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May 6, 1999

Chicago District
300 S. Riverside Plaza, Suite 550 South
Chicago, Illinois 60606
Telephone: 312-353-5863

WARNING LETTER
CHI-16-99

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Pradeep Aggarwal, President
Medefil, Inc.
492 W. Lunt Avenue
Schaumburg, IL 60193

Dear Mr. Aggarwal:

During an inspection of your firm from February 1 to February 25, 1999, Investigators Ruben DeLaGarza, Lisa Hornback, and Sue Bruederle determined that your firm manufactures prefilled heparin and/or saline syringe products which are drugs within the meaning of Section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act).

The investigators documented serious deviations from the Current Good Manufacturing Practice regulations (CGMP) as specified in Title 21, Code of Federal Regulations (CFR), Parts 210 & 211. The following deviations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Act:

1. Failure to perform adequate sterility testing. For example, your firm:
 - a) Failed to perform sterility testing per the following USP XXIII requirements:
 - Use thioglycollate media for product sterility testing
 - Incubate the soybean-casein media at the required temperature of 20-25°C
 - b) Failed to perform growth promotion testing on sterility media to assure the media is capable of supporting microbial growth.
 - c) Failed to validate the sterility test method to show adequate recovery of microorganisms.
 - d) Lacked procedures that require an investigation be conducted for an initial failing sterility test.

2. Failure to maintain stability data to support the expiration dates for your drug products.
3. Failure to maintain adequate stability test procedures. For example, your procedures lacked the following: a written description of the sample size and test intervals; requirement to test the drug in the same container-closure system as that in which it is marketed; and assurance that the test methods are stability-indicating.
4. Failure to perform adequate process validation. For example, your process validation studies lacked the following: a written validation protocol; documentation of the amount of Heparin Sodium injected into each [REDACTED] mL bag of [REDACTED] Sodium Chloride when validating the manufacturing process for Heparin-Sodium-for-Injection drug products; and assessment of the uniformity of dosage within a bag and within a batch of multiple bags.
5. Failure to perform container-closure integrity studies for drug products.
6. Failure to adequately monitor and control Class 100 room where aseptic-fill and other associated operations take place. For example:
 - a) The following were not routinely performed during aseptic fill operations: non-viable particle counts, quantitative air sampling for microbial analysis, and microbial monitoring of personnel performing manual aseptic fill operations in Class 100 areas.
 - b) Particle count testing and microbial air quality testing (using microbial settle plates) were not performed during aseptic fill activity in the rooms.
 - c) On January 29, 1999, air flow velocity in [REDACTED] of [REDACTED] HEPA filters did not meet specifications.
 - d) HEPA filters were not tested for leaks using an aerosol challenge.
7. Failure to adequately test finished drug product to assure it meets specifications. For example:
 - a) There was no assurance that low levels of microbial growth can be observed visually through translucent plastic syringes.
 - b) Procedures did not require an investigation be conducted for an initial failing concentration test.

8. Failure to maintain adequate master production and control records. For example, master production and control records for all products:
 - a) Did not indicate the size of the batch.
 - b) Did not specify a measure for the heparin dosage unit or the total measure of dosage unit for the size of the batch.
 - c) Did not contain an accurate statement of the amount of component to be used for the preparation of a specific batch size.
9. Failure to assure that the sampling method during finished product testing is representative of the entire lot.
10. Failure to review all drug production and control records, including packaging and labeling, before a batch is released or distributed.
11. Failure to test each drug component or obtain a Certificate of Analysis from the component supplier to assure the drug component meets specifications.

During a meeting with you and your firm's corporate officers on February 5, 1999, you were informed that it appeared your firm was in violation of the law for marketing and distributing prefilled heparin and/or saline syringes without obtaining an Abbreviated New Drug Application (ANDA) from FDA. Your firm's pre-filled syringe products are labeled for use as drugs. During that meeting, you informed us that you would immediately stop production and distribution of all pre-filled syringes and you agreed to recall all your firm's pre-filled syringes in commercial distribution. You agreed to destroy all remaining product in your inventory and all product returned during the recall.

Please send a written response to the following questions and requests:

1. Have you destroyed all remaining product in inventory?
2. For all products that have been destroyed, please describe the method of destruction and the locations and dates it took place. Please provide a list of the lot numbers that were destroyed and the quantity in each lot or batch that were destroyed.
3. For all product that has not been destroyed, please provide the following: lot numbers and quantity in each, the location, and a schedule for planned destruction.
4. Please provide Ms. Kathy Haas, Recall and Complaint Coordinator, the monthly recall status reports she requested in her telephone call with you on March 9, 1999. She can be reached at (312) 353-5863, ext. 143.

During our meeting on February 5, 1999, you also promised to stop all marketing and distribution of prefilled syringes until you changed the labeling of your prefilled syringe products for use as medical devices (catheter lock flush) and received FDA approval of a Premarket Notification 510(k). Please confirm in writing that you have ceased all production and distribution of your prefilled saline and heparin syringe products. Please confirm in writing your intent to begin distribution of your prefilled syringe products, labeled for use as medical devices (catheter lock flush), only after you receive FDA approval of a Premarket Notification 510(k).

This letter, as well as the Inspectional Observations, Form FDA 483, issued to you at the conclusion of the inspection, 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 Current Good Manufacturing Practice regulations. Federal Agencies are advised of the issuance of all warning letters about drugs and devices so that they may take this information into account when considering the award of contracts. Additionally, pending NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

You should ensure that prompt action is taken to correct the deviations noted during this inspection. Failure to adequately correct these deviations may result in regulatory actions, including seizure or injunction, without further notice.

Please notify this office within 15 working days of the receipt of this letter of the specific steps you have taken to correct the noted violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your reply should be sent to Michael Lang, Acting Compliance Officer.

Sincerely,

/s/

Raymond V. Mlecko
District Director