



Food and Drug Administration  
New Orleans District  
Nashville Branch Office  
297 Plus Park Blvd.  
Nashville, TN 37217  
Telephone: 615-781-5380  
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September 17, 2004

**Warning Letter No. 2004-NOL-36**

**FEDERAL EXPRESS  
OVERNIGHT DELIVERY**

Tommy T. Simpson, MD  
President  
Delta Pharma, Inc.  
114 W. Mulberry Street  
Ripley, Mississippi 38663-1709

Dear Dr. Simpson:

On March 8-10, 2004, investigators from the Food and Drug Administration (FDA) conducted an inspection of your facility located at 114 W. Mulberry Street, Ripley, Mississippi. This inspection disclosed serious violations of the Federal Food, Drug and Cosmetic Act (the Act).

As you may be aware, Section 127 of the FDA Modernization Act of 1997 amended the Federal Food, Drug, and Cosmetic Act (the Act) by adding section 503A, which specified certain conditions under which compounded human drugs could be exempt from particular requirements of the Act. In April 2002, however, the United States Supreme Court struck down the commercial speech restrictions in section 503A of the Act as unconstitutional. Accordingly, all of section 503A is now invalid.

As a result, the agency now utilizes its longstanding policy of exercising its enforcement discretion as articulated in Compliance Policy Guide (CPG), section 460.200, issued on June 7, 2002. The CPG contains factors the agency considers in deciding whether to exercise its enforcement discretion. One factor is whether a firm is extemporaneously compounding reasonable quantities of drugs based on valid prescriptions from licensed practitioners for individually identified patients. Another factor is whether a firm is compounding outside the traditional patient-pharmacist-physician relationship, which requires a valid prescription to precede the compounding of the drug product. The agency also considers whether a firm compounds commercially available drug products or essentially copies of commercially available FDA-approved products. In this regard, the agency expects documentation of a particular patient's medical need for the variation from the commercially available product.

In addition, FDA remains seriously concerned about the public health risks associated with the large-scale production of injectable drugs by manufacturers that do not meet the laws and regulations applicable to drug manufacturing.

While your firm purports to be a compounding pharmacy, our investigation has determined it is more consistent in size and production volume with a drug manufacturer. Your firm makes [REDACTED] injectable products, in large volume, including methylprednisolone acetate 80mg/mL, dexamethasone sodium phosphate 4mg/mL, estradiol cypionate 5mg/mL, promethazine hydrochloride 50mg/mL, dexamethasone sodium phosphate 10mg/mL, estrone injectable suspension 5mg/mL, and estradiol valerate 40mg/ml. None of these or your firm's other products are dispensed directly to patients. They are instead sold only to physicians as "office stock," without requiring individual prescriptions. Typical batch sizes range from [REDACTED], which equates to as many as [REDACTED]. From August 2003 to March 2004, your firm produced [REDACTED], for a total of approximately [REDACTED]. And during the March 2004 inspection, your firm had on hand approximately [REDACTED] products. The volume of products that your firm manufactures, and the manner in which it dispenses those products, exceeds the scope of permissible pharmacy compounding.

The inspection also noted your firm uses three wholesalers to obtain physician orders for Delta Pharma's products. Customers may also telephone orders to each of the wholesalers or directly to your firm. Each wholesaler sets their own price, invoices customers, and receives payment for the products shipped. In at least one case, your firm ships products on the wholesaler's behalf. Each month, the wholesalers itemize their sales of Delta Pharma products and send payment to your firm based on its "Wholesale Products and Price List." This activity is not consistent with that of a pharmacy extemporaneously compounding drugs at retail.

In addition, many of the products made by your firm are essentially copies of commercially available products, including the following:

- methylprednisolone acetate 80mg/mL ([REDACTED])
- dexamethasone sodium phosphate 4mg/mL ([REDACTED])
- estradiol cypionate 5mg/mL ([REDACTED])
- promethazine hydrochloride 50mg/mL ([REDACTED])
- dexamethasone sodium phosphate 10mg/mL ([REDACTED])
- estrone injectable suspension USP 5mg/mL ([REDACTED])
- estradiol valerate USP 40mg/mL ([REDACTED])

It appears your firm cannot document a medical need for particular patients for these versions of otherwise commercially available products.

### Violations

The products compounded by your firm are drugs within the meaning of section 201(g) of the Act. As they are not generally recognized by qualified experts as safe and effective for their labeled uses, the products are new drugs, as defined by section 201(p) of the Act. No approved application pursuant to section 505 of the Act is effective with respect to these products. Accordingly, their introduction or delivery for introduction into interstate commerce violates section 505(a) of the Act.

In addition, your firm's drug products are misbranded under section 502(f)(1) of the Act because their labeling fails to bear adequate directions for use and they are not exempt from this requirement under 21 CFR § 201.115.

The products are also misbranded under section 502(o) of the Act because they are manufactured in an establishment not duly registered under section 510 of the Act, and the articles have not been listed as required by section 510(i) of the Act. Your facility is not exempt from registration and drug listing requirements under 21 CFR § 207.10 or section 510(g) of the Act.

Your drug products are also adulterated under Section 501(a)(2)(B) of the Act because the controls and procedures used in the manufacture, processing, packing, and holding of drug products 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:

The inspection revealed the following violations:

1. Your firm failed to design procedures to prevent microbiological contamination of sterile drug products, as required by 21 CFR 211.113(b). Specifically, no media fills have been conducted to validate the aseptic fill operations, and the sterilization cycles of the steam autoclave have not been validated. [Reference: Form FDA 483, Observation 2]
2. Your firm failed to establish a system for monitoring environmental conditions in the aseptic processing area as required by 21 CFR 211.42(c)(10)(iv). Specifically, routine environmental monitoring of the aseptic filling area for viable and non-viable particulates is not done. Routine microbiological monitoring of the gowns and gloves of the employees working in the class 100 area is not done. [Reference: Form FDA 483, Observation 4]
3. Your firm failed to establish written procedures for production and process control designed to assure the drug products have the identity, strength, quality and purity they are purported to have as required by 21 CFR 211.100(a). Specifically, your manufacturing process has not been validated for any of your drug products. [Reference: Form FDA 483, Observation 1]
4. Your firm failed to verify the identity of each component of drug product and its conformance with all appropriate written specifications for purity, strength, and quality as required by 21 CFR 211.84(d)(2). Specifically, incoming components are not tested but are accepted only on the basis of the supplier's Certificate of Analysis (COA). Acceptance of components based on a supplier's COA is allowable provided at least one specific identity test is conducted and the reliability of the suppliers' analyses has been established through appropriate validation. Neither of these two provisions is met. [Reference: Form FDA 483, Observation 10]
5. Your firm failed to test containers and closures for conformance with all appropriate written procedures as required by 21 CFR 211.84(d)(3). Specifically, containers and closures are not tested but are accepted only on the basis of the supplier's Certificate of Analysis (COA). Acceptance of containers and closures based on a supplier's COA is allowable provided at least a visual identification is conducted and the reliability of the suppliers' analyses has been established through appropriate validation. Neither of these two provisions is met. [Reference: Form FDA 483, Observation 11]

6. Your firm failed to establish written procedures which include standards or specifications, methods of testing, methods of cleaning, sterilizing, and processing to remove pyrogenic properties for drug product containers and closures, as required by 21 CFR 211.94(d). Specifically, you failed to have any written procedures for the washing, depyrogenation, and sterilization of containers and closures, and these systems are not validated. [Reference: Form FDA 483, Observation 3]
7. Your firm failed to establish a written testing program designed to assess the stability of your drug products, as required by 21 CFR 211.166(a). Specifically, you failed to conduct stability testing on your drug products. [Reference: Form FDA 483, Observation 5]
8. Your firm failed to conduct appropriate laboratory testing prior to the release for distribution of drug products as required by 21 CFR 211.165(a). Specifically, you released finished product for sale without the preservative being assayed or antimicrobial effectiveness tested. [Reference: Form FDA 483, Observation 6]
9. Your firm failed to establish written procedures for cleaning and maintenance of equipment used in the manufacture, processing, packing, or holding of a drug product, as required by 21 CFR 211.67(b). Specifically, you do not have written cleaning procedures and have not validated your cleaning practices. [Reference: Form FDA 483, Observation 7]
10. Your firm failed to establish written procedures to cover the receipt, identification, storage, handling, sampling, examination, and/or testing of labeling and packaging materials, as required by 21 CFR 211.122(a). Specifically, you do not have written procedures to assure the quality of the incoming packaging or labeling. [Reference: Form FDA 483, Observation 8]
11. Your firm failed to determine all equipment used in the manufacture, processing, packing, or holding of a drug product is of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance, as required by 21 CFR 211.63. Specifically, you have not qualified the dry heat oven or the steam autoclave used in your manufacturing process. [Reference: Form FDA 483, Observation 9]
12. Your firm failed to establish written procedures which describe in sufficient detail the receipt, identification, storage, handling, sampling, testing, approval, and rejection of components, drug product containers, and closures, as required by 21 CFR 211.80(a). Specifically you have no written procedures to describe in detail the receipt, identification, storage, handling, sampling, testing, approval, and rejection of components, drug product containers, and closures. [Reference: Form FDA 483, Observation 13]
13. Your firm failed to appropriately identify each lot of components, drug product containers, and closures as to its status of quarantine, approved, or rejected, as required by 21 CFR 211.80(d). Your firm has not established quarantine, approval or rejection procedures or practices. [Reference: Form FDA 483, Observation 12]
14. Your firm failed to establish written procedures for the responsibilities and procedures applicable to the quality control unit, as required by 21 CFR 211.22(d). Specifically, you failed to have a true quality control unit, whose authority and responsibility are clearly outlined in writing. [Reference: Form FDA 483, Observation 14]

15. Your firm failed to establish written control procedures for the issuance of drug labeling, as required by 21 CFR 211.125(f). There is no label accountability procedure in writing or in practice. [Reference: Form FDA 483, Observation 16]
16. Your firm failed to establish and follow adequate written procedures for evaluation, at least annually, of the quality standards of each drug product (including complaints and investigations) to determine the need for changes in drug product specifications or manufacturing or control procedures as required by 21 CFR 211.180 (e)(2). [Reference: Form FDA 483, Observation 20]

Because you are producing large volumes of drugs without valid prescriptions for individually identified patients, and because many of these drugs are essentially copies of commercially available products, we will not exercise enforcement discretion with regard to the above violations.

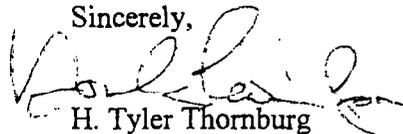
We note your firm's response to the Form FDA 483 issued at the close of the last inspection and your assurance that Delta Pharma, Inc. will not compound copies of commercially available products. Nevertheless, for the reasons noted above, we do not agree that your firm is operating as a compounding pharmacy. Also, your firm's response was largely inadequate for many of the FDA Form 483 observations, as there was either no commitment to correct the deficiency or only partial correction was promised. Therefore, we find your response deficient in addressing the stated violations.

The above violations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that all drug products compounded and processed by your firm are in compliance with federal laws and regulations, including adherence to each requirement of the Current Good Manufacturing Practice Regulations, and you must correct the violations noted in this letter.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in additional regulatory action without further notice. These actions include, but are not limited to, seizure of your products or injunction. Federal agencies are routinely advised of warning letters issued so that they may take this information into account when considering the award of government contracts.

Please notify this office in writing within 15 working days of receipt of this letter of the specific steps you will take to correct these violations, including an explanation of each step being taken to prevent the recurrence of the violations. You should address your reply to this letter to Kari L. Batey, Compliance Officer, Food and Drug Administration, 297 Plus Park Boulevard, Nashville, Tennessee 37217.

Sincerely,



H. Tyler Thornburg  
Director, New Orleans District

Enclosure:  
21 CFR Part 211