DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

Dallas District
4040 North Central Expressway
Dallas, Texas 75204-3128

May 8, 2008

2008-DAL-WL-10

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Larry Gremminger, R.Ph.
President
Elge, Inc.
P.O. Box 944
Richmond, Texas 77406

Dear Mr. Gremminger:

An inspection of your facility, located at 1000 Cole Avenue, in Rosenberg, Texas, which manufactures prescription and over-the-counter (OTC) drug products for human use, was conducted on January 14 through February 14, 2008, by investigators of the U.S. Food and Drug Administration (FDA). The inspection revealed that your drug products are adulterated within the meaning of Section 501(a)(2)(B) [21 U.S.C. § 351(a)(2)(B)] of the Federal Food, Drug, and Cosmetic Act (Act) in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing or holding do not conform to or are not operated or administered in conformity with Current Good Manufacturing Practices (CGMP) regulations for drugs Title 21, Code of Federal Regulations (CFR), Part 211.

In addition, this inspection also revealed your firm is marketing unapproved drugs in violation of Section 505(a) of the Act [21 U.S.C. 355(a)] and the drugs are also misbranded in violation of Section 502(f)(1) [21 U.S.C. 352(f)(1)] and Section 502(c) [21 U.S.C. 352(c)].

The violations observed during our inspection and listed on FDA-483 include, but are not limited to, the following:

1. Failure to establish laboratory controls, including determination of conformance to appropriate written specifications for the acceptance of each lot within each shipment of components used in the manufacture, processing, packing, or holding of drug products as required by 21 CFR 211.160(b)(1). Specifically, during review of laboratory documentation obtained as part of your supplier qualification program for Dextromethorphan Tannate lot no. 104053; Pseudoephedrine Tannate lot

no. 106043R1; and d-Chlorpheniramine Tannate lot no. 103014R1, a recurrent failure to identify each peak (or absorption band) of spectra obtained using USP <197K> FT-IR "Identity" test for functional groups characteristic of Dextromethorphan Base, Pseudoephedrine Base and d-Chlorpheniramine Base, was noted.

Review of the USP <197K> FT-IR Identity test spectra obtained for the stated APIs revealed that all of the spectra generated for each API had comparable peaks in all areas of the mid-IR spectrum when processing the sample tested as described in USP <197K>. The established USP <197K> Identity test method lacks the capability to detect physico-chemical changes of incoming API raw materials or distinguish one of the above referenced API's from another. Therefore, your firm's Identity test method is considered an inadequate analysis for the identification and quantitation of in-coming tannate containing API's (i.e., Dextromethorphan Tannate, Pseudoephedrine Tannate, Chlorpheniramine Tannate). In addition, your firm fails to document that your identity testing procedures can detect extraneous materials in lots of incoming API's salt/base forms, that should then result in rejection of the lot.

2. Failure to establish adequate laboratory controls, including the establishment of scientifically sound and appropriate specifications designed to assure conformance with appropriate standards of identity, strength, quality, quality and purity as required by 21 CFR § 211.160(b). Specifically, your firm has not established specifications for the amount of free Tannic Acid in drug products containing tannate compounds and for Benzalkonium Chloride in Otozone Otic drops. In addition, your firm has failed to establish specifications or testing procedures for dissolution or rate of drug release for drug products containing tannates.

3. Failure to thoroughly investigate any unexplained discrepancy or the failure of any batch to meet any of its specifications, whether or not the batch has already been distributed, as required by 21 CFR § 211.192. Specifically, PediaTan D Suspension, lot # 70810 failed the assay specification for Chlorpheniramine Tannate (Specification (b)(4) (b)(4) %) with an averaged result of (b)(4) %. The other active ingredient used in the product, Phenylephrine Tannate, was within assay specification. Your firm's investigation revealed that laboratory error did not contribute to the OOS Assay result and that the probable cause was a insufficient quantity of water added during the QS phase of mixing, resulting in a higher concentration of all ingredients. However, the investigation did not document any explanation for the normal assay values observed for the second active ingredient, Phenylephrine Tannate.

In addition, review of the HPLC assay chromatograms for release testing

for another drug product, Ed Bron G, lot #70615 revealed the presence of an unidentified peak at approximately (b)(4) RRT. There was no investigation by your firm in regard to the unidentified peak.

4. Failure to establish the reliability of the supplier's analysis, through appropriate validation of supplier's test results at appropriate intervals, as required by 21 CFR § 211.84(d)(2). Supplier's reports of analysis are routinely accepted without this assurance. For example, the supplier's test results for limit of ketones in shipments of Phenylephrine HCL have not been verified by the firm's own testing.

5. Failure to test an adequate number of batches of each drug product to determine an appropriate expiration date, as is required by 21 CFR § 211.166(b). Specifically, your firm's SOP-82-01 entitled "Stability Program" requires in part that accelerated stability testing be conducted for all new drug products at (b)(4) days and allows for use of bracketing and matrixing of products in obtaining representative accelerated stability data. Your firm has generated long-term room temperature stability data for (b)(4) months for PediaTan suspension. This product has a (b)(4) expiration date. Additionally, review of the stability data for PediaTan revealed that accelerated stability testing was not conducted to justify the established expiration date and the accelerated and long-term stability data from other products used for 'bracketing" was not appropriate to support the proposed shelf life of this product. In the case of the PediaTan product, the other products chosen for "bracketing" were not appropriate because their formulations differed from that of the "bracketed" product (i.e.PediaTan) in that these had additional active ingredients. Further, you firm failed to establish a stability testing program which includes reliable, meaningful, and specific test methods as required by 21 CFR § 211.166(a)(3).

Unapproved Drugs

In addition to the cGMP violations, you manufacture and market unapproved new drugs in violation of the Act at your facility at 1000 Cole Avenue, Rosenberg, Texas 77471-3949. Based on the information your firm submitted to FDA's Drug Registration and Listing System and the labeling collected during the inspection of your facility, you manufacture the following prescription drugs:

- Tan Dur DM Suspension (Pseudoephedrine Tannate 50 mg, Dextromethorphan Tannate 27.5 mg & 3-Chlorpheniramine Tannate 3 mg per 5 mL);
- C-Tanna 12 Suspension(Carbetapentane Tannate 30 mg & Chlorpheniramine Tannate 4 mg per 5 mL); and

- Dicel DM Suspension (Pseudoephedrine Tannate 5 mg, Chlorpheniramine Tannate 5 mg & Dextromethorphan Tannate 25 mg per 5 mL).

The above products are drugs within the meaning of Section 201(g) of the Act, [21 U.S.C. § 321(g)] because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases. Further, they are "new drugs" within the meaning of Section 201(p) of the Act [21 U.S.C. § 321(p)] because they are not generally recognized as safe and effective for their labeled uses. Under Sections 301(d) and 505(a) of the Act [21 U.S.C. §§ 331(a), (d) and 355(a)] a new drug may not be introduced into or delivered for introduction into interstate commerce unless an FDA-approved application is in effect for the drug. Based on our information, you do not have any FDA-approved applications on file for these drug products.

Additionally, the above products are misbranded because, as prescription drugs, adequate directions cannot be written for them so that a layman can use these products safely for their intended uses. Consequently, their labeling fails to bear adequate directions for use as required under Sections 502(f)(1) of the Act [21 U.S.C. § 352(f)(1)] and because they lack required approved applications, they are not exempt from this requirement under 21 C.F.R. § 201.115. The introduction or delivery for introduction into interstate commerce of these products without approved new drug applications violates Section 301(a) and (d) of the Act [21 U.S.C. §§ 331(a) and (d)].

Misbranded Over-the-Counter (OTC) Drugs

Moreover, your firm also manufactures numerous drug products for over-the-counter use. Specifically, several products that you manufacture inappropriately bear the Rx (prescription) legend because they are OTC drug products based on their formulation and directions for use as described in the final regulations covering Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for OTC use, 21 C.F.R. Part 341. Since these products are not subject to Section 503(b)(1) of the Act [[21 U.S.C. § 353(b)(1)], they are misbranded under Section 503 (b)(4)(B) of the Act [[21 U.S.C. § 353(b)(4)(B)] because they inappropriately bear the Rx legend. These products include:

- Alacol DM (Dextromethorphan HBr 10 mg, Phenylephrine HCl 5 mg, & Brompheniramine Maleate 2 mg per 5 mL);
- Norel DM (Dextromethorphan HBr 15 mg, Phenylephrine HCl 10 mg & Chlorpheniramine Maleate 4 mg per 5 mL) and;
- M-End DM (Dextromethorphan HBr 15 mg, Pseudoephedrine HCl 15 mg, & Chlorpheniramine Maleate 2 mg per 5 mL).

Additionally, the product M-End DM is an unapproved new drug because it does not meet the OTC monograph described above. Under sections 301(d) and 505(a) of the Act (21 U.S.C. §§ 331(d) and 355(a)) a new drug may not be introduced or delivered for introduction into interstate commerce unless it is subject to an FDA-approved application. Since this product does not have an approved application, its introduction and delivery into interstate commerce violates these provisions of the Act.

In addition to the above violations, the products Alacol DM, Norel DM, and M-End DM, do not contain the required labeling information in a drug facts panel in accordance with 21 C.F.R. 201.66. Therefore, these products are misbranded under section 502(c) of the Act [21 U.S.C. § 352(c)] because the information that is required to appear on the labeling is not prominently placed thereon with such conspicuousness and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

During the regulatory meeting conducted on April 18, 2007, at the Dallas District's office you were informed of the need to remove the prescription logo (Rx) from the drug products and the requirements to market these drug products following pertinent OTC monographs. You stated that continued dialog was critical between both parties to ensure Elge is on the right path to compliance. This compliance has not been attained.

We acknowledge your "January 31, 2008, Status Report for Observations (483) of 2/14/07," given to the Investigator as an outline of the current status of corrective action of the issues previously identified during the inspection dated 2/14/07. We note that you have not suspended production and distribution of tannate containing drug products at your site.

We received your written response dated March 26, 2008, addressing the deviations noted on the 483 issued to Mr. Douglas E. Smith at the conclusion of the inspection dated February 14, 2008. A preliminary review of the response revealed that your firm failed to provide sufficient information to fully assess the adequacy of the proposed corrective actions. Furthermore, the information submitted to address many of the inspectional observations only indicate that the observations will be corrected, however, you failed to provide specific timeframes for implementing the proposed corrective actions.

The issues and violations cited in this letter are not intended to be an all-inclusive list of violations that exist at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence or the occurrence of other violations. It is your responsibility to conduct a comprehensive audit of your facility and operations and assure compliance with all requirements of the Act and FDA regulations.

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in regulatory action without further notice, including, without limitation, seizure and/or injunction. Other federal agencies may take this Warning Letter into account when considering the award of contracts. Additionally, FDA may withhold approval of requests for export certificates, or approval of new drug applications listing your facility as a manufacturer until the above violations are corrected. A reinspection may be necessary.

Within 15 working days of receipt of this letter please notify this office in writing of the specific steps you have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of similar violations as well as copies of related documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the time within which you will complete the correction. If you no longer manufacture or market any products, your response should so indicate, including the reasons for, and the date on which you ceased production.

Your reply should he directed to Edwin Ramos, Compliance Officer, U.S. Food and Drug Administration, 4040 N. Central Expressway, Suite 300, Dallas, Texas 75204. If you have any questions regarding any issue in this letter, please contact Mr. Ramos at (214) 253-5218.

Sincerely,

Reynaldo R. Rodriguez, Jr.
Dallas District Director

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