



CBER-00-014

MAR 9 2000

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

William White, Jr.
President and CEO
Greer Laboratories, Inc.
639 Nuway Circle, NE
Lenoir, NC 28645

Dear Mr. White:

The Food and Drug Administration (FDA) conducted an inspection of Greer Laboratories, Inc., located at 639 Nuway Circle, NE, Lenoir, North Carolina, between December 6 and December 16, 1999. During the inspection, FDA investigators documented violations of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and deviations from the applicable standards and requirements of Subchapter C Parts 210 and 211, and Subchapter F Parts 600-680, Title 21, Code of Federal Regulations, (21 CFR). The deviations noted on the Form FDA 483, Inspectional Observations, issued at the conclusion of the inspection include, but are not limited to the following:

1. 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], as follows:
 - a) No investigations were conducted for allergenic extracts [REDACTED] lots 40-39-1A and 40-339-2A, and [REDACTED], lot M1-176-2X2, that failed general safety testing.
 - b) No investigations were conducted to determine the cause and effects of the precipitation or to characterize the nature of the precipitates found in the final allergenic extract products.
 - c) No investigations were conducted to determine the cause of leaking vials of allergenic extract products.
 - d) Sterilizing filter integrity failures were not investigated.

2. Failure to establish appropriate time limits for the completion of each phase of production to assure quality of the drug product [21 CFR 211.111], in that hold times have not been established for standardized bulk extracts.
3. Failure to visually examine reserve samples of drug products at least once a year for evidence of deterioration, and to record and maintain the results of the examination [21 CFR 211.170(b) and 21 CFR 680.2(f)], in that there were no written procedures for examining retention samples and there was no documentation of the results for the visual examinations conducted on retention samples.
4. Failure to ensure that reprocessed batches of product will conform with all established standards, specifications, and characteristics [21 CFR 211.115(a) and 211.110(a)], in that there were no written procedures and validation data that support the reprocessing, refiltering, and revalidating of bulk and finished allergenic extract products.
5. Failure to 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 container and closure validation studies were not performed to ensure the integrity of sealed vials.
6. Failure to establish and follow written procedures for evaluating the quality standards of drug products to determine the need for changes in drug product specifications, manufacturing or control procedures [21 CFR 211.180(e)], in that annual record reviews are not conducted.
7. Failure to assure that drug product container and closures are processed to remove pyrogenic properties [21 CFR 211.94(c)], in that vial stoppers are not processed to assure depyrogenation.

We acknowledge receipt of your firm's written responses dated December 27, 1999, January 14, 2000, and February 16, 2000, which address the inspectional observations on the Form FDA 483 issued at the close of the inspection. We have reviewed the contents of your December 27, 1999, and January 14, 2000, responses and will address your February 16, 2000, response under separate cover. Corrective actions addressed in your letters may be referenced in your response to this letter, as appropriate; however, your responses did not provide sufficient detail to fully assess the adequacy of the corrective actions. Our comments and requests for further information regarding corrective action are detailed below. The items correspond to the observations listed on the Form FDA 483:

Item 1

Your response fails to address reprocessing of batches that fail the general safety test. Please comment. In addition, please indicate what disposition procedures are in place to address an initial general safety test failure of product if the decision of the Quality Assurance and production personnel is not to conduct a repeat test.

Item 3

Your response states that you are "currently evaluating the impact of both product and capacity of various options to tap water as the dialyzing medium." Please provide the results of this study when completed.

Items 4 and 6

We agree with your assessment that precipitates may be an inherent characteristic of allergenic extracts, however, please be advised that investigations should be conducted to characterize the nature of the precipitation and to determine their effect on the stability and potency of the final product.

Item 8

Your response states that the personnel who work in the Order Processing department have received no formal training. Please indicate when these individuals will be certified under your newly implemented training program.

Item 11

We acknowledge your commitment to discontinue refiltering confirmed sterility failures until this practice has been adequately evaluated with respect to the absence of potential deleterious effects on the product. However, please be advised that if the sterility tests are performed in accordance with 21 CFR 610.12 and the bulk material or final container material fail initial and repeat testing, then the product does not meet the requirements for sterility and should be discarded. It is our view that refiltering of product that does not meet the requirements for sterility is an unacceptable practice. Please comment.

Item 15

Please provide a time frame for the completion of bioburden studies and the establishment of bioburden limits.

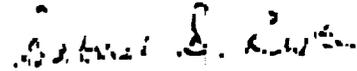
Neither this letter nor the list of inspectional observations (Form FDA 483) is meant to be an all-inclusive list of deficiencies that may exist at your facility. It is your responsibility as management to assure that your establishment is in compliance with all requirements of the federal regulations. 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.

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Please notify this office in writing within 15 working days of receipt of this letter, of any 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. Failure to promptly correct these deviations may result in regulatory action without further notice. Such action includes license suspension, revocation, injunction, and seizure. Your reply should be sent to the U.S. Food and Drug Administration, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200 N, Rockville, Maryland 20852-1448; Attention HFM-610.

If you have any questions regarding this letter, please contact Ms. Cathy Conn, Director, Division of Case Management, at (301) 827-6201.

Sincerely,



Deborah D. Ralston
Director
Office of Regional Operations