DEPARTMENT OF HEALTH AND HUMAN SERVICE

Food and Drug Administration
New Orleans District
297 Plus Park Boulevard
Nashville, TN 37217-1003

Telephone: 615-781-5380
FAX: 615-781-5391

February 15, 2006

WARNING LETTER NO. 2006-NOL-04

FEDERAL EXPRESS
OVERNIGHT DELIVERY

Mr. Woody R. Gamble, President/Owner
Southern Meds Joint Venture, LLC
2561 Pass Road, Suites B & C
Biloxi, Mississippi 39531

Dear Mr. Gamble:

On August 3-5 and 11, 2005, a U.S. Food and Drug Administration (FDA) investigator inspected your facility, located at 2561 Pass Road, Suites B & C, Biloxi, Mississippi. The investigator documented serious violations of the Federal Food, Drug, and Cosmetic Act (the Act). The sterile injectable drug products manufactured by your firm are drugs within the meaning of Section 201(g) of the Act [21 *United States Code* (USC), Section 321 (g)], and are unapproved new drugs under Section 505 of the Act [21 USC 355]. These drug products also are adulterated within the meaning of Section 501(a)(2)(B) of the Act [21 USC 351(a)(2)(B)], and they are misbranded within the meaning of Section 502 of the Act (21 USC 352).

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

As a result, FDA utilizes its longstanding policy of exercising its enforcement discretion regarding certain types of pharmacy compounding. This policy is articulated in FDA's Compliance Policy Guide (CPG), Section 460.200, issued on June 7, 2002. The CPG contains factors FDA considers in deciding whether to exercise enforcement discretion. One factor FDA considers is whether a compounded product is a copy of a commercially available product and, if so, whether there is any documentation of a medical need for the compounded product.

The inspection disclosed your firm manufactures thirteen sterile injectable drug products; eight of these injectable drug products have the same strength as the commercially available products:

- The compounded estradiol valerate 40 mg/ml is supplied in [redacted] ml vials and the commercially available product is supplied in 5 ml vials;
- The compounded pyridoxine HCL, USP, 100 mg/ml is supplied in [redacted] ml vials and the commercially available product is supplied in 1 ml vials;
- The compounded methylprednisolone acetate 40 mg/ml and 80 mg/ml is supplied in [redacted] ml vials and the commercially available product is supplied in 10 ml and 5 ml vials;
- The compounded dexamethasone acetate 8 mg/ml is supplied in [redacted] ml vials and the commercially available product is supplied in 5 ml vials;
- The compounded betamethasone sodium phosphate 3 mg/ml is supplied in [redacted] ml vials and the commercially available product is supplied in 5 ml vials;
- The compounded adenosine phosphate 25 mg/ml is supplied in [redacted] ml vials and the commercially available product is supplied in 10 ml vials; and,
- The compounded triamcinolone acetonide 40 mg/ml is supplied in [redacted] ml vials and the commercially available product is supplied in 1 ml and 5 ml vials.

For the purpose of the agency's exercise of its enforcement discretion, the availability of different size vials are not a meaningful distinction between your products and the commercially available products. Further, we found no documentation of the medical need for the variation between solutions and suspensions.

The inspection revealed your firm manufactured/distributed approximately [redacted] vials of injectable drug products within 12 months (August 2004 to August 2005). This included shipments of [redacted] units on May 26, 2004, [redacted] units on May 27, 2004, [redacted] units on February 25, 2005, and [redacted] units on June 29, 2005, all to [redacted] We do not believe your firm's production volume is consistent with traditional pharmacy compounding operation.

In light of the above factors, FDA will not exercise its enforcement discretion for your firm's manufacturing and distribution of these products. Your firm's compounded products are unapproved new drugs, and their introduction or delivery for introduction into interstate commerce violates Sections 505(a) and 301(d) of the Act [21 USC 355(a), 331(d)]. Further, these compounded drugs are misbranded under Section 502(f)(1) of the Act [21 USC 352(f)(1)] because their labeling fails to bear adequate directions for use and they are not exempt from this requirement under 21 CFR 201.115. These drugs also are misbranded under Section 502(o) of the Act [21 USC 352(o)] because they are produced in an establishment not duly registered under Section 510 of the Act [21 USC 360], and they have not been listed as required by Section 510(j) of the Act [21 USC 360(j)]. Your facility is not exempt from registration and drug listing requirements under Title 21 *Code of Federal Regulations* (CFR), Part 207.10 (21 CFR 207.10) and Section 510(g) of the Act [21 USC 360(g)] because it is engaged in the manufacture and distribution of drugs.

In addition, the inspection found significant violations of the Current Good Manufacturing Practice (CGMP) regulations for drug products, set forth in 21 CFR 210 and 211. The CGMP violations include, but are not limited to, the following:

1. You have not established and followed appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile, as required under 21 CFR 211.113(b). For example, you do not perform media fills, you have not validated the sterilization process (steam autoclave) for terminally sterilized products, and you have not conducted smoke studies in your Class 100 hood.

2. You do not have control systems to prevent contamination, as required under 21 CFR 211.42(c)(10)(i). For example, you do not perform environmental monitoring for viable and non viable organisms in your aseptic areas.

3. On August 5, 2005, our investigator noted residues on your HEPA filter, HEPA filter plastic retainer screen, and plastic light cover inside your Class 100 hood indicating equipment was not cleaned, maintained, and sanitized, as required under 21 CFR 211.67(a) to prevent contamination which could alter the safety, identity, strength, quality, or purity of the drug product.

4. Your firm does not have written standards or specifications and methods of testing to remove pyrogenic properties and your dry heat oven used for depyrogenation of glass vials, glassware, and closures has not been validated, as required under 21 CFR 211.94(d).

5. You do not test each batch of drug product purporting to be sterile by appropriate laboratory determination of satisfactory conformance to final specifications, as required under 21 CFR 211.165(a). For example, eight lots (Lot # [redacted] thru [redacted]) of betamethasone sodium phosphate 4 mg/mL – betamethasone acetate 3 mg/mL were distributed without finished product testing, including sterility testing.

6. Twelve lots of prescription, injectable drug products were distributed even though these drug products failed to meet the established USP standards, recognized as your firm's finished product specifications, as required under 21 CFR 211.165(f).

7. You have not established and followed written procedures for production and process control designed to assure the drug products have the identity, strength, quality, and purity they purport or are represented to possess, as required under 21 CFR 211.100(a). For example, you have not validated the manufacturing process for any of your sterile injectable drug products. In addition, your firm does not perform integrity testing on microbial retentive filters.

8. You do not identify and handle filled drug product containers set aside and held unlabeled for future labeling operations to preclude mislabeling, as required under 21 CFR 211.130(b). For example, on August 3, 2005, our investigator noted several metal trays and cardboard boxes containing unlabeled glass vials filled with drug product stored in the processing areas.

9. All of your finished injectable drug products bear an 18 month expiration date which has not been determined by appropriate stability testing to assure these products meet applicable standards of identity, strength, quality, and purity at the time of use, as required under 21 CFR 211.137 (a).

10. You have no written testing program designed to assess the stability characteristics of your injectable drug products, as required under 21 CFR 211.166(a).

11. Batch production and control records have not been prepared and maintained for each batch of prescription injectable drug product produced by your firm, as required under 21 CFR 211.188.

12. You have not performed at least one specific identity test on each component or established the reliability of the supplier's test results, as required under 21 CFR 211.84(d)(2). For example, although you receive a Certificate of Analysis, you do not perform identity testing on incoming raw materials and you have not established the reliability of the supplier's test results.

13. You have not conducted a visual identification on each lot of container and closure or established the reliability of the supplier's test results, as required under 21 CFR 211.84(d)(3). For example, although you receive a Certificate of Analysis, you do not perform a visual examination on containers and closures and you have not established the reliability of supplier's test results.

14. You do not have appropriate written procedures. For example, you do not have written procedures for handling returned products (21 CFR 211.204) or complaints [21 CFR 211.198(a)], and you have no written calibration program for equipment [21 CFR 211.68(a)].

In light of the above inspectional observations, your drug products are adulterated within the meaning of Section 501(a)(2)(B) of the Act [21 USC 351(a)(2)(B)] as the methods, controls, and procedures, used in the drugs' manufacture, processing, packing, and holding, do not conform to CGMP regulations set forth in 21 CFR 210 and 211.

The above violations are not intended to be an all-inclusive list, as other deficiencies may exist at your facility. It is your responsibility to assure your facility is operating in compliance with each requirement of the CGMP regulations and applicable statutes enforced by the FDA. Federal agencies are advised of the issuance of all warning letters about drugs so they may take this information into account when considering the award of contracts.

You should take prompt action to correct all of the violations noted in this letter, and you should establish procedures whereby such violations do not recur. Failure to promptly correct violations may result in regulatory action without further notice, such as seizure and/or injunction.

You should notify this office in writing, within fifteen (15) working days from your receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step taken to prevent recurrence of similar violations. You should include in your response documentation, such as documentation of validation of the sterilization process for terminally sterilized products, corrected process control procedures, or other useful information to assist us in evaluating your corrections. If you cannot complete all corrections before you respond, you must explain the reason for your delay and state when you will correct

any remaining deviations. Your responses will be reviewed and any corrective actions will be verified during our next inspection at your facility. You can find guidance and information for the regulated industry regarding regulations for drug products through links at FDA's website at http://www.fda.gov/oc/industry/.

Your reply should be directed to the U.S. Food and Drug Administration, Attention: Cynthia R. Crocker, Compliance Officer, at 100 W. Capitol Street, Jackson, Mississippi 39269. If you have questions regarding any issue in this letter, please contact Ms. Crocker at (601) 965-4581, extension 106.

Sincerely,

H. Tyler Thornburg
District Director
New Orleans District

Enclosure: Form FDA 483