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CBER-99-013

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

MAR 17 1999

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Alister Stokes
Chief Operating Officer
Speywood Biopharm Ltd.
1 Bath Road
Maidenhead
Berkshire SL6 4HH
United Kingdom

Dear Dr. Stokes:

An inspection of Speywood Biopharm Ltd., located at Ash Road, Wrexham, United Kingdom was conducted from November 30 through December 7, 1998. During the inspection, violations of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act and Title 21, Code of Federal Regulations (21 CFR), Subchapter C Parts 210 and 211, and Subchapter F Parts 600-610 were documented, as follows:

1. Failure to establish and/or follow written testing programs designed to assess the stability characteristics of drug products [21 CFR 211.166 and 211.137(a)] in that at the time of the inspection there was no approved stability program.
2. Failure to establish an adequate system for monitoring environmental conditions of aseptic processing areas [21 CFR 211.42(c)(10)(iv) and 600.11(a)] in that active air sampling is not performed during aseptic filling but rather immediately after every filling operation.
3. Failure of personnel engaged in the manufacture, processing, packing, or holding of a drug product to wear, as necessary, protective apparel such as head and face coverings to protect drug products from contamination [21 CFR 211.28(a) and 600.10(c)] in that fill room operators' eyes and eyebrows are not covered.
4. Failure to establish appropriate time limits for the completion of each phase of production to assure the quality of the drug product [21 CFR 211.111] in that production time limits for formulation, sterile filtration, and aseptic filling operations have not been established.

5. Failure to assure that container closure systems provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product [21 CFR 211.94(b)] in that validation studies for container closure integrity have not been conducted.
6. Failure to establish 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 [21 CFR 211.165(e)] in that the _____ determination of _____ and the method for determining _____ although included in the firm's analytical method validation plan, have not been validated.
7. Failure to assure that air filtration systems are adequate [21 CFR 211.46(c) and 211.100(a)] in that smoke studies to evaluate laminar flow in the filling area have not been conducted since 1985, are not documented, and there are no written procedures for such studies.
8. Failure to thoroughly investigate any unexplained discrepancy or the failure of a batch or any of its components to meet any of its specifications [21 CFR 211.192] in that :
 - a. The failure to meet the lower limit flow rate specification for the _____ was not fully investigated prior to changing the specification.
 - b. Deviation reports contain the statement "No flow rate and temperature due to _____" but no information is given as to problems with the thawing process or corrective action to be taken.

We acknowledge receipt of your February 15, 1999, written response which addresses the inspectional observations on the Form FDA 483 issued at the close of the inspection, and we will respond to your letter under separate cover. Corrective actions addressed in your February 15, 1998, letter may be referenced in your response to this letter, as appropriate.

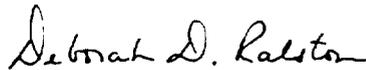
Neither this letter nor the list of inspectional observations (Form FDA 483) is meant to be an all-inclusive list of deficiencies at your facilities. It is your responsibility as management to assure that your facilities are in compliance with all the provisions of the Federal Food, Drug and Cosmetic Act and all applicable regulations. Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these deviations. Failure to correct these deviations may result in regulatory action without further notice. Such action includes seizure, license suspension and/or revocation.

Please notify FDA in writing, within 15 working days of receipt of this letter, of any additional steps you have taken or will take to correct the noted violations and to prevent their recurrence. If corrective actions 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, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200 N, Rockville, Maryland 20852-1448, Attention: Division of Case Management, HFM-610.

Sincerely,



Deborah D. Ralston
Acting Director
Office of Regional Operations

cc: John Savage
General Manager
Speywood Biopharm Ltd.
Ash Road
Wrexham Industrial Estate
Wrexham LL13 9UF
United Kingdom