



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
g 3500d

September 3, 2002

Dallas District
4040 North Central Expressway
Dallas, Texas 75204-3145

Ref: 2002-DAL-WL-19

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Norman Kalmin, M.D.
President and CEO
South Texas Blood and Tissue Center
6211 Interstate 10 West
San Antonio, TX 78201

Dear Dr. Kalmin:

During an inspection of South Texas Blood and Tissue Center located in San Antonio, Texas, conducted May 13 through 28, 2002, our investigators documented significant deviations of regulations for human tissue intended for transplantation set forth at Title 21, Code of Federal Regulations (21 CFR), Part 1270, promulgated under the authority of Section 361 of the Public Health Service Act. We found that your firm failed to prepare, validate, and follow written procedures for prevention of infectious disease contamination and cross-contamination during processing as required by 21 CFR 1270.31(d). Our observations included:

1. Failure to validate written procedures. For example:
 - a. There was no documentation to demonstrate that twelve (12) procedures pertaining to sterilization, decontamination, and/or cleaning had been validated.
 - b. Although you attempted to validate your tissue Pre-Processing Tissue Disinfection (TS02.0220) and Tissue Sterilization/Irradiation (TS02.040) procedures, validation was not adequate. The Soaking and Irradiation Validation study you used for validation of these procedures did not demonstrate that the pre-processing antibiotic solution soak and irradiation

sterilization processes would effectively eliminate all organisms present in tissue components, in that:

- You did not assess the average bioburden of tissues received from your suppliers.
 - You did not determine worst-case situations for disinfection.
 - Tissue from Donor [REDACTED], used in this validation study, had a post-irradiation positive culture for *Actinobacillus ureae*.
- c. You have not validated that the [REDACTED] system used to conduct microbial testing will perform as you intend. You use this system to conduct sterility testing of rinsates from aseptically processed tissues. However, there is no evidence that residue from solutions used during aseptic processing do not inhibit growth of the sterility test media, and thereby confound the validation results. In addition, the comparison study conducted by STBTC did not adequately demonstrate that the [REDACTED] system favorably compares to the reference laboratory against which the study was conducted. We also note that the [REDACTED] system has not been cleared for use in testing of human tissue for the recovery and detection of aerobic and anaerobic microorganisms. FDA cleared indications reference recovery and detection of aerobic and anaerobic microorganisms from clinical blood specimens, other normally sterile body fluids, and platelets. Since the system has not been cleared for sterility testing of rinsates from aseptically processed tissues, you must demonstrate that the device will accurately and effectively perform in the manner you intend.
- d. Failure to follow written procedures, as follows:
- Your Tissue Pre-Processing Record Review (TS02.0145) procedure states that all donor records will be reviewed prior to processing of tissue. However, a review of [REDACTED] donor charts dated between May 14, 2001 and May 16, 2002 found that all [REDACTED] records were reviewed between 36 and 129 days after the tissue had been processed, with an average review time occurring 72.8 days post-processing.
 - Your Inoculation of Bottles for [REDACTED] (TS02.0702) procedure requires that the time for mixing of sample swabs in preparing the [REDACTED] be [REDACTED]. However, there is no timing device present in the laboratory to measure the time [REDACTED].

- Your Bone Tissue [REDACTED] (TS02.0224) procedure instructs that tissue is to undergo [REDACTED] and your Cleaning and Disinfecting Instruments (TS02.0350) procedure includes instructions to clean instruments in [REDACTED]. In fact, [REDACTED] is not used in either of these procedures. During the inspection, you indicated that the use of [REDACTED] was deleted from both of these processes. However, the procedures were not updated to reflect these current practices.
- Your Pre-Processing Tissue Disinfection TS02.0220 procedure requires that tissue contaminated with Class I or II organisms to be disinfected using [REDACTED] during processing, and requires that tissue contaminated with Class III organisms should be [REDACTED]. The procurement culture of the Left Achilles Tendon from Donor [REDACTED] had a positive culture for *Pseudomonas aeruginosa*, a Class III organism, however this tissue was processed using [REDACTED] rather than [REDACTED].

2. Failure to prepare written procedures to prevent contamination or cross-contamination of tissue during processing, in that there are no procedures to perform culture testing of tissue following the [REDACTED] process, which would be necessary to adequately prevent contamination and cross contamination.

The above-identified deviations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the regulations. The specific deviations noted in this letter and the FDA-483, Inspectional Observations (copy enclosed), issued at the conclusion 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 causes of the deviations identified by FDA. If the causes are determined to be systems problems, you should promptly initiate permanent corrective actions.

You should take prompt measures to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Such action may include an order of retention, recall, and destruction of human tissue, and/or injunction.

We acknowledge receipt of your response letter to the inspectional observations, which was received in our office on July 8, 2002. Dallas District Office, and FDA's Center for Biologics Evaluation and Research (CBER), have reviewed your response and offer the following comments. We acknowledge your commitment to renovation of the tissue production facility, and implementation of your master validation plan upon completion of these renovations. However, you did not comment on interim steps to be taken to prevent infectious disease contamination or cross-contamination of tissue during

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processing. Please comment.

Please notify this office, in writing, within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted deviations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar deviations will not recur. If corrective actions cannot be completed within fifteen (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 the Food and Drug Administration, Dallas District Office, 4040 North Central Expressway, Dallas, Texas 75204, Attention: Brenda Baumert, Compliance Officer.

Sincerely yours.

A handwritten signature in black ink, reading "Michael A. Chappell". The signature is written in a cursive style with a large, sweeping flourish at the end.

Michael A. Chappell
District Director

Enclosure