Press Release

Dr.Reddy's

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Hyderabad, India – 26 November, 2015

For Immediate dissemination

Update on USFDA warning letter

Dr. Reddy's Laboratories (BSE: 500124, NSE: DRREDDY, NYSE: RDY)

Further to our Press Release dated November 6, 2015, this is to inform you that the U.S. Food and Drug Administration ("FDA") warning letter to the Company dated November 5, 2015 has been made available to the public on the FDA's web site at: http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm473604.htm.

The Company is in the process of preparing a response to FDA's warning letter. The FDA has granted an extension until December 7, 2015 for the submission of the Company's response to its warning letter.

Dr. Reddy's Laboratories Ltd. Dr.Reddy's Hyderabad - 34

About Dr. Reddy's: Dr. Reddy's Laboratories Ltd. is an integrated pharmaceutical company, committed to accelerating access to affordable and innovative medicines, because it believes Good Health Can't Wait. Through its three businesses - Pharmaceutical Services & Active Ingredients , Global Generics and Proprietary Products – the company offers a portfolio of products and services that include active pharmaceutical ingredients, (APIs), custom pharmaceutical services, generics, biosimilars and differentiated formulations. With operations in 26 countries across the globe, the major therapeutic areas of Dr. Reddy's are gastro-intestinal, cardiovascular, diabetology, oncology, pain management and anti-infectives. For more information, log on to: www.drreddys.com

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U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Dr. Reddy's Laboratories Limited 11/5/15

Department of Health and Human Services

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

Warning Letter

Via UPS

WL: 320-16-02

November 5, 2015

Mr. Satish Reddy
Chairman
Dr. Reddy's Laboratories Ltd.
8-2-337, Road No 3
Banjara Hills, Hyderabad 500034
Andhra Pradesh 530 046
India

Dear Mr. Reddy:

The U.S. Food and Drug Administration (FDA) inspected the following three Dr. Reddy's Laboratories Ltd. pharmaceutical manufacturing facilities in India:

A. November 17-21, 2014: Dr. Reddy's Laboratories Limited CTO Unit VI, located at APIIC Industrial Estate, Pydibhimavarma (Village), Ranasthalam Mandai, Srikakulam District, Andhra Pradesh;

B. January 26-31, 2015: Dr. Reddy's Laboratories Limited CTO Unit V, located at Peddadevulapally Village, Tripuraram, Mandal, Miryalguda Taluk, Nalgonda District, Telangana; and
C. February 26 to March 6, 2015: Dr. Reddy's Laboratories Ltd., Unit-VII located at Plot No. P1 to P9, Phase III, Duvvada, VSEZ, Visakhapatnam, Andhra Pradesh.

At Dr. Reddy's Laboratories Limited CTO Units VI and V facilities, we identified significant deviations from current good manufacturing practice (CGMP) for the manufacture of active pharmaceutical ingredients (APIs). At Dr. Reddy's Laboratories Limited Unit-VII facility, we found significant violations of CGMP regulations for finished pharmaceuticals, Title 21, Code of Federal Regulations, Parts 210 and 211.

These deviations and violations cause your APIs and finished drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), 21 U.S.C. 351(a)(2)(B). 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 reviewed your firm's responses of December 15, 2014, February 19, 2015, and March 27, 2015. We note that they lack sufficient corrective actions. We received your additional correspondence of January 31, April 9, May 13, May 21, July 14, and September 14, 2015.

Our investigators observed specific deviations and violations during the inspection, including, but not limited to, the following.

A. Dr. Reddy's Laboratories Limited CTO Unit VI Facility (FEI: 3002949085)

1. Failure to maintain complete data derived from all laboratory tests conducted to ensure compliance with established specifications and standards.

Your laboratory records did not contain all raw data generated during each test for API batches manufactured at your firm. The investigator found that batch samples were routinely re-tested following failing or atypical results until acceptable results were obtained, and that failing or atypical results were not investigated or included in the official laboratory control records.

During the inspection, the presence of an uncontrolled "Custom QC laboratory" (CQC) was discovered by our inspection team. The existence of this laboratory was previously unknown to

FDA. Your QC Associate Director acknowledged that the CQC laboratory was involved in CGMP analysis of APIs intended for export to the United States through 2012. This discovery was made one day before the end of the inspection, but during FDA's brief evaluation of the high performance liquid chromatography (HPLC) electronic records generated by the CQC, our investigators found the following examples.

a. **(b)(4)** (raw material) batch #**(b)(4)**
You performed assay/related substances by HPLC at **(b)(4)** on January 23, 2012. The sample failed the specification limit for purity, with a result of **(b)(4)**% (specification: NLT **(b)(4)**%). This failing result was not documented or reported. You repeated the analysis at **(b)(4)** on January 24, 2012, with a failing result of **(b)(4)**%. Again, you did not document or report it. On January 25, 2012, you conducted a third analysis at **(b)(4)** Your laboratory's "Record of Analysis" for this batch, which you used to support batch disposition decisions, contained only the passing results obtained during the third and final test.

b. **(b)(4)** batch #**(b)(4)**
You conducted purity testing by HPLC at **(b)(4)** on January 27, 2012. This sample failed the purity specification limit (NLT **(b)(4)**%) with a result of **(b)(4)**%, but you did not document, report or investigate the failure. Your QC data package, which you used to support batch disposition decisions, showed passing results from **(b)(4)** on the same day but does not include the initial failing results.

c. **(b)(4)** U.S. DMF batch #**(b)(4)**
The first sample analysis for related substances by HPLC was performed in duplicate at **(b)(4)** February 10, 2012. The second injection of this first sample contained an extra peak. Sample preparation information was not documented, and the test result with the extra peak was not reported. Your QC records for this batch, which you used to support your Drug Master File for this product and to support batch disposition decisions, included results only from a later analysis that you conducted at **(b)(4)** on February 11, 2012.

d. **(b)(4)** batch #**(b)(4)**
The first sample analysis for assay/related substances by HPLC was performed at **(b)(4)** January 14, 2012. The sample failed the specification limit for known and unknown impurities. The second sample analysis, performed the same day at **(b)(4)**, also failed the specification limits for known and unknown impurities. A third test, performed at **(b)(4)**, January 14, 2012, also failed the specification limits for known and unknown impurities. Only the third failure was reported in your QC data package, which you used to support batch disposition decisions. Sample preparation information for the first two sequence runs was not documented.

In your December 15, 2014 response, you stated that tests were repeated because your analysts observed:

- significant drifts in the base line
- chromatograph peak shapes inconsistent with the usual peaks
- delays between sample preparation and injection
- an injection of a sample before the previous sample was fully eluted from the column
- incorrect vial numbers entered into the auto injector

None of these explanations justify your failure to maintain complete records, nor do they support your practice of substituting repeat tests after failing results. You acknowledged that your analysts failed to document and start investigating OOS results, as required by your SOP 01-045/03 "Handling of Incidents" and SOP 08-004/12 "Laboratory Investigation of Out of Specification Results." However, you have not assessed how your reliance on the incomplete and inaccurate data generated by the CQC laboratory, which was operational until April 2012, may have affected the quality of your APIs.

In response to this letter, address how your firm intends to ensure the reliability and completeness of all records of analytical data generated at your facility. Specify the measures you have implemented to ensure your quality unit oversees documentation procedures and reviews all test results generated by all of your laboratories, including the electronic data generated for drugs manufactured and tested at your facility.

2. Failure to prevent unauthorized access or changes to data, and to provide adequate controls to prevent omission of data.

During the inspection we found the following examples of uncontrolled access to electronic systems used to generate data in your Product Development Laboratory (PD Lab).

a. Your HPLC systems are configured so that no passwords are required to log in. Credentials are unverified. Anyone who accesses the system can use software administrator privileges, which means that there is no electronic or procedural control to prevent manipulation of data.

b. Your HPLC system had no access controls to prevent alteration or deletion of data. Furthermore, your HPLC software lacked an audit trail feature to document all activities related to the chromatographic analysis. Because of this failure, neither your quality unit nor your laboratory

staff could demonstrate that HPLC records included complete and unaltered data. They were also unable to verify that there had been no alterations or deletions.

c. One of your analysts stated that another, unknown individual had logged into the system using the analyst's credentials. This unknown individual performed injections and deletions without the analyst's knowledge.

According to your December 15, 2014 response, you used the equipment and systems in the PD Lab to conduct non-CGMP activities, which you characterize as "extended" investigations to identify impurities in APIs and intermediates, improve processes, qualify sources of key starting materials, and conduct laboratory experiments to address Drug Master File (DMF) deficiencies. Your response is inadequate, because many of these activities are subject to CGMP. Additionally, you based final disposition decisions on uncontrolled investigations conducted in the PD Lab.

In your response to this letter, explain how you will ensure that all analyses performed in support of product disposition decisions and other CGMP activities will be reviewed, approved, and overseen by your quality unit. Provide specific details of the steps you have taken to prevent unauthorized access to your electronic data systems and to ensure that data systems retain complete, accurate, reliable, and traceable results of analyses performed.

3. Failure to record activities at the time they are performed.

Your employees did not complete batch production and control records immediately after activities were performed. When QA reviewers noticed missing entries in the batch records, they made a list of all the missing items on separate, uncontrolled pieces of paper that were provided to the production manager. Data were later entered into CGMP documents after operations had already ended as though they had been entered at the time of the operation.

For example, on November 17, 2014, we saw eight production records for **(b)(4)** and **(b)(4)** that had blank entries for weights of material used for production, checked-by signatures, accessories used, in-house batch numbers, quantity added, and product labeling for material dried specimens. The yield report sheet and batch summary sheet were also incomplete.

Missing information was recorded on uncontrolled sheets of paper instead of in your official records. Your staff told us that they write on sheets of paper to make management aware of missing data in the batch record. Your December 15, 2014 response to this finding stated, "[w]e acknowledge and regret that some of the data such as weights, checked by signature etc…were not entered" (*sic*). You claim this practice was only observed in records related to the manufacture

of **(b)(4)** active ingredients, and that the missing entries for weights were due to manufacturing equipment inadequacies.

These explanations do not justify your use of uncontrolled paper for documenting CGMP-relevant data, nor do they justify your failure to document events and information contemporaneously. For example, it is unacceptable to use uncontrolled sheets of paper to document deviations from the manufacturing process, regardless of whether such deviations are critical or non-critical. Even non-critical deviations from established procedures should be documented and explained, and reviewed and approved by your quality unit prior to the release of your intermediates or APIs.

In response to this letter, provide an assessment of the effects of your poor documentation practices on the quality of other batches produced in your facility. Specify when you discontinued using unofficial paper records, how you will prevent this practice from reoccurring, and the controls you are implementing to ensure that all CGMP-related operations are documented as they occur.

4. Failure to control the issuance, revision, superseding and withdrawal of all documents with maintenance of revision histories.

a. Your SOP 01-017/02 “Documentation Practices” requires that all controlled documents are completed and archived. However, on November 17, 2014, our investigator observed copies of issued, partially-used and unused batch records, analytical raw data, analytical results, training records, and cleaning validation protocols in the waste area. These controlled documents had not been completed or archived in accordance with your SOP on documentation practices.

b. During the inspection, investigators observed master batch records in the manufacturing areas, even though they were required to remain under the control of the quality unit. We also found a production employee with a quality unit document control stamp. In your response to the Form FDA-483, you confirmed that your amended SOP 01-018 “Preparation, Issue, Filling and Verification of Batch Production Record” (*sic*) stipulates that this stamp should remain in the possession of only quality unit personnel.

In your December 15, 2014 response, you stated, “[w]e regret that the documents referred under this observation were scrapped and found disposed of in the waste area without adhering to proper verification and authorization procedures. There was a lapse in the document control system…” You proposed a revised procedure and staff re-training.

We acknowledge your commitment to retrain your employees on your revised procedure. However, your response is inadequate because revising your SOP and re-training staff do not provide a

comprehensive assessment of the extent of your practice of placing controlled records in the waste area, outside of the document control system. You also have not evaluated all records of products that remain within a retesting period to determine whether any records related to such products were discarded without quality unit approval.

In your response to this letter, provide specific changes made to your procedures, and how you intend to ensure oversight from your quality unit over the management of batch production records. Provide details on how you will implement a reliable document control system to ensure that batch records are only generated and approved by your quality unit.

B. Dr. Reddy's Laboratories Limited CTO Unit V (FEI: 3005447965)

1. Failure to adequately investigate out-of-specification results and implement appropriate corrective actions.

a. Our investigator documented that five batches of **(b)(4)** intermediate failed the optical purity test by HPLC, which test is included in your Drug Master File for **(b)(4)**. In your response of February 19, 2015, you acknowledged that, since 2012, 11 batches had failed the optical purity test, and that you had been unable to determine a root cause for such failures. Although all batches passed the optical rotation test found in the United States Pharmacopeia, you did not establish a correlation between the optical purity and optical rotation tests or report that you had identified an alleged root cause until May 19, 2015.

Your response is inadequate in that you provide no data to demonstrate that the conditions identified as the alleged root causes for the failures were actually observed in the failing batches. Moreover, you did not assess passing batches to determine if any of these same alleged conditions were present.

b. Our investigator documented 13 instances of out of specification results for a single impurity found in your **(b)(4)** intermediate for **(b)(4)**. In your February 19, 2015 response, you indicate that, since 2012, 65 batches of this intermediate failed to meet the single impurity specification. This represents **(b)(4)** of your entire production of this intermediate, a failure rate you acknowledged as high. In your response, you described your efforts to characterize and identify the impurity, determine the chemistry formation of the impurity, and your on-going work to try to minimize the formation of the impurity, identified as **(b)(4)**.

Although we acknowledge these efforts, your response is inadequate because you have yet to find a process solution to minimize the formation of this impurity, and propose continuing to reprocess

those batches that do not meet the established specifications. Your response lacks a justification for not including the reprocessing step as part of your routine manufacturing process.

In response to this letter, explain your plans to revalidate the manufacturing process for **(b)(4)** API.

2. Failure to maintain all quality-related documents appropriately.

Although your SOP GQA018-00, "Documentation Control, Archival and Destruction," does not permit photocopying labels, during the inspection we observed numerous pre-filled, photocopied labels for **(b)(4)** API in the garbage. These photocopied labels included the name of the product, material code, batch number, drum number, net weight, batch quantity, signature and date.

According to your February 19, 2015 response, "photocopying of the labels has not been a routine practice." Your investigation found that these labels "were intended for process/equipment status identification, which will be destroyed after completion of the process step" and are used for blend material in your **(b)(4)** blending, **(b)(4)** and packing area.

Your response to this observation does not adequately explain how the use of pre-filled photocopied labels may have affected the quality and traceability of the APIs you manufacture, nor does it indicate your plans for implementing procedures to prevent the use of uncontrolled photocopied labels.

In your response to this letter, provide your improved procedures to reconcile the quantities of labels issued, and for ensuring that you use the correct labels in your manufacturing operations.

3. Failure to prevent unauthorized access or changes to data.

During the inspection, we found that QC laboratory analysts were authorized to release finished product in your firm's computerized SAP inventory management system. Release or rejection of finished product is a non-delegable responsibility of the quality unit, and cannot be shared with laboratory analysts or other personnel. However, your SAP system permitted QC laboratory analysts to release intermediates from one process to the next process, as well as to release finished product into the market without requiring quality unit oversight.

In your February 19, 2015 response, you acknowledged that your SAP system permitted QC laboratory analysts to release intermediates and APIs, including release of finished API for distribution. However, you claimed that QC did not *actually* release finished API for commercial distribution using SAP because your quality unit is bound by SOP #01-021, "QA Release," which

provides for quality unit oversight. You also stated that you had "unambiguously verified that not a single commercial API batch has been released by QC alone" *(sic)* within the timeframe of January to December 2014. You acknowledged the need to build additional controls into your SAP system, and committed to amend the SAP configuration and stop solely relying on the SOP as the control tool. You also committed to review all batches manufactured and distributed from the site to determine if any products had been released for commercial distribution by QC alone.

On May 21, 2015, you reported that three batches of an API (not identified in your correspondence) *were* released for commercial distribution by a QC analyst in 2013. You concluded that this was an isolated incident.

In subsequent correspondence dated September 14, 2015, you stated that allowing QC analysts to release batches of intermediates was a deliberate part of Dr. Reddy's control strategy: this "functionality in SAP was given to QC personnel to allow the release of intermediates only for internal use in additional processing without QA intervention." You reiterated that your review of the release process over two years indicated that "the process operated as intended with no deviations," even though you had just reported such a deviation to the FDA in your May 2015 correspondence.

In your response to this letter, explain the discrepancy between your May 2015 report regarding release of API by a QC analyst and your September 2015 assertion that no such deviations had transpired over the course of two years. Describe the improvements made to the configuration of your SAP system, including controls to limit analyst functions and specifically to prevent QC analysts from releasing finished API or intermediates for commercial distribution. Explain further how your SAP system has been re-configured to reflect the quality unit's oversight of QC decisions to release intermediate for further use. Finally, show how your SOP on commercial release is aligned with the configuration and functionality of your SAP system.

4. Failure to identify storage containers for intermediates in batch production records.

During the inspection, we observed that you had not recorded identification numbers in your product batch records for drums used to hold intermediates during manufacturing. We also observed that you had not implemented necessary controls to prevent mix-ups and contamination.

In your February 19, 2015 response, you acknowledged these problems. You indicated that you have revised your batch records to require identification of equipment, replaced dedicated **(b)(4)** drums with **(b)(4)** bags, and amended your cleaning SOP.

In response to this letter, provide data to demonstrate that the **(b)(4)** bags you have substituted do not affect the quality of the intermediates you store in them.

C. Dr. Reddy's Laboratories Limited Unit VII (FEI: 3006549835)

1. Your firm failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed. (21 CFR 211.192)

On March 3, 2015, during the filling operation for **(b)(4)** injection **(b)(4)**mg/ml, batch **(b)(4)** in Block **(b)(4)**, our investigator documented a malfunction in the **(b)(4)** mechanism used to transport **(b)(4)** filled vials **(b)(4)** headed towards the **(b)(4)**. The **(b)(4)** mechanism **(b)(4)** the **(b)(4)** approximately **(b)(4)** of the correct **(b)(4)** before it malfunctioned and stopped.

On March 3, 2015, our investigator notified your Associate Director of Quality Assurance, your Resource Manager of Quality Assurance, and your Associate Director and Head Operations about the **(b)(4)** mechanism failure. However, contrary to your SOP FTCQA011-08, "Reporting, Investigating and Disposition of Incidents," your management failed to intervene, and allowed the filling process to continue uninterrupted.

During the filling operation, our investigator observed an operator repeatedly using forceps and an **(b)(4)** hand to **(b)(4)** the **(b)(4)** manually and align the **(b)(4)** with the **(b)(4)** conveyor belt. The operator intervened again to **(b)(4)** the **(b)(4)** onto the **(b)(4)** conveyor belt. Because the conveyor belt was not operational, an operator manually intervened to **(b)(4)** the vials into the **(b)(4)** loading area, where the **(b)(4)** the **(b)(4)** into the **(b)(4)**.

Your production manager said that approximately **(b)(4)** filled vials on approximately **(b)(4)** were transported in this manner. He said that the filling operation had to be completed within **(b)(4)** due to **(b)(4)** issues with the product in **(b)(4)**.

Each of these manual interventions risks compromising the sterility of the product and is a deviation from your approved SOP No. OPR052-05, "Operation of **(b)(4)** Filling Line **(b)(4)**" for filling **(b)(4)** injection **(b)(4)** mg/ml.

You did not simulate these critical manual interventions during media fills, so you have no basis to know whether they may compromise the sterility of your products. Understanding the effects of these interventions is especially important because the exposed product **(b)(4)**.

Even though your senior management was notified of this failure, you did not initiate an incident report to investigate the equipment malfunction or determine the effects of this discrepancy on the quality of the product until we concluded our inspection and issued a Form 483.

Your March 27, 2015 response stated "we recognize and accept that there was a malfunction of the **(b)(4)** assembly… this was a unique and a 'one off' failure which has not occurred in the past." You acknowledged that, in accordance with your own SOP, you should have registered a formal incident. You attributed the malfunction to a failed **(b)(4)** holding the **(b)(4)** of the **(b)(4)** mechanism. Your investigation concluded that, since all operations are carried out **(b)(4)**, the sterility hazard is remote.

Your response is inadequate. Although you acknowledged the unwarranted delay in initiating your investigation into the **(b)(4)** mechanism breakdown, your conclusion that potential effects on sterility were remote is unjustified because you have not simulated the manual interventions in your media fills.

We note that the lack of adequate investigations is a repeat violation from our February 2008 inspection.

In response to this letter, provide your plan to improve your investigations of critical process deviations. Include the changes you will implement to ensure that media fills provide adequate simulations. Detail how the critical interventions that may compromise the sterility of a product will be minimized in your aseptic processing operation.

2. Your firm failed to follow appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

Your media fill record reconciliation documentation failed to include a full accounting and description of the units rejected from each batch. Although a significant number of media-filled units were rejected with no written justification, we found the following media fills runs deemed as acceptable.

Media fill batch #	*Run date*	*Filled units*	*Rejected units*
(b)(4)	October 30, 2014	**(b)(4)**	81
(b)(4)	October 27, 2014	**(b)(4)**	21
(b)(4)	September 14, 2014	**(b)(4)**	36

(b)(4)	August 1, 2014	**(b)(4)**	249
(b)(4)	May 26, 2014	**(b)(4)**	64
(b)(4)	December 20, 2013	**(b)(4)**	121
(b)(4)	November 28, 2013	**(b)(4)**	5
(b)(4)	November 27, 2013	**(b)(4)**	35
(b)(4)	November 19, 2013	**(b)(4)**	185

According to your March 27, 2015 response, you explained the kind of defects observed, and revised your procedures to clarify the type of rejects.

Your response is inadequate. The media-fill records do not include reasons why filled vials were rejected. In addition, the total number of rejected media-filled vials does not include the vials that the **(b)(4)** automatically rejected. Your justification is not acceptable for excluding units removed during processing, or excluding units that were not incubated because of interventions.

In response to this letter, provide the findings of a risk assessment to determine the effects of your exclusion criteria on all the products manufactured during the period of the referenced media fills. Provide your revised media fill procedures to demonstrate how you have modified your exclusion criteria and ensured that your media fills accurately reflect the process you use to manufacture sterile products.

The lack of appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile is a repeat violation from our February 2008 inspection. For our current thinking on how to meet CGMP when manufacturing sterile drugs using aseptic processing, we recommend you review the FDA's guidance for industry, *Sterile Drug Products Produced by Aseptic Processing —Current Good Manufacturing Practice*, available at **http://www.fda.gov/downloads/Drugs/.../Guidances/ucm070342.pdf (http://www.fda.gov/downloads/Drugs/.../Guidances/ucm070342.pdf)**.

3. Your firm failed to establish adequate written procedures for production and process controls designed to assure that the drug products you manufacture have the identity, strength, quality, and purity they purport or are represented to possess, and your firm's quality control unit did not review and approve those procedures, including any changes. (21 CFR 211.100(a))

Parenteral drugs must be essentially free of particulates. However, during the inspection, we observed that your procedure for qualifying the operators who perform visual inspection is unacceptable because you did not document the creation of inspectors' qualification kits. The challenge test set vials used to qualify your operators were inadequate because particle size in the

kits is not specified. There is thus no way to determine if the kits themselves are sufficient to qualify inspectors under the essentially-free standard. Our investigators also documented that your qualification kits for visual inspectors are created **(b)(4)** and destroyed after use.

In your March 27, 2015 response, you stated that you will create a protocol for preparing new qualification kits and documenting employees' qualifications. Your response is inadequate. You did not indicate how previously inspected products may have been affected by your substandard visual inspection procedures and qualification kits. You also failed to provide the new protocol. Additionally, you did not provide any details on how you intend to train and qualify operators or measure the effectiveness of the new qualification kits.

In response to this letter, assess the effects of your lack of adequate visual inspection procedures and training on all the quality of all batches inspected by operators who were improperly trained and qualified, and provide a summary of your findings. In your summary, note whether each affected product has been distributed or rejected. Also describe the actions you have implemented to ensure that the finished parenteral drugs you manufacture are essentially free of particulate matter.

Conclusion

Violations and deviations cited in this letter are not intended as an all-inclusive list. You are responsible for determining the causes of these violations and deviations, for preventing their recurrence, and for preventing other violations and deviations.

These items, as well as other deficiencies our investigators found, lead us to question the effectiveness of your current corporate quality system to achieve overall compliance with CGMP.

Several violations are recurrent or represent long-standing failures to adequately resolve significant manufacturing quality problems. It is apparent that you have not implemented a robust quality system at your sites.

Dr. Reddy's corporate management is responsible for ensuring the quality, safety, and integrity of all drugs you manufacture. FDA strongly recommends that you evaluate global manufacturing operations to ensure compliance with CGMP regulations and requirements, comprehensively and immediately.

If, as a result of receiving this warning letter or for other reasons, you are considering a decision that could reduce the number of active pharmaceutical ingredients and/or finished products

produced by your manufacturing facility, FDA requests that you contact CDER's Drug Shortages Staff immediately, as you begin your internal discussions, at **drugshortages@fda.hhs.gov (mailto:drugshortages@fda.hhs.gov)**. so that we can work with you on the most effective way to bring your operations into compliance with the law. Contacting the Drug Shortages Staff also allows you to meet any obligations you may have to report discontinuances in your drug manufacture under 21 U.S.C. 356C(a)(1) and allows FDA to consider, as soon as possible, what actions, if any, may be needed to avoid shortages and protect the health of patients who depend on your products. In appropriate cases, you may take corrective action without interrupting supply, or to shorten any interruption, thereby avoiding or limiting drug shortages.

Until you complete all corrections and FDA confirms your compliance with CGMP, FDA may withhold approval of any new applications or supplements listing your firm as a drug product or API manufacturer. If you fail to correct these violations, under Section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3), FDA may also refuse admission of articles into the United States manufactured at:

A. Dr. Reddy's Laboratories Limited, CTO Unit VI, APIIC Industrial Estate, Pydibhimavarma (Village), Ranasthalam Mandai, Srikakulam District, Andhra Pradesh, India
B. Dr. Reddy's Laboratories Limited, CTO Unit V, Peddadevulapalli, Tripuraram, Mandal, Miryalguda Taluk, Nalgonda District, Telangana, India
C. Dr. Reddy's Laboratories Limited Unit VII, Plot No. P1 to P9, Phase III, Duvvada, VSEZ, Visakhapatnam, Andhra Pradesh, India

Under Section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3), articles may be refused admission because manufacturing methods and controls do not appear to conform to CGMP within the meaning of Section 501 (a)(2)(B) of the FD&C Act, 21 U.S.C. 351 (a)(2)(B).

Within 15 working days of receipt of this letter, please notify this office, in writing, of the specific steps that you have taken to correct and prevent repeating these deviations and violations. In addition to the specific requests noted above, supporting documentation should include a third party assessment of the following:

1. A comprehensive evaluation of the extent of inaccuracies in recorded and reported data. Include a detailed action plan to fully investigate the extent and root causes of your deficient documentation and data management practices.

A risk assessment of the potential effects of observed failures on the quality of your drug products, including the effects of your deficient practices on the quality of drug products released for

distribution and whether submissions to FDA may have been impacted. Conduct the same assessment for APIs that are components of drugs in applications that not yet been approved but which are pending before the FDA.

2. A management strategy for your firm that includes the details of your global corrective action and preventive action plan. Actions you have taken or will take may include:

- contacting your customers
- recalling product
- conducting additional testing
- adding lots to your stability programs to assure stability
- monitoring complaints
- revising procedures
- implementing new controls
- training or re-training personnel

If you cannot complete corrective actions within 15 working days, state the reasons for the delay and the date by which you will have completed the corrections. If you no longer manufacture or distribute the drug products or APIs at issue, provide the date(s) and reason(s) you ceased production. Send your reply to:

Maan Abduldayem, Compliance Officer
Office of Manufacturing Quality
Food and Drug Administration
White Oak, Building 51, Room 4212
10903 New Hampshire Ave.
Silver Spring, MD 20993

Please identify your response with FEI 3002949085 (CTO Unit VI), FEI 3005447965 (CTO Unit V), and FEI 3006549835 (Unit VII).

Sincerely,
/S/
Thomas Cosgrove, J.D.

Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

More in 2015 (/ICECI/EnforcementActions/WarningLetters/2015/default.htm)