U.S. Department of Health & Human Services

U.S. Food & Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

B.M.P. Pharma Trading AG 5/4/12

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Silver Spring MD 20993

Warning Letter

VIA UPS MAIL

WL: 320-12-15

May 4, 2012

Mr. Bernd M. Joerss
President
B.M.P. Pharma Trading AG
Bornbarch 16
D-22848 Norderstedt, Germany

Dear Mr. Joerss:

During our November 14-16, 2011, inspection of your active pharmaceutical ingredient (API) manufacturing facility, B.M.P. Bulk Medicines & Pharmaceuticals GmbH, located at Bornbarch 16, Norderstedt, Germany, 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 considered your firm's response of November 30, 2012 prior to issuing this warning letter.

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

1. Failure to use dedicated production areas, including facilities and air handling equipment, when performing operations with beta-lactam products.

   For example, your firm performs sampling, an open operation involving powders, on both beta-lactam antibiotics and non-beta-lactam products in a shared facility, using shared equipment and a shared dust collection hood. The procedures in place at your facility, as discussed in your response, are insufficient to prevent beta-lactam cross-contamination of your non-beta-lactam products. Additionally, your facility is not designed to prevent beta-lactam cross-contamination into products that you repackage in the production room. We note in particular that the dust collection hoods in the sampling room and production room share common ductwork. For FDA's current thinking on this topic, please consult the Agency's Draft Guidance for Industry entitled "Non-Penicillin Beta-Lactam Risk Assessment: A CGMP Framework."[1]

   In your response, please commit to cease all beta-lactam operations until you have addressed this issue. Your response to this letter should address how you will completely segregate facilities where operations (including but not limited to sampling and repacking) for beta-lactam antibiotics occur from non-beta lactam facilities. Your response should describe procedures that you will implement to prevent cross-contamination by beta-lactams or any other compounds with high pharmacological activity, toxicity, or of infectious nature.

   In addition, please address your plans for decontaminating your facility, which has been exposed to multiple beta-lactams during the course of operations. Include your sampling plan, baseline of contamination on all potentially contaminated surfaces, and analytical methodology that will be used to demonstrate that the deviations discussed in this letter have been remediated. Your methodology should include a demonstration that the decontamination agents are effective at inactivating all the beta-lactams your facility has sampled on all potentially contaminated surfaces and equipment with an acceptable limit of detection. Where sufficient decontamination cannot be conclusively demonstrated, we expect you will remove those potentially contaminated surfaces or equipment. Affected areas may include but are not limited to all duct work connected to areas where beta-lactam sampling occurred; the sampling hood; and walls, floors, and ceiling of the sampling room. Note that you must provide descriptions of your decontamination, renovation, and requalification plans even if your firm decides that it will no longer perform open operations with beta-lactams.

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 continue 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.

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, failure to correct these deviations may result in FDA refusing admission of articles manufactured at B.M.P. Bulk Medicines & Pharmaceuticals GmbH 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)].

If, as a result of receiving this Warning Letter or in general, you are considering making a decision that will result in a decreased number of finished drug products or active pharmaceutical ingredients produced by your manufacturing facility, FDA requests that you contact CDER's Drug Shortages Program immediately, as you begin your internal discussions, at drugshortages@fda.hhs.gov in order to ensure that your action(s) does not adversely affect the public health.

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 the drug product(s) manufactured or processed at this facility, and provide the date(s) and reason(s) you ceased production. Please identify your response with FEI #3002174993.

If you have questions or concerns regarding this letter, contact Mary E. Farbman, Compliance Officer, at the below address and telephone number.

U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Office of Manufacturing and Product Quality
Division of International Drug Quality
White Oak, Building 51, Room 4214
10903 New Hampshire Ave
Silver Spring, MD 20993
Tel: (301) 796-4171
Fax: (301) 847-8741

Sincerely,

/S/

/Steven Lynn/
Steven Lynn
Director
Office of Manufacturing and Product Quality
Office of Compliance
Center for Drug Evaluation and Research

1 This draft guidance is available on the World Wide Web at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM246958.pdf[1].

Links on this page:

1. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM246958.pdf

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