



October 10, 2001

Dallas District
4040 North Central Expressway
Dallas, Texas 75204-3145

Ref: 2002-DAL-WL-02

WARNING LETTER

CERTIFIED MAIL RETURN RECEIPT REQUESTED

Mr. Daniel F. Volney, President
Unique Pharmaceuticals, Ltd.
5920 S. General Bruce Drive, #500
Temple, TX 76505

An inspection of your firm conducted by the Food and Drug Administration (FDA), the Texas Department of Health, and the Texas State Board of Pharmacy, on August 2/4 & 16, and September 5, 2000, revealed serious violations of the Federal Food, Drug, and Cosmetic Act (the Act).

While your firm purports to be a compounding pharmacy (as noted in your September 27, 2000, letter to the FDA Investigator), the inspection disclosed that in the case of numerous drug products, your firm is not preparing the drugs pursuant to valid prescription orders from licensed practitioners for individual patients. Rather, Unique Pharmaceuticals, Ltd., an entity not registered with FDA, is manufacturing and distributing drug products in large quantities, including drugs appearing to be copies of commercially available drug products, to wholesale drug distributors for their subsequent distribution to hospitals, pharmacies, and physicians. Eighty percent of the drugs prepared by your firm are not dispensed or sold directly to individual patients.

During a three-month period, your firm prepared and distributed inordinate quantities of drug products appearing to be copies of commercially available drugs, including, but not limited to, the following:

- Dexamethasone Acetate for Injection 8mg/mL - 38,650 vials
- Triamcinolone Acetonide for Injection 40mg/mL - 38,400 vials
- Methylprednisolone Acetate for Injection 80mg/ml - 18,400 vials
- Methylprednisolone Acetate for Injection 40mg/mL - 10,750 vials
- Promethazine for Injection 50mg/mL - 5000 vials
- Estradiol Valerate for Injection 40mg/mL - 2000 vials
- Triamcinolone Diacetate for Injection 40mg/mL - 2000 vials
- Estradiol Cypionate for Injection 5mg/mL - 1250 vials
- Diphenhydramine for Injection 50mg/mL - 1000 vials
- Dicyclomine for Injection 10mg/mL - 650 vials.

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These activities plainly exceed the scope of the regular course of business of a pharmacy dispensing or selling drugs at retail. Our findings are consistent with the Texas Department of Health Warning Letter dated September 29, 2000, which indicates that your firm is manufacturing and distributing drugs to wholesalers in Texas and other states and not exclusively to practitioners.

As you are aware, section 127 of the FDA Modernization Act of 1997 (FDAMA) amended the Federal Food, Drug, and Cosmetic Act, adding section 503A. This provision became effective on November 21, 1998, and sets forth the requirements that compounded products must meet to qualify for exemption from the new drug (Section 505), certain adulteration (501(a)(2)(B)), and misbranding (502(f)(1)) provisions of the Act. On February 6, 2001, the United States Court of Appeals for the Ninth Circuit declared Section 503A of the Act to be invalid in its entirety (*Western States Medical Center v. Shalala*, 238 F.3d 1090 (9th Cir. 2001)). On August 24, 2001, the United States Department of Justice appealed this decision to the U.S. Supreme Court. During the time that the appeal is pending it is FDA's position that section 503A is valid outside of the Ninth Circuit.

The drug products prepared by your firm do not qualify for exemptions from section 505, 502(f)(1), and 501(a)(2)(B) provided under section 503A of the Act in that:

(1) Drug products including, but not limited to, the following:

- Dexamethasone Acetate for Injection 8mg/mL
- Triamcinolone Acetonide for Injection 40mg/mL
- Methylprednisolone Acetate for Injection 80mg/ml
- Methylprednisolone Acetate for Injection 40mg/mL
- Promethazine for Injection 50mg/mL
- Estradiol Valerate for Injection 40mg/mL
- Triamcinolone Diacetate for Injection 40mg/mL
- Estradiol Cypionate for Injection 5mg/mL
- Diphenhydramine for Injection 50mg/mL
- Dicyclomine for Injection 10mg/mL

are not being compounded for identified, individual patients based on prescription orders from licensed practitioners as required by section 503A(a) of the Act. Instead, they are being distributed to wholesale drug distributors for further sale to hospitals, pharmacies, and physicians; and

(2) Drug products including, but not limited to, the following:

- Boron PF 2mg/mL for Injection
- Cesium CL 100mg/mL for Injection
- Co-Enzyme Q 20mg/mL for Injection
- DHEA 10mg/mL for Injection

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- Echinacea 2% for Injection
 - Germanium Sesq 132 for Injection
 - Glucosamine 200mg/mL for Injection
 - Glycerrhizic Acid PF 8mg/mL for Injection
 - Lipoic Acid PF 25mg/mL for Injection
 - Melatonin 2.5mg/mL for Injection
 - Molybdenum 200mcg/mL for Injection
 - Pangamic Acid 250mg/mL for Injection
 - Rubidium 200mcg/mL for Injection
 - Strontium 1mg/mL PF for Injection
 - Vanadium 200mcg/mL PF for Injection
- are being prepared using bulk drug substances that do not meet the requirements of section 503A(b)(1)(A) of the Act; and

(3) A drug product that you prepare, Adenosine M.P. 250mg/mL for Injection, appears on the "Withdrawn or Removed Drug Product List" that was published in the Federal Register as a final rule and became effective on April 7, 1999, and, therefore, does not comply with section 503A(b)(1)(C) of the Act; and

(4) Drug products, including, but not limited to, the following:

- Dexamethasone Acetate for Injection 8mg/mL
- Triamcinolone Acetonide for Injection 40mg/mL
- Methylprednisolone Acetate for Injection 80mg/ml
- Methylprednisolone Acetate for Injection 40mg/mL
- Promethazine for Injection 50mg/mL
- Estradiol Valerate for Injection 40mg/mL
- Triamcinolone Diacetate for Injection 40mg/mL
- Estradiol Cypionate for Injection 5mg/mL
- Diphenhydramine for Injection 50mg/mL
- Dicyclomine for Injection 10mg/mL

appear to be copies of commercially available drugs, are being prepared regularly or in inordinate quantities, and therefore, do not comply with section 503A(b)(1)(D) of the Act.

The drug products that your firm prepares, as noted above, are in violation of the Federal Food, Drug, and Cosmetic Act as follows:

Section 505

The referenced products are drugs within the meaning of section 201(g) of the Act which may not be introduced or delivered for introduction into interstate commerce under section 505(a), since they are new drugs within the meaning of section 201(p)

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and no approvals of any applications filed pursuant to section 505(b) or (j) are in effect for such drugs.

Section 502(f)(1)

The referenced drug products are misbranded within the meaning of section 502(f)(1) because they are prescription drugs and their labeling fails to bear adequate directions for use under which a practitioner licensed by law can use the drugs safely and for the purposes for which they are intended.

Section 502(o)

The referenced drug products are misbranded within the meaning of section 502(o) in that they were manufactured in an establishment not duly registered under section 510 of the Act; and, they have not been listed as required by section 510(j).

Section 502(a)

The referenced drug products are misbranded within the meaning of section 502(a) because they bear an NDC number that is false and misleading in that the drugs are manufactured by your firm but the NDC numbers present on the label are those that identify other firms (21 CFR 207.35). For example, the NDC number used on your drug product, Dexamethasone Acetate, is the NDC number assigned to [REDACTED]

Section 501(a)(2)(B)

The drug products are adulterated within the meaning of section 501(a)(2)(B) in that the controls and procedures used in their manufacture, processing, packing, and holding do not conform to current good manufacturing practice regulations, 21 CFR, Parts 210 and 211. Deviations from these regulations include, but are not limited to, the following:

1. Failure to establish a stability testing program that demonstrates that all products are stable and will retain their identity, strength, quality, and purity they purport at the end of 1 year and 2 year expiry assigned to the drug products (21 CFR 211.137 and 211.166).
2. Failure to establish complete master production and control records to ensure drug product uniformity from batch to batch (21 CFR 211.186).
3. Failure to establish complete batch production and control records for each batch of drug products (21 CFR 211.188 (b) (11)). For example, batch production records lack identification of the person supervising or checking each step in the manufacturing of a drug.
4. Failure to establish written procedures to assure that correct labels, labeling, and packaging materials are used for drug products (21 CFR 211.130).

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5. Failure to validate the Pressure Vessel Cleaning system (21 CFR 211.67).

In addition, based upon the documentation that you have supplied to FDA to date, there is no evidence that you have established:

- (a) adequate written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess (21 CFR 211.100); and
- (b) validation procedures and data to support the adequacy of sterilization of the drug products purporting to be sterile (21 CFR 211.113 (b)). For example, there is no documentation of equipment qualification or validation of sterilization processes; and
- (c) adequate control over design and construction features for the manufacturing facility (21 CFR 211.42). For example, there is no documentation of the validation of the air handling system or the water system used in production.

We acknowledge receipt of your September 27, 2000, letter responding to the form FDA-483, Inspectional Observations. As noted above, your firm must comply with current good manufacturing practice regulations for those drug products that your firm manufactures. You also indicate in your letter your plan to restructure your operations and to ship compounded drugs directly to physicians, without the use of third party distributors. Your plan does not appear to comply with sections 503A(a)(2)(A) and 503A(a)(2)(B) of the Act because: (1) from the nature and scope of your firm's operations, it does not appear that it would involve preparing limited quantities of compounded drug products before receipt of valid prescription orders for identified individual patients (503A(a)(2)(A)); and (2) such preparation of compounded drug products before the receipt of valid prescription orders for individual patients, would not appear to be based on a history of receiving valid prescription orders for compounded drug products where such orders have been generated solely within established relationships between the pharmacist-physician-patient as contemplated by section 503A(a)(2)(B).

We note that some of the products prepared by your firm may have reportedly been in short supply for brief periods of time. However, the large quantities of products prepared by your firm exceed the limited quantities that may be needed to meet temporary inventory shortages. As discussed above, your products are not being prepared for identified, individual patients based on prescription orders from licensed practitioners within an established relationship. Instead, they have been distributed to wholesale drug distributors for further sale to hospitals, pharmacies and physicians, which goes beyond the regular course of selling or dispensing drugs at retail.

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The above violations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure that all drug products manufactured and processed at Unique Pharmaceuticals, Ltd., are in compliance with federal laws and regulations. Failure to promptly correct these violations and prevent future violations may result in regulatory action, such as seizure and/or injunction, without further notice.

Please notify this office within 15 working days of receipt of this letter of the specific steps you have taken to correct these violations, including an explanation of each step being taken to prevent the recurrence of the violations.

In addition to responding to the above violations, you should provide us with the assurance you have that the bulk drug substance used in the preparation of Dexamethasone Acetate for Injection 8mg/mL is not derived from cattle born, raised, or slaughtered in countries where bovine spongiform encephalopathy (BSE) is known to exist.

You should address your reply to this letter to the U. S. Food and Drug Administration, Attention: Jim Lahar, Compliance Officer, at the above address.

Sincerely,


Michael A. Chappell
Director, Dallas District

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