sections 501 (a)(2)(B) [21 U.S.C. 351(a)(2)(B)], 501(c) [21 U.S.C. 351(c)], 502(a) [21 U.S.C. 352(a)], 502(f) [21 U.S.C. 352(f)], and 502(j) [21 U.S.C. 352(j)]. Violations of these and other sections of the FD&C Act may result in additional regulatory action without further notice. Such actions include, but are not limited to, seizure, injunction, and/or civil penalties.

The Commissioner will proceed pursuant to 21 CFR 601.6(b)(1) to revoke establishment license number 1059 and your product licenses for Source Plasma unless you do the following: 1) telephone Mr. Simmons within ten (10) working days of receipt of this letter to request that the matter of revocation be held in abeyance pending resolution of the matters involved, as provided in 21 CFR 601.6(b)(2), and confirm the telephone call in writing. Any request that revocation be held in abeyance will be evaluated by the agency.

Number SF-001-8 has been assigned to this suspension. All correspondence with the Office of Compliance concerning this suspension should reflect this number. The appropriate state officials will also be notified of your suspension. In addition, this administrative action does not preclude the agency from taking additional regulatory action, including seizure and or injunction, without further notice.

Sincerely yours,



Ronald G. Chesemore
Associate Commissioner for
Regulatory Affairs

Effective Date October 20, 1997 Time 11:15 AM