Department of Health and Human Services

Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

CBER- 04 -06

By Certified Mail - Return Receipt Requested
And by Facsimile Transmission

MAY 13, 2004

Warning Letter

Ritchie C. Shoemaker, M.D.
500 Market Street, Suite 102
Pocomoke City, Maryland 21851

Dear Dr. Shoemaker:

During an inspection that was conducted from January 13-15, 2004, Food and Drug Administration (FDA) investigators Lynette P. Salisbury and Gale L. Glinecki determined that you administered and instructed subjects to self-administer the FDA-approved veterinary product Staphage Lysate to human subjects in violation of the Public Health Service Act (PHS Act) and the Federal Food, Drug, and Cosmetic Act (FD&C Act). The veterinary drug is not licensed for human use.

Although the manufacturer is licensed to manufacture a human form of Staphage Lysate, that human form has not been manufactured for approximately [redacted] The human form of Staphage Lysate is a biological product as defined in Section 351 (i) of the PHS Act in that it is analogous to a virus and is applicable to the prevention, treatment, or cure of a disease or condition of human beings, and is subject to Section 351 (a) of the PHS Act. Staphage Lysate 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 the following violations:

1. Section 351 (a) of the PHS Act was violated in that unlicensed biological product Staphage Lysate was introduced or delivered for introduction into interstate commerce 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.

2. The Staphage Lysate used in your study is misbranded under Section 502(f)(1) of the FD&C Act because the labeling fails to bear adequate directions for use. You administered

and instructed subjects to self-administer the veterinary form of Staphage Lysate by nasal instillation using atomizers intended for another purpose. The product did not bear directions for that use, but instead was labeled "For investigational Use Only." Although 21 C.F.R. 201.115(b) exempts investigational drugs from the adequate-directions-for-use requirement in Section 502(f)(1), and permits them to bear the investigational use caution set forth in 21 C.F.R. 312.6(a), that exemption is limited to drugs that comply with Section 505(i) of the F D&C Act and the regulations authorized by that section. The Staphage Lysate used in your study did not comply with those regulations because, among other reasons, it was not subject to an IND that was in effect, as required by 21 C.F.R. 312.20(b). Therefore, the Staphage Lysate was subject to Section 502(9(1), and failed to satisfy that statutory requirement.

3.You violated 21 C.F.R. 312.20 and 312.40 by failing to submit an investigational new drug application (IND) to FDA prior to conducting a clinical investigation. The inspection revealed that you administered and instructed 78 subjects to self-administer Staphage Lysate from October 2001 to November 2003.

4.You violated 21 C.F.R. 312.23(a)(6) by failing to have a written protocol during the time of the study.

5. You violated 21 C.F.R. 50.20 and 312.60 by failing to obtain the informed consent of seven subjects.

6. You did not submit the clinical study or the informed consent form to an IRB for review and approval prior to initiating the study, as required by 21 C.F.R. 56.103(a).

7. You violated 21 C.F.R. 312.60 and 312.62(a) by failing to maintain any records of the receipt and disposition of the investigational drug Staphage Lysate, and by failing to record the lot numbers of Staphage Lysate you supplied or administered to the 78 subjects.

This letter is not intended to be an all-inclusive list of deficiencies. It is your responsibility to ensure adherence to each requirement of the law and applicable regulations, and to protect the rights, safety, and welfare of subjects under your care.

We received and reviewed your letter dated January 16, 2004, written in response to the Form FDA 483 observations left with you at the conclusion of the inspection. Your response letter states that: (1) you have ceased all use of Staphage Lysate, (2) you now have an IRB approved protocol and informed consent form, (3) you have reviewed a manual on Good Clinical Practices and the regulations regarding investigational new drugs, (4) a clinical coordinator will be added to your staff, and (5) you have discussed proper documentation procedures with your staff.

Your written response indicates that you are preparing to submit an IND to FDA in the future. Unless the manufacturer resumes production of the approved human Staphage Lysate, the veterinary product may only be studied as an investigational human drug in the United States if there is an IND in effect, You may submit an IND application to the FDA pursuant to Title 21, Code of Federal Regulations Part 312 (21 C.F.R. Part 312). If an IND is submitted, no clinical investigation is permitted to proceed until the IND is in effect, as described in 21 C.F.R. 312.20 and 312.40. These regulations are available at http://www.access.gpo.gov/nara/cfr/index.html.

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.

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 the failure to effectively put into practice the corrective actions

you plan to implement and/or the commission of other violations may result in the initiation of enforcement action(s) without further notice. These actions could include initiation of clinical investigator disqualification proceedings, which may render a clinical investigator ineligible to receive investigational new drugs, and/or injunction.

We do not require a response to this letter. If you have any questions or comments. about the contents of this letter or any aspects of clinical testing or investigational drugs, you may contact:

Debra Bower
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Sincerely,

/s/

James S. Cohen
Acting Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

This page was posted on November 18, 2005.
