U.S. Department of Health & Human Services

U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Yag Mag Labs Private Limited 9/12/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Silver Spring, MD 20993

Warning Letter

VIA UPS MAIL **WL: 320-11-20**

12 September 2011

Mr. M. Soma Raju
Yag-Mag Labs Private Limited
Plot 7, Flat 301
Besides Andhra Bank, Sundar Nagar, Near ESI
Hyderabad 500 038, Andhra Pradesh, India

Dear Mr. M. Soma Raju,

During our June 27 to July 2, 2011 inspection of your active pharmaceutical ingredient (API) manufacturing facility, Yag-Mag Labs Private Limited located at Survey No. 10, Gaddapotharam Village, Jinnaram Mandal, Medak District, Andhra Pradesh 502 319, India, an investigator from the Food and Drug Administration (FDA) identified significant deviations from Current Good Manufacturing Practice (CGMP) for the manufacture of APIs. These deviations cause your API(s) to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 351(a)(2)(B)] 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, CGMP.

We have reviewed your firm's response of July 18, 2011, and note that it lacks sufficient corrective actions.

Specific deviations observed during the inspection include, but are not limited to, the following:

1. Failure to document the manufacturing operations at the time they are performed.

For example, you manufactured approximately **(b)(4)** batches of **(b)(4)**, USP, from April 2009 through March 2010, but the batch records were admittedly written months after the batches were manufactured and released for shipment. You are responsible for the accuracy of the information included in manufacturing records and the integrity of the data generated by your firm, including assuring appropriate sign-off and review of the records from operations before batch disposition. Batch records must be completed at the time of batch manufacture, and backdating of records is not an acceptable practice. This finding that manufacturing batch records are untrustworthy represents a basic systemic failure by your company.

2. Failure to have API manufacturing facilities of appropriate design and construction suitable for their intended use.

For example, the inspection revealed the facility was not adequately designed to facilitate cleaning and minimize the potential for contamination. This was evidenced by the observed residues and corrosion on processing equipment, materials and processing equipment exposed to the outside elements without adequate protection; poorly identified and leaking piping; recessed ground-level floor susceptible to flooding and observed with substantial standing water; and inadequate unsanitary restroom facilities.

3. Failure to have appropriate procedures or practices in place to prevent cross-contamination.

For example, prior to April 2011, you did not use cleaning logs and it was reported to our investigator, by your personnel, that no cleaning was performed. There was no evidence that any cleaning between batches or between product changeovers occurred for non-dedicated equipment. It is a critical responsibility of your firm to clean non-dedicated equipment between production of different materials to prevent cross-contamination, using validated procedures. The cleaning program should include strong justification for acceptance criteria for any permitted residues, choice of cleaning procedures, and cleaning agents.

4. Failure to prepare, review, and approve documents related to the manufacture of APIs, in accordance with written procedures.

For example, you manufactured, released, and distributed batch **(b)(4)** of **(b)(4)** USP to the United States in April 2010. You performed these manufacturing operations without written procedures for change control, out-of-specification test results, laboratory deviations, investigation of production discrepancies or deviations, consumer complaint handling, or annual product reviews.

In addition, the batch record for batch **(b)(4)** is inadequate. The batch record failed to include manufacturing or processing instructions, limits, controls or actual test result values. It is your responsibility to ensure that your quality system, basic written procedures, and essential quality assurance functions are in place prior to performing drug manufacturing. Your quality system will be thoroughly reviewed during the next FDA inspection.

5. Failure to adequately control, process, analyze, and approve or reject raw materials and finished APIs.

For example, **(b)(4)** batches of **(b)(4)** USP were released for distribution from April 2010 through March 2011 without adequate sampling of starting materials. It was observed within the in-house analysis records and through discussion with a firm employee that starting material **(b)(4)**, internal lot **(b)(4)** had come from an unknown supplier via a distributor without product label or manufacturer information. According to the in-house records, it was tested by GC, KF and MP, but no raw data could be found to support the testing, nor records of instrument use logs.

Additionally, there is no traceability of the finished APIs as the completed batches were not properly identified and were then comingled, allowing for commercial lots to contain an unknown blend of manufactured batches.

Your response acknowledges that your facility "was not up to the mark of FDA...." and that corrective and preventative actions are needed, but are not completed at this time. We recommend that you conduct a complete and extensive evaluation of your overall quality and manufacturing controls to ensure that all APIs manufactured at your facility meet the quality and purity characteristics they purport to possess. We highly recommend that you hire a third party auditor with

experience in detecting data integrity problems, who may assist you in evaluating your serious CGMP deviations. Your firm's broad-based CGMP compliance issues will require significant remediation and substantial investment of time and resources. Among the areas needing global attention include but are not limited to facility improvements, process validation, complete and accurate manufacturing procedures, training programs, quality unit effectiveness, and an overall effective quality system.

The deviations detailed in this letter are not intended to be an all-inclusive statement of deviations that exist at your facility. You are responsible for investigating and determining the causes of the deviations identified above and for preventing their recurrence and the occurrence of other deviations. If you wish to ship APIs to the United States, it is the responsibility of your firm to ensure compliance with all U.S. standards for CGMP and all applicable U.S. laws and regulations.

Additionally, your firm is neither registered nor has it listed every API in commercial distribution in the United States with FDA, as required by 21 C.F.R. § 207.40 and section 510(i) of the Act [21 U.S.C. § 360(i)]. The FDA investigators discussed this issue with you during the inspection. Your response did not address this issue. Information on how to register and list is available at the following internet website: http://www.fda.gov/cder/drls/registration_listing.htm. You must complete the required registration and listing and provide evidence that you have fulfilled these requirements in your response to this letter.

Until all corrections have been completed and FDA has confirmed corrections of the deviations and your firm's compliance with CGMP, FDA may withhold approval of any new applications or supplements listing your firm as an API manufacturer. In addition, until such time as your manufacturing practices are verified to comply with CGMPs, your firm will remain under FDA Import Alert and FDA will continue to refuse admission of all articles manufactured at Yag-Mag Labs Private Limited, India into the United States. The articles are subject to refusal of admission pursuant to section 801(a)(3) of the Act [21 U.S.C. § 381(a)(3)] in that the methods and controls used in their manufacture do not appear to conform to Current Good Manufacturing Practice within the meaning of section 501(a)(2)(B) of the Act [21 U.S.C. § 351(a)(2)(B)].

Failure to promptly correct violations affecting your products that are being marketed within United States commerce may also result in legal action without further notice, including, without limitation, seizure and injunction. Other federal agencies may take this Warning Letter into account when considering the award of contracts.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct deviations. Include an explanation of each step being taken to prevent the recurrence of deviations and copies of supporting documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the date by which you will have completed the correction. Additionally, your response should state if you no longer manufacture or distribute active pharmaceutical ingredients, and provide the date(s) and reason(s) you ceased production. Please identify your response with FEI # 3004896339.

If you have questions or concerns regarding this letter, contact Elizabeth L. Philpy, Compliance Officer, at the below address and telephone number.

U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Division of Manufacturing and Product Quality
International Compliance Branch
White Oak, Building 51, Room 4225
10903 New Hampshire Ave
Silver Spring, MD 20993
Tel: (301) 796-3334
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Sincerely,
/S/
Steven Lynn
Director
Office of Manufacturing and Product Quality
Office of Compliance
Center for Drug Evaluation and Research

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