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April 20, 2001

Food and Drug Administration
466 Fernandez Juncos Avenue
Puerta De Tierra
San Juan, Puerto Rico 00901-3223

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER
SJN-01-10

Carlos Fortier Quintana
Owner and Manager
Grafor Manufacturing, Inc.
Street 4, #376, La Rambla
Ponce, PR 00731

Dear Mr. Fortier:

From February 1 to February 13, 2001, our personnel conducted an inspection of your OTC drug manufacturing facility, Grafor Manufacturing, Inc., Street 4, # 376, La Rambla, Ponce, PR. Our evaluation of the information obtained during the inspection determined that the pharmaceutical products manufactured by the facility are adulterated within the meaning of section 501 (a)(2)(b) of the Federal Food, Drug and Cosmetic Act (the Act) because they were not manufactured in accordance with Good Manufacturing Practice Regulations (GMP) as defined by Title 21, Code of Federal Regulations, Part 211 (21 CFR 211).

The deviations from GMP's found during the inspection, and reported on the List of Inspectional Observations, FD-483, presented at the conclusion of the inspection, include the following:

- 1) Failure to have laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient prior to release, as required by 21 CFR 211.165 (a). No chemical or physical analytical test is performed before release of any of the Pasmol™ drug product batches.
- 2) Failure to have a written testing program designed to assess the stability characteristics of drug products as required by 21 CFR 211.166 (a).

- 3) Failure to test an adequate number of batches of Pasmol drug products to determine an appropriate expiration date, or to determine if they are stable for at least three years and do not need an expiration date, as required by 21 CFR 211.166 (b) and 211.137 (g).
- 4) Failure to identify drug products with a lot or control number that permits determination of the history of the manufacture and control of the batch as required by 21 CFR 211.130 (b). The finished product containers of Pasmol™ drug products do not bear a lot or control number.
- 5) Failure to prepare batch production and control records that include complete information relating to the production and control of each batch as required by 21 CFR 211.188. For example, the batch production records for Pasmol™ drug products do not include:
 - a) an accurate reproduction of the appropriate master production record, checked for accuracy, dated and signed;
 - b) specific identification of each batch of component used;
 - c) inspection of the packaging and labeling area before and after use;
 - d) a statement of the actual yield and a statement of the percentage of theoretical yield at appropriate phases of processing;
 - e) complete labeling control records, including specimens or copies of all labeling used; and
 - f) identification of the persons performing and directly supervising or checking each significant step in the operation.
 - g) failure to retain reserve samples for each lot of active ingredient and drug product as required by 21 CFR 211.170.
- 6) Failure to have written procedures for the distribution of drug products that include a system by which the distribution of each lot of drug product can be readily determined to facilitate its recall, if necessary, as required by 21 CFR 211.150 (b).
- 7) Failure to have written procedures that describe the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components as required by 21 CFR 211.80 (a).
- 8) Failure to conduct at least one test to verify the identity of each component of a drug product as required by 21 CFR 211.84 (d) (1).

- 9) Failure to test each component for conformity with all appropriate written specifications for purity, strength and quality, or to establish the reliability of the supplier's analyses in order to accept their reports of analysis, as required by 21 CFR 211.86 (d) (2). The components used in the manufacture of Pasmol™ drug products are released for production based solely on the supplier's certificate of analysis without validating the supplier's test results at appropriate intervals.
- 10) Failure to establish written procedures describing the warehousing of drug products as required by 21 CFR 211.142.
- 11) Failure to establish written procedures that describe the handling of all oral and written complaints regarding a drug product as required by 21 CFR 211.198 (a).
- 12) Failure to calibrate automatic, mechanical or electronic equipment used for drug product manufacturing to assure proper performance, as required by 21 CFR 211.68 (a). For example, the weighing scale used to manufacture Pasmol™ drug products has not been calibrated.
- 13) Failure to train personnel engaged in or responsible for supervising the manufacture, processing, packing or holding of drug products in the particular operations that the employee performs and in current good manufacturing practice as they relate to the employee's functions, as required by 21 CFR 211.25 (a) and (b).

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practice Regulations. 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.

Please notify the San Juan District office in writing within 15 working 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 prevent the recurrence of these or similar violations.

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

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Your reply should be sent to the Food and Drug Administration, San Juan District Office, 466 Fernandez Juncos Ave., San Juan, Puerto Rico 00901-3223, Attention: Rebeca Rodríguez, Acting Compliance Officer.

Sincerely,

A handwritten signature in cursive script that reads "Mildred R. Barber". The signature is written in black ink and is positioned above the printed name and title.

Mildred R. Barber
District Director