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Food and Drug Administration
Rockville MD 20857

Certified-Return Receipt Requested

MAR 1 1999

Warning Letter

Nicholas Kipshidze, M.D., Ph.D.
Medical College of Wisconsin
Divisions of Cardiovascular Medicine
9200 W. Wisconsin Avenue
Milwaukee, Wisconsin 53226

CBER - 99 - 010

Dear Dr. Kipshidze:

During an inspection ending December 22, 1998, Mr. Jerome Wytrykus and Ms. Connie Coates, investigators from the Food and Drug Administration, documented that you administered _____ to human subjects in violation of the Public Health Service Act (PHS Act) and the Federal Food, Drug, and Cosmetic Act (FD&C Act).

_____ is a biological product as defined in Section 351(i) of the PHS Act (as amended November 21, 1997), in that it is a biological product applicable to the prevention, treatment, or cure of diseases or injuries to human beings, and is subject to Section 351(a) of the PHS Act. _____ also is a drug within the meaning of Section 201(g) of the FD&C Act in that it is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man.

The inspection revealed that Section 505(a) of the FD&C Act is being violated through introduction into interstate commerce of a new drug _____ with no approved biologics license application (BLA) in effect, nor any investigational new drug application (IND) in effect, pursuant to Section 505(i) of the FD&C Act.

The _____ formulations used in your studies involving human subjects are misbranded under Section 502(f)(1) of the FD&C Act, in that the labeling fails to bear adequate directions for use for the purposes for which the drug is intended because adequate directions cannot be written for unapproved drugs. The _____ you obtained from _____ which you administered to at least one human subject, bears the description "Usage: For research use only. Not for use in diagnostic or therapeutic procedures." The _____ you obtained from _____ which you administered to at least one human subject, bears the description "Usage: This material is offered by _____ for research, laboratory, or further manufacturing purposes only. Not for human use."

In addition, the unapproved _____ biologic drugs are in violation Section 351(a) of the PHS Act and Section 505 of the FD&C Act in that you exported unlicensed biological drugs to _____ for the purpose of a clinical investigation without receiving FDA authorization to export pursuant to Title 21, Code of Federal Regulations, Section 312.110.

This letter is not intended to be an all-inclusive list of deficiencies observed at your facility. It is your responsibility to ensure adherence to each requirement of the FD&C and PHS Acts and relevant regulations.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure and/or injunction, and disqualification.

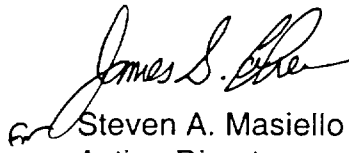
You should notify this office in writing, within 15 business days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step taken to prevent a recurrence of similar violations. If corrective action cannot be completed within 15 business days, state the reason for the delay and the time within which the corrections will be completed. Corrective actions would include, but are not limited to, discontinuing administration of _____ to human subjects, halting the shipment of _____ to colleagues overseas, and the submission of an IND.

An IND application and information packet is enclosed. Any IND application should be submitted to Dr. Kathryn Zoon, Center for Biologics Evaluation and Research, HFM-99, Suite 200N, 1401 Rockville Pike, Rockville, Maryland 20852-1448. Questions regarding submission of an IND application and assistance may be directed to the Office of Communications, Training, and Manufacturers Assistance at (800) 835-4709.

Your response to this letter should be sent to the following address:

Mr. Joseph P. Salewski
Division of Inspections and Surveillance HFM-650
Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

Sincerely,



Steven A. Masiello
Acting Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation
and Research

Enclosure

Information on Submitting a Sponsor-Investigator IND
including Title 21 of the Code of Federal Regulations Part 312

cc: Institutional Review Board
Medical College of Wisconsin
