HFD-205
FOI

DEPARTMENT OF HEALTH & HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

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WARNING LETTER

APR 23 1997

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Liu Gui Lian
Factory Director
Guangdong Pharmaceutical Factory
91 Fungcun Dadao
Guangzhou City 510380
China

Dear Mr. Lian :

This is regarding an inspection of your active pharmaceutical ingredient (API) manufacturing facility in Guangzhou City, China by FDA Investigator Ted L. Anderson on January 27-29, 1997. The inspection revealed numerous deviations from U.S. current good manufacturing practices in the manufacture of active pharmaceutical ingredients. The deviations were presented to your attention on an FDA-483 List of Observations at the close of the inspection. These deviations cause these API products to be adulterated within the meaning of Section 501(a)(2)(B) of the U.S. Federal Food, Drug, and Cosmetic Act. Section 501(a)(2)(B) of the Act requires that all drugs be manufactured, processed, packed, and held according to current good manufacturing practice (CGMP). No distinction is made between active pharmaceutical ingredients and finished pharmaceuticals, and failure of either to comply with CGMP constitutes a failure to comply with the requirements of the Act. Some of these deviations were similar to those observed during the previous inspection in September, 1994, which resulted in a Warning Letter to your firm on March 10, 1995.

We have also reviewed your February 28, 1997 written response to the List of Observations. We conclude that this response lacks sufficient details, satisfactory

commitments, or documentation to adequately address all of the deviations observed during the January, 1997 inspection. Specific areas of concern include, but are not limited to the following:

FACILITY AND EQUIPMENT DESIGN:

The inspection revealed numerous deficiencies regarding inadequate design of equipment,

CGMP requires equipment to be designed to facilitate operations, cleaning, and maintenance.

Your response indicates that the specific equipment design deficiencies listed on the FDA-483 have been, or will be,

Similar deficiencies were observed during the previous inspection in September, 1994. We are concerned that your firm has allowed these conditions to continue and that your response indicates that full corrections will not be completed until the end of 1997.

You should reconsider your time frames for corrective action. Please advise this office within 30 days of what prompt action will be implemented to correct existing deficiencies and prevent repetition of this deficiency.

EQUIPMENT MAINTENANCE

The inspection revealed numerous instances of inadequate equipment maintenance, including paint residues and rough welds on product contact surfaces, holes in walls, rusty utensils used to transfer product, an inoperative temperature recorder, loose fitting doors, and cracks, etc. Again, similar deficiencies were observed during the previous inspection. CGMP requires the proper cleaning and maintenance of equipment as well as written procedures for, and a record of such cleaning and maintenance.

We are concerned that your firm has allowed these deficiencies to continue and has not taken adequate steps to properly maintain all equipment in your facility. Your response states that the observations noted have been corrected, but does not provide assurance that an adequate maintenance program for the entire facility has been implemented. Please advise this office within 30 days of what action your firm has implemented to preclude repetition of this deficiency.

VALIDATION

The inspection revealed incomplete

Your response provided validation data

production facility only. Please provide additional assurances to this office within 30 days, that the facilities for all products have been validated or qualified and meet air and water specifications.

The CGMP deviations identified above or on the FDA-483 issued to your firm are not to be considered an all-inclusive list of the deficiencies at this facility. FDA inspections are audits which are not intended to determine all deviations from CGMPs that exist at a firm. We recommend that you evaluate your facility on an overall basis for CGMP compliance. Until the deficiencies noted during the inspection have been corrected, and

Failure to promptly correct these deficiencies may result in FDA denying entry into the U.S. of drug products manufactured by your firm. Such drugs could be subject to refusal of admission pursuant to Section 801(a)(3) of the Act in that the methods and controls used in their manufacture do not appear to conform to current good manufacturing practices within the meaning of Section 501(a)(2)(B) of the Act.

Please address your response to this letter to Compliance Officer John M Dietrick at the address provided above. In your response, please include a timetable of when the corrections will be completed and attach supporting documents. Any documents provided should be in English or accompanied by an English translation.

To schedule a reinspection after corrections have been completed, contact Deborah S Browning, Consumer Safety Officer, Drug Group, Division of Emergency and Investigational Operations (HFC-133), 5600 Fishers Lane, Rockville, Maryland 20857. You may wish to contact that office at (301) 827-5653 or by FAX at (301) 443-6919.

Sincerely,

Douglas I. Ellsworth

Douglas I. Ellsworth, Director
Division of Manufacturing and Product Quality