



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Atlanta District Office

60 8th Street, N.E.
Atlanta, Georgia 30309

June 13, 2000

VIA FEDERAL EXPRESS

Dr. Terry W. Osborn
President
Pharmaceutical Development Center
280 Calhoun Street
QE-113
Charleston, South Carolina 29403

WARNING LETTER
(00-ATL-46)

Dear Dr. Osborn:

Investigator Robert L. Lewis conducted an inspection of your firm (PDC) on May 23-25, 2000. Investigator Lewis conducted a preapproval inspection for [REDACTED]. Our investigator documented several significant deviations from the Current Good Manufacturing Practice Regulations (GMPs) as set forth in Title 21 of the Code of Federal Regulations (21 CFR), Part 211. These deviations cause this product to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act).

You have failed to formally establish written procedures that would clearly define and describe the responsibilities and procedures applicable to the quality control functions associated with the manufacture of this product. Neither your firm nor the applicant had clearly assumed the responsibilities of a quality control unit for such critical functions as in-process review testing, review prior to product release, review of third party laboratory results, and initiation of investigation into out-of-specification (OOS) results. These quality control responsibilities should be clearly established prior to initiation of manufacturing at a contract site.

Your firm released three lots of this product to a contract packager without any in process or release testing being performed. No evaluation was conducted of their conformance to established specifications prior to shipment. Release testing was finally conducted seven months after the lots were manufactured. This testing revealed one of the lots failed finished assay release specifications. There apparently were no procedures in place for the analytical lab or the applicant to forward these results to your firm in a timely manner. It is not clear when these results were actually submitted to your firm.

You failed to conduct an investigation as required when a drug batch fails to meet its specifications. One of the three lots under stability study was found to fail assay testing at the "initial" test date (approximately seven months after manufacture). Although the applicant became aware of the OOS results by at least September 1999, Investigator Lewis was given conflicting information in regards to when your firm became aware of the problem. No investigation had been initiated when our inspection at PDC was completed.

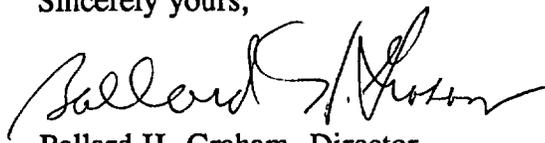
You could not provide documented evidence which established a high degree of assurance that the current manufacturing procedures and processes were effective and could consistently produce a product meeting its predetermined specifications and quality attributes. Your firm lacked sufficient data to justify the proposed manufacturing process for this product. One of the three initial lots failed release assay testing. There was also no data establishing the ability of the manufacturing process to produce a homogeneous suspension. Although in-process samples were taken at various points during the manufacture of the three initial lots, none of the samples was ever analyzed.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. At the close of the inspection, the Inspectional Observations (FDA 483) was issued to and discussed with you. The specific violations noted in this letter and in the FDA 483 could be symptomatic of underlying problems in your firm's quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

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

Please notify this office in writing within fifteen (15) days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. 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 response should be sent to Philip S. Campbell, Compliance Officer, at the address noted in the letterhead.

Sincerely yours,



Ballard H. Graham, Director
Atlanta District