



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

By Certified Mail - Return Receipt Requested
And By Facsimile Transmission

Center for Biologics Evaluation and
Research
1401 Rockville Pike
Rockville MD 20852-1448

CBER - 07 - 003

Warning Letter

Ralph M. Conti, M.D.
6301 Mountain Vista Road # 205
Henderson, Nevada 89014

NOV 22 2006

Dear Dr. Conti:

This letter describes the results of a Food and Drug Administration (FDA) inspection conducted between July 20 and July 24, 2006. FDA investigator Anthony Keller met with you to review your conduct of an experimental procedure to implant [redacted] tissue to treat a variety of illnesses. FDA conducted this inspection under the agency's Bioresearch Monitoring Program, which includes inspections designed to review the conduct of clinical research involving investigational new drugs.

The investigator issued and discussed the Form FDA 483, Inspectional Observations, with you at the end of the inspection.

The inspection revealed that you obtained human [redacted] from a local hospital, carried them to your office, processed the tissue, and implanted it in at least 16 subjects. As a pediatrician you were not otherwise involved with the care of the recipients, who are adults diagnosed with illnesses such as [redacted]

Based on this information, we have determined that your actions have violated the Public Health Service Act (PHS Act) and the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The [redacted] tissue and cells are a biological product as defined in section 351(i) of the PHS Act [42 U.S.C. § 262(i)], in that they are a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product or analogous product, or arsphenamine or derivative of arsphenamine, applicable to the prevention, treatment, or cure of a disease or condition of human beings. The [redacted] tissue and cells are also a drug within the meaning of section 201(g) of the FD&C Act [21 U.S.C. § 321(g)], in that they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man.

In order to introduce or deliver for introduction a biological product into interstate commerce, a valid biologics license (BLA) must be in effect [21 U.S.C. § 355(a); 42 U.S.C. § 262(a)]. A BLA is issued only after a showing of safety, purity and potency for the product's intended use. Before approval, biological products may generally be distributed for clinical use in humans only if the sponsor has an investigational new drug (IND) application in effect [21 U.S.C. § 355(i); Title 21, Code of Federal Regulations (21 CFR) Part 312]. The [redacted] tissue and cells are not the subject of an approved BLA, and you do not have an IND in effect.

The [redacted] tissue and cells you implanted are human cells, tissues, or cellular and tissue-based products (HCT/Ps) as defined in 21 CFR § 1271.3(d). Under 21 CFR Part 1271, HCT/Ps are not subject to license or IND requirements if certain criteria are met. However, these criteria are not met here. An IND application is required for the [redacted] tissue and cell implants

because they are intended for non-homologous use (21 CFR § 1271.10(a)(2); 21 CFR 1271.3(c)).

As a result, you violated applicable regulations governing the proper conduct of clinical studies involving investigational new drugs. For example:

- You failed to submit an IND application to FDA (21 CFR § 312.20(a); 21 CFR § 312.40(a)).
- You initiated a clinical investigation without an IND application in effect (21 CFR § 312.20(b)).
- You initiated a clinical investigation without institutional review board (IRB) review or approval (21 CFR § 56.103; 21 CFR § 312.40(a)).
- You did not obtain and document adequate informed consent, including the required elements specified in 21 CFR § 50.25(a) (21 CFR § 50.27; 21 CFR § 312.60).

Moreover, as explained in 21 CFR § 1271.20, your [REDACTED] tissue implants are subject to the requirements of 21 CFR Part 1271, subparts B (Procedures for Registration and Listing), C (Donor Eligibility), and D (Current Good Tissue Practice). Our inspection revealed multiple violations of these requirements. For example:

- You did not register with FDA or submit a list of HCT/Ps that you manufacture (including recovery, processing, storage, labeling, packaging, and distribution) (21 CFR § 1271.21).
- You failed to determine donor eligibility, as required by 21 CFR § 1271.50, based upon the results of donor screening in accordance with 21 CFR § 1271.75 and donor testing in accordance with 21 CFR §§ 1271.80 and 1271.85. Specifically, you did not obtain a health history of the [REDACTED] donors or test the [REDACTED] to reduce the risk of transmission of relevant communicable diseases.
- You did not establish and maintain procedures for all steps to be performed in testing, screening, determining donor eligibility, and complying with other applicable requirements of 21 CFR Part 1271, subpart C, as required by 21 CFR § 1271.47(a). Specifically, you did not follow any written standard operating procedures for the processing, storage, and disposition of the [REDACTED] during and after the experimental procedure.
- You did not maintain records concurrently with performance of each step of the required donor eligibility determination or the required current good tissue practices set forth in 21 CFR part 1271, subpart D (21 CFR § 1271.270). Specifically, you did not maintain records about the processing of the [REDACTED] or about each subject's procedure.

This letter is not intended to contain an all-inclusive list of deficiencies in your clinical study of this biological product. It is your responsibility to ensure adherence to applicable requirements of the FD&C Act, the PHS Act, and applicable FDA regulations and to protect the rights, safety, and welfare of subjects under your care.

You should notify this office, in writing, within fifteen (15) business days of receipt of this letter of the steps you have taken or will take to correct the noted violations and prevent their recurrence. Your response should include any documentation necessary to show that correction has been achieved.

Page 3 - Dr. Conti

You may submit an IND application to the FDA pursuant to Title 21 CFR Part 312. Information to assist you in submitting an IND application is available at <http://www.fda.gov/cber/ind/ind.htm>. Questions regarding submission of an IND application and assistance may be directed to the FDA's Center for Biologics Evaluation and Research Office of Communications, Training, and Manufacturers Assistance at (800) 835-4709. If an IND application is submitted, no clinical investigation is permitted to proceed until the IND application is in effect, as described in 21 CFR §§ 312.20 and 312.40. These regulations are available at <http://www.gpoaccess.gov/cfr/index.html>.

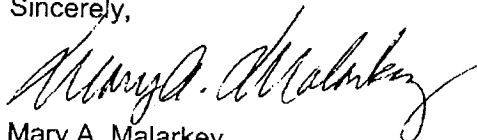
This Warning Letter is issued to you because of the serious nature of the observations noted at the time of the FDA inspection. Please be advised that failure to implement effective corrective actions and/or the commission of further violations may result in the initiation of enforcement action(s) without further notice. These actions could include injunction and initiation of clinical investigator disqualification proceedings, which may render you ineligible to receive investigational drugs.

Please send your written response to:

Ms. Bhanu Kannan
Division of Inspections and Surveillance (HFM-664)
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
1401 Rockville Pike, Suite 200N
Rockville, Maryland, 20852-1448
Telephone: (301) 827-6221

We request that you send a copy of your response to the FDA District Office listed below.

Sincerely,



Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc:
Barbara Cassens, District Director
Food and Drug Administration
1431 Harbor Bay Parkway
Alameda, California 94502-7070

