U.S. Department of Health & Human Services

U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Dr. Reddys de Mexico 6/3/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Silver Spring MD 20993

Warning Letter

VIA UPS MAIL

WL: 320-11-014

June 3, 2011

Mr. G.V. Prasad, CEO
Dr. Reddy's Laboratories Limited
7-1-27 Ameerpet
Hyderabad 500 016
Andra Pradesh India

Dear Mr. Prasad:

During our November 8-11, 2010 inspection of your active pharmaceutical ingredient (API) manufacturing facility, Industrias Quimicas Falcon de Mexico, S.A. de C.V. (also known as Dr. Reddy's Mexico) located at Km. 4.5 Carretera Federal Cuernavaca-Cuautla, 62578 Jiutepec, Morelos Mexico, 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 APIs 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 December 1, 2010, and note that it lacks sufficient corrective actions.

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

1. Your firm did not validate analytical methods used to test APIs.

For example, the inspection revealed that your firm had not validated the HPLC method for assay and related substances of **(b)(4)** (finished API **(b)(4)** for human use). This is just one example of numerous methods used by your firm that had not been validated according to approved procedures.

Your response states that of the **(b)(4)** APIs manufactured at your facility, **(b)(4)**% are compendial products. The remaining roughly **(b)(4)** non-compendial APIs had no method validation. You committed to complete these method validations by April 30, 2011. However, this does not address product currently on the market, or product that will enter the market tested with an unvalidated method. Your proposal to verify "key parameters" for the first API batch produced does not provide the same level of assurance as method validation.

In your response to this letter, provide us with a plan that details a greater level of assurance that adulterated API will not reach the U.S. market. Additionally, advise what you will do with adulterated API on the U.S. market that has been tested with methods that are not validated (for non-compendial products). In your response of December 1, 2010, you commit to verify all methods (for compendial products) by June 30, 2011. Include in your response to this letter the actions taken to ensure that all products tested with methods that have not been verified are in conformance to established quality and/purity standards.

Please also clarify if your test methods are stability indicating.

2. Your firm's cleaning validation was incomplete for non-dedicated manufacturing equipment.

For example, during the inspection the investigator observed a chart, dated November 11, 2010, showing your firm's cleaning validation progress by area that indicated the manufacturing equipment in Bay 2 (containing non-dedicated equipment) had no documented cleaning validation. This is just one example of several areas lacking cleaning validation for manufacturing equipment.

Your response states that you commit to start cleaning validation activities once a validated analytical method is available. We are concerned about the impact that the lack of cleaning validation has on marketed product. Provide us your action plan to determine that cleaning procedures are effective, and ensure that marketed product is not cross-contaminated.

3. Your firm's out-of-specification (OOS) investigations did not include analysis of all available data.

For example, the inspection revealed that your firm rejected three consecutive lots of **(b)(4)** (an intermediate used in the manufacture of an API for the product "**(b)(4)**") on February 26, 2010, for appearance problems. The deviation investigation into the cause of the failure did not include an analysis of all available data including batches manufactured prior to the failures.

The inspection also found many deficiencies regarding handling OOS investigations. These include the timeliness of closing investigations, notification of the quality unit (including four to eight-month delays for reporting failing stability batches), and failure to follow written procedures. Although some of your proposed corrections to these individual items appear to be adequate, we remain concerned that a thorough evaluation of your investigation approach has not been conducted. Please include in your response a corrective and preventive action plan regarding handling investigations.

4. Your firm's quality unit did not exercise its responsibility to ensure the APIs manufactured were in compliance with CGMP, and met intended specifications for quality and purity.

As evidenced by the previous deviations, your quality unit has not overseen the controls required under CGMP to properly produce APIs. Your December 1 response stated that you will assess your firm's quality needs by April 30, 2011. A quality unit is a basic requirement to ensure that quality APIs are produced at your

facility. Please provide a detailed current assessment of this deficiency.

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 Industrias Quimicas Falcon de Mexico, S.A. de C.V. (also known as Dr. Reddy's Mexico) 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)].

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. Please identify your response with FEI #3002808297.

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

U.S. Food and Drug Administration
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Division of Manufacturing and Product Quality
International Compliance Branch
White Oak, Building 51
10903 New Hampshire Ave
Silver Spring, MD 20993
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Sincerely,
/S/
Carmelo Rosa on behalf of Richard L. Friedman
Richard L. Friedman
Director
Division of Manufacturing and Product Quality
Office of Compliance
Center for Drug Evaluation and Research

/S/
Eric Nelson
Acting Director
Division of Compliance
Center for Veterinary Medicine

Cc:
Mr. Francisco Casillas, Site Manager
Industrias Quimicas Falcon de Mexico, S.A. de C.V.
(also known as Dr. Reddy's Mexico)

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