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U.S. FOOD AND DRUG ADMINISTRATION

NEW YORK DISTRICT
850 THIRD AVENUE, BROOKLYN, NEW YORK 11232

Telephone: [718]340-7000 [Ext 5053]

WARNING LETTER

June 24, 1997

CERTIFIED MAIL RETURN RECEIPT REQUESTED

Mrs. Tasrin Hossain, President
Advance Pharmaceutical Inc.
2201-F Fifth Avenue
Ronkonkoma, New York 11779

Ref: 61-NYK-97

Dear Mrs. Hossain:

An inspection of your drug manufacturing facility located at 2201-F Fifth Avenue, Ronkonkoma, New York 11779 was conducted between April 16 and May 14, 1997. This inspection documented deviations from the Current Good Manufacturing Practice Regulations for Finished Pharmaceuticals [Title 21, Code of Federal Regulations (CFR), Part 211]. Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act) requires that drugs be manufactured in conformance with Good Manufacturing Practices.

At the conclusion of our inspection our investigator presented the firm with a list of inspectional observations (copy attached) that shows deviations from the Current Good Manufacturing Practice Regulations for Finished Pharmaceuticals [Title 21, Code of Federal Regulations (CFR), Part 211]. Our findings are listed below:

1. Failure to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug process, such as:
 - a) process validation had not been conducted on Simethicone 80 mg tablets and Children's Chewable Acetaminophen 80 mg, both grape and fruit flavored.
 - b) validation was only performed on one lot of Diphenhydramine HCl 25 mg capsules.
 - c) validation was not completed on the Children's Chewable Aspirin tablets 81 mg.
 - d) validation samples collected were from only one side of the blender.

2. Failure to have adequate written manufacturing process validation procedures which are designed to assure that the drug products produced have the identity, strength, quality and purity they purport or are represented to possess. Specifically, manufacturing process validation protocols are inadequate because they fail to:
 - a) indicate the number of drug batches per product to be validated;
 - b) include installation qualification studies for equipment used to manufacture tablets and capsule;
 - c) describe the equipment used for manufacturing and sampling, the sample collection method, a description of length and duration of the study, criteria for study, and the reasons for revalidation.

3. Failure to follow the written production and process controls procedures in the execution of various production and process control functions in that your firm did not perform U.S. P. testing on stability tests for ID A & B and uniformity of dosage units for Children's Chewable Aspirin 81 mg and Diphenhydramine HCl 25 mg capsules.

4. Failure to withhold from use components that had been tested inappropriate for use by the quality control unit. Specifically, the active ingredients for Simethicone lots numbered R-1453, R-1477 and R-1488; Acetaminophen 90% lot numbers R-1675, R-1720 and R-1464; and Diphenhydramine HCl lot numbers R-1753, R-1754 and R-1691 failed to meet your firms specifications for particle size and /or bulk density.

5. Failure to have written procedures to assure the proper performance of automatic, mechanical or electronic equipment such that they will perform satisfactorily when used in the manufacture, process, packing and holding of a drug product. Specifically, there are no protocols for the [REDACTED]

6. Failure to have written procedures and to follow them for the cleaning and validation of your tablet and capsule machine. In addition, the written procedures for the [REDACTED] are inadequate and incomplete, as well as there is no documentation of maintenance or a maintenance schedule for the [REDACTED]
7. Failure to maintain records and to document the maintenance of the [REDACTED] machine, and the tablet and capsule machines. In addition, you failed to follow the manufacturer's instructions for the maintenance of the tablet and capsule equipment and the [REDACTED]
8. Failure to have established written procedures for the calibration of equipment used in manufacture, processing, packaging and holding of a drug product to assure proper performance. Specifically, the [REDACTED] was not calibrated.
9. Failure to follow your Standard Operating Procedures for stability testing and process testing and to record and justify the deviations.
10. Failure to annually evaluate the quality standards of each drug component to determine the need for changes in drug product specifications or manufacturing or control procedures. Specifically, there are no written procedures established to follow for such evaluations of the Children's Chewable Acetaminophen 80 mg tablets, Simethicone 80 mg tablets and Children's Aspirin 81 mg tablets.
11. Failure to have written procedure describing the handling of all written and oral complaints and to thoroughly document complaint investigations.

The above list of violations is not intended to be an all-inclusive list of deficiencies at your firm. It is your responsibility to ensure that all of your firm's products are in compliance with all requirements of the Act and its implementing regulations. Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

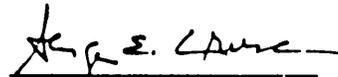
You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These include seizure and/or injunctions.

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You should 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. 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 reply should be sent to Domestic Compliance Branch, Food and Drug Administration, 850 Third Avenue, Brooklyn, New York 11232, Attention: Anita Fenty, Compliance Officer.

Very truly yours,



Alonza E. Cruse
Acting District Director
New York District Office
Food and Drug Administration

Attachment: FD form 483