

d1565b

HFI-35

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Refer to: CFN 1120199

Baltimore District
900 Madison Avenue
Baltimore, Maryland 21201
Telephone: (410) 962-4040

March 27, 1998

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Bernard J. Poussot, President
Wyeth-Ayerst Laboratories, Inc.
P.O. Box 8299
Philadelphia, Pennsylvania 19101

Dear Mr. Poussot:

The Food and Drug Administration (FDA) conducted a pre-approval inspection of your A. H. Robins facility located at 2248-2300 Darbytown Road, Richmond, Virginia, on March 17-20, 1998. During the inspection, our investigators documented several significant deviations from the Current Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Parts 210 & 211) regarding your microbiological testing laboratory as it relates not only to the NDAs referenced above, but products you currently market. These deviations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act.

You have failed to establish laboratory controls based on scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity.

Significant findings include:

- Failure to perform and/or complete the validation and qualification of the autoclaves to sterilize media and laboratory testing equipment. This equipment is used to test raw materials for release and in stability testing of finished drug products;
- One autoclave undergoing validation failed to meet operational and performance requirements for the sterilization of media and equipment, yet it was in use during the inspection;

Mr. Bernard J. Poussot

Page 2

March 27, 1998

- Failure to have written procedures reviewed and approved by the quality control unit prior to implementation;
- Some written procedures were out-of-date or obsolete, while some laboratory operations had no documented approved procedures in place. For example, there were no procedures for the discard or retention of media that had been under or over processed during autoclaving;
- Failure to follow written procedures, in that:
 - Validation was not performed on the autoclaves used in sterilization of test media and laboratory equipment. Such autoclaves should not have been used for media or equipment sterilization until validation was completed and established specifications met;
 - Preventative maintenance was not performed on two autoclaves as required by the manufacturer's operation manual and your draft SOP;
 - Media was autoclaved for extensive periods of time beyond the established specifications for media sterilization, causing lack of assurance that the media will perform during the growth promotion phase or otherwise meet acceptance criteria;
 - Autoclave control bioindicator checks were not performed on a monthly basis per written instructions;
 - The growth promotion and sterility testing of media was not documented in the media QC log.

The above deviations were included on a written list of inspectional observations (FDA-483, enclosed) issued to Mr. Michael L. Berg, Managing Director, at the conclusion of the inspection. The violations discussed above and included on the FDA-483 are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure that your establishment is in compliance with all requirements of the federal regulations.

Until it has been determined that corrections are adequate, federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, as a result of these deficiencies, Baltimore District is recommending to the Center for Drug Evaluation and Research that the approval of pending [REDACTED], and [REDACTED] be withheld.

Mr. Bernard J. Poussot

Page 3

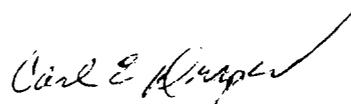
March 27, 1998

You should take prompt action to correct these deviations. Failure to do so may result in regulatory action without further notice, such as seizure and/or injunction.

Please notify this office in writing, within 15 working days of receipt of this letter, of any additional steps you have taken to correct the noted violations and to prevent their recurrence. If corrective action cannot be completed within 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, Richmond Resident Post, 10710 Midlothian Turnpike, Suite 424, Richmond, Virginia 23235, to the attention of Scott J. MacIntire, Compliance Officer. Mr. MacIntire can be reached at (804) 379-1627, Ext. 14.

Sincerely,



Carl E. Draper
Acting Director, Baltimore District

Enclosure

cc: Mr. Michael L. Berg
Managing Director
Wyeth-Ayerst Laboratories
P.O. Box 26609
2248 Darbytown Road
Richmond, Virginia 23261-6609