



9/20/01

Food and Drug Administration
Detroit District
1560 East Jefferson Avenue
Detroit, MI 48207-3179
Telephone: 313-226-6260

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER
2000-DT-36

August 3, 2000

Paul R. Ervin, Ph.D.
CEO and Chief Scientific Officer
Biotherapies, Inc.
5692 Plymouth Road
Ann Arbor, MI 48105

Dear Mr. Ervin:

A May 3 through 26, 2000 inspection of your firm's drug manufacturing operations found that your firm is operating in serious violation of the Federal Food, Drug, and Cosmetic Act (the Act). During the inspection, our investigators documented numerous significant deviations from the Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Part 211), which cause your drug products to be adulterated within the meaning of section 501 (a) (2) (B) of the Act. While examples are as follows, we suggest you refer to the list of inspectional observations [the FDA-483] which was issued at the conclusion of the inspection for additional details:

1. Failure to have a quality control unit adequate to perform its functions and responsibilities, as required by 21 CFR 211.22. Your failure to have an adequate quality control unit is demonstrated by the number and types of inspectional observations made during this inspection.
2. Failure to have an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of a drug product and /or failure to ensure that each person engaged in such activities has the education, training, and experience, or any combination thereof, to enable them to perform their assigned functions, as required by 21 CFR 211.25. Your failure to have a staff adequate to perform their assigned functions, is demonstrated by the number and types of inspectional observations made.
3. Failure to have a building or facility designed and constructed to prevent contamination during the course of aseptic processing operations, as required by 21 CFR 211.42 (c) (10). For example, see FDA-483 observations 3 and 4.

4. Failure to have, follow, and have a record justifying any deviations from, adequately designed procedures for production and process control designed to assure that aseptic drug products have the identity, strength, quality, and purity they purport or are represented to possess, as required by 21 CFR 211.100. For example, see FDA-483 observations 1, 2, 3, 5, 6, 7 and 8.
5. Failure to establish and to follow appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile, as required by 21 CFR 211.113. For example, see FDA-483 observations 1 and 2.
6. Failure to establish and to follow written control procedures, designed to assure batch uniformity and the integrity of drug products, that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch, as required by 21 CFR 211.110. For example, see FDA-483 observations 5, 6 and 7.
7. Failure to make an appropriate laboratory determination of satisfactory conformance of each batch of drug product to its final specifications prior to its release, as required by 21 CFR 211.165. For example, see FDA 483- observation 5.
8. Failure to have laboratory controls which 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, as required by 21 CFR 211.160. For example, see FDA-483 observations 5, 6 and 7.
9. Failure to have, and to follow, a stability testing program adequate to assess the stability characteristics of drug products, as required by 21 CFR 211.166. For example, see FDA-483 observations 5 and 9.

The above list of deviations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence to each requirement of the Good Manufacturing Practice Regulations. Other Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information in account when considering the award of contracts. Additionally, pending NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

We request that you take prompt action to correct these violations. Failure to promptly correct these violations may result in enforcement action being initiated by the Food and Drug Administration without further notice, such as seizure and/or injunction.

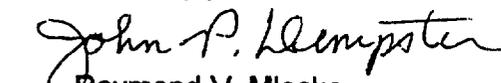
We request that you thoroughly evaluate the adequacy of your procedures and controls,

and that you take whatever actions are necessary to make systemic corrections and to assure that similar violations will not recur.

Please notify this office in writing, within fifteen (15) working days of your receipt of this letter, of any additional steps you have taken to correct these violations, including an explanation of steps being taken to identify violations and to make corrections 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 frame within which the corrections will be implemented.

Your reply should be directed to Sandra Williams, Compliance Officer, at the above address.

Sincerely yours,


for Raymond V. Mlecko
District Director
Detroit District

Cc via certified mail: Mr. Thomas Trimmer, President