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July 6, 2001

Chicago District
300 S. Riverside Plaza, Suite 550 South
Chicago, Illinois 60606
Telephone: 312-353-5863

WARNING LETTER
CHI-38-01

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Hector Ortino, President & CEO
Ferro Corporation
1000 Lakeside Avenue East
Cleveland, Ohio 44114

Dear Mr. Ortino:

During an inspection of Ferro Pfanstiehl Laboratories, Inc. [FPL], 1219 Glen Rock Avenue, Waukegan, IL, between December 21, 2000 and January 19, 2001, our investigator documented the failure of FPL to manufacture active pharmaceutical ingredients (API's) in conformance with Current Good Manufacturing Practice (CGMP). These deviations cause these APIs to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act).

Section 501(a)(2)(B) of the Act requires that all drugs be manufactured, processed, packed, and held in accordance with CGMPs. No distinction is made between active pharmaceutical ingredients and finished pharmaceuticals. Failure to comply with CGMPs constitutes a failure to comply with the requirements of the Act.

During the meeting held on March 13, 2001, between FPL and Chicago District representatives, FPL's FDA 483, List of Inspectional Observations response letter dated February 10, 2001, was discussed. In this meeting, we indicated that the responses appeared adequate, however, we also indicated we would verify the corrective active actions during the next inspection.

Examples of failure to follow CGMPs in the production of APIs by FPL include, but are not limited to the following:

1. Adequate cleaning procedures have not been established in that FPL has not conducted cleaning validation studies for non-dedicated manufacturing equipment. For example, the cleaning procedures have not been validated to demonstrate removal of API residues, cleaning agents, and impurities in buildings 1, 2 & 7. We acknowledge that FPL provided FDA with a cleaning validation priority list both during the inspection and at the March 13th meeting. Also during the March 13th meeting with our office, you and FPL representatives indicated that the firm would meet the targeted completion dates. However, we remind you that following an inspection from January 20, 1998 to February 6, 1998, item #1 of the FDA 483 cited the firm for failing to perform cleaning validation studies for the non-dedicated equipment in building 2. In the response letter dated March 4, 1998, FPL promised to correct this deviation by September 1, 2000.
2. Cleaning verification testing methods for Ammonium Lactate, Inulin, and Decitabine are not validated. A similar observation was cited on the FDA 483 (item #2) for the February 1998 inspection and FPL committed at that time to correcting this observation.
3. Manufacturing processes have not been validated for several products. These products include Ammonium Lactate, Egg Phosphatide, and Sucrose (High Purity, Low Endotoxin). We acknowledge that during our March meeting, FPL officials indicated that the process validation study for Ammonium Lactate has been completed and that Ferro Pfanstiehl is committed to meeting the targeted completion dates listed on the master validation priority list provided our investigator during the inspection.
4. Investigations are not completed in a thorough and timely manner. For example, investigations were not completed for several incidents of Purified Water not meeting specifications for microbial contamination and endotoxin levels during the Performance Qualification testing for building 7 and 8 RO water system that occurred during the period of November 1999 to December 2000.
5. Representative samples of components are not collected for testing and examination. For example, the inspection revealed that the microbiological samples of Purified Water collected at the points of use are not drawn through the same equipment as water used in product.

This letter, as well as the Form FDA 483, List of Inspectional Observations, issued to Mr. A. George Holstein, President, at the conclusion of the inspection, are not intended to be an all inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with the requirements of the Federal Food, Drug, and Cosmetic Act and that your API products are manufactured, processed, packed and held according to current good manufacturing practice. Failure to promptly correct these deviations may result in regulatory action without further notice. Possible actions include seizure and/or injunction. A copy of the FDA 483 is enclosed.

Please notify this office, in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations and prevent the recurrence of similar violations. 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.

Please direct your response to the attention of George F. Bailey, Compliance Officer, at the address listed above.

Sincerely,

\s\
Raymond V. Mlecko
District Director
Chicago District

Attachments: Form FDA 483, List of Observations dated 1/19/01

cc: A. George Holstein, President
Ferro Pfanstiehl, Inc.
1219 Glen Rock Ave.
Waukegan, IL 60085

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