

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857 Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 07/08/19 - 07/12/19
	FEI NUMBER 3005448030

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO: Mr. RV Sai Prasad, Site Head

FIRM NAME Dr. Reddy's Laboratories Limited (Unit II)	STREET ADDRESS Plot 1, 75A/B, 105, 110 & 111-112, Sri Venkateswara Co-Op Ind.
CITY, STATE AND ZIP CODE Bollaram, Medak Dist., Andhra Pradesh, 502325, India	TYPE OF ESTABLISHMENT INSPECTED API Manufacturer

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS; AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

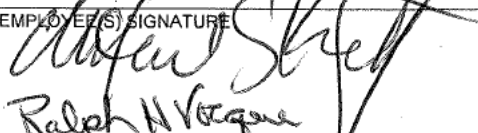
DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

1. Investigations into product complaints and out-of-specification QC analytical results, related to finished API product quality failures, are not adequate.

Specifically, your company has received several complaints from customers regarding out-of-specification (OOS) results, observed when the customer performs API acceptance tests, after an API is shipped by and received from your company. OOS results upon customer receipt and testing include, but not limited to, low assay (anhydrous basis), microbiological (TAMC and bioburden) failures, high water content and loss on drying. Your own pull and testing of your retention samples have confirmed some customer OOS results (microbiological TAMC and bioburden).

The OOS results confirmed by your retention sample tests were not in accordance with respect to the original QC release test results performed by your QC department at end of production of your finished APIs. In these instances, your investigations do not determine root causes for the drug substance failures and you accept the returned material without an adequate conclusion and reprocess the material upon return.

For example, your firm has had 3 complaints (Nos.: 200165824, 200166193, 200184440) related to microbiological failures (TAMC, bioburden) for ^{(b) (4)} [redacted] USP/Ph.Eur, which did not meet the customer specification for the API lots of concern mentioned in the complaints. Your retesting of your retain samples confirmed the OOS microbiological failures. However, you did not determine a root cause of the increase in TAMC and bioburden counts and just accepted the returned material. You did not evaluate whether the finished APIs and retention samples, which are stored in areas not controlled or monitored for relative humidity, are affected by extreme fluctuations in humidity. While you do record the humidity data in some of the finished API and retention sample areas (WH-20, QC Lab), you do not monitor or evaluate the humidity data you collect; in many of the retention sample storage areas ^{(b) (4)} [redacted] Block), you do not even record the humidity values.

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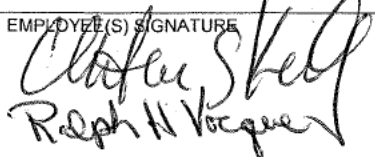
Review of OOS investigations noted that you have had several confirmed OOS failures in the QC laboratory for water content of APIs (OOS17516, OOS17616), where the conclusion was determined as "exposure of batch material to high humidity". The proposed corrective actions for OOS17516 and OOS17616 was to install portable dehumidifiers in the QC laboratory, which was confirmed by your QC department. Note that the environmental conditions for the QC laboratory are identical to the storage conditions of the retention sample rooms (QC Lab, ^(b)₍₄₎ Block) and the Finished API storage warehouses (WH-14 and WH-20).

Additionally, you have several OOS results for water content and assay (anhydrous) during long term and accelerated stability testing of your finished APIs, where the humidity is controlled at 25 +/- 2 C and 60 +/- 5% relative humidity. Note that the humidity conditions of your storage areas can exceed 80% during the year for uncontrolled storage areas. Since you do not actively monitor humidity conditions in your finished API and retention sample storage areas, you have not established action or alert levels for humidity.

You did not evaluate the storage conditions of the finished APIs and finished API retention samples, which are held in areas not controlled or monitored for humidity. Furthermore, you hold finished APIs and retention samples in environmental conditions which are not aligned with the conditions used for validation of the expiry date of your APIs. You have not adequately assessed whether the uncontrolled humidity conditions can affect the quality, purity and potency of your finished APIs and API retention samples during long-term storage.

2. Preventative controls over your electronic inventory and warehousing management systems are not effectively established to prevent product mix-ups and ensure traceability for the life cycle of the material.

Specifically, you did not appropriately qualify/validate your SAP inventory management system in accordance with ICH and Part 11 requirements for validation of electronic systems. You did not effectively develop the qualification protocol (in-house design) with the required challenges of your barcode scanning system to ensure that the system would prevent product mix ups for raw materials and finished APIs. During the inspection, your SAP validation team admitted that they did not perform the required negative challenges to the barcode system in the raw material and finished product warehouses to ensure the system would reject a material if it was incorrectly scanned for a bill of materials/pick list, placed in the wrong location in the warehouse, or incorrectly scanned against a purchase order to prevent the wrong lots from being shipped. Note that we reviewed several confirmed

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complaints (Nos.: 200262668, 200136344, 200161118) where the customer was shipped the wrong type of finished API (incorrect lot number, different pharmacopeial grade, wrong process validation lot), which confirms the barcode system was not effectively challenged.

Additionally, your barcode scanning system is deficiently qualified in that it is not capable of performing the following tasks:

- * During the inspection we observed that the barcode scanner could not perform its intended functions in the cold storage warehouses (WH-18). The scanner would lose the connection to the SAP wireless network.
- * When a raw material is scanned against a pick list, the container disappears from the SAP database. During the inspection, we challenged container locations of several raw materials, which returned the result "does not exist" in the SAP database, despite its confirmed physical presence in the warehouse. Note that all dispensing of raw materials is performed entirely in the warehouse.
- * You do not enter all relevant product information for raw materials held in the warehouses. For example, you often use the same SAP material code for two different manufacturers of the same raw material; however, the raw material approved vendor may be specific to a customer DMF filing. Since you have not challenged the system by setting different vendor codes for the same material (or use entirely different SAP material codes), you cannot guarantee that the scanner can differentiate between same raw material manufactured by different vendors.

3. Materials are not stored under appropriate conditions and according to the manufacturer's specifications that guarantee no adverse effect on the material's quality, purity, and potency and are not appropriately re-evaluated to determine their suitability for use after prolonged storage in and exposure to heat and humidity.

Specifically, your firm holds raw materials in environmental conditions which are not in accordance with the manufacturer's storage specifications. During the inspection, we observed raw materials held in extreme heat and humidity conditions which were not in accordance with the manufacturers' storage requirements on the material labels. We also observed raw materials stored in open areas (uncontrolled for temperature or humidity) which were required to be protected from moisture, oxygen or air. Note that the temperature and humidity of Warehouses

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1, 3, and 7 can exceed 45 C and 80% relative humidity during the year. You cannot guarantee that the storage conditions in which you hold these products do not affect the quality, purity, and potency of the raw materials used in the manufacture of your finished APIs, since you do not consider the manufacturers' storage requirements.

4. Written protocols for qualification of (b) (4) water systems are not followed.

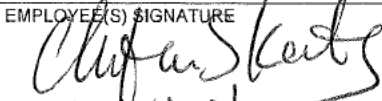

Specifically, you did not perform all required water quality testing during Phase (b) (4) trials for the performance qualification of your (b) (4) water (b) (4) system installed in the (b) (4) Block of your site. You did not perform any total organic carbon (TOC) or endotoxin testing at any of your (b) (4) points-of-use (in the (b) (4) recirculating loop) for Phase (b) (4) as specified in your protocol, with the justification that an inline TOC monitor is an acceptable substitute for performing TOC analysis at all points-of-use during PQ. Note that TOC is a required parameter for USP (b) (4) water.

Additionally, you do not perform TOC testing for any points of use during routine monitoring of your (b) (4) water system, with the justification that there is an inline TOC monitor on the recirculating loop. However, you did not select the location of the inline TOC monitor in the (b) (4) recirculation loop using a worst-case approach during the qualification, by determining where the highest TOC values appear at the points-of-use, since you did not perform the TOC testing specified in your protocol.

5. Records not made readily available during an FDA inspection.

Specifically, your lack of organization and preparation for this inspection delayed the progress of this inspection due to lack of timely delivery of documents, photographs, and personnel. Examples include, but are not limited to:

You were not able to provide the requested photographs of raw materials located in Warehouses 1, 3, 7, and 18 in a timely fashion. Because of the materials stored in your warehouses, we allowed your personnel to collect photographs using firm-provided explosion proof cameras that we requested. However, it took several attempts to collect proper photos even after we personally escorted your staff and instructed them how to collect the photos. The photos came back incomplete, blurry, partially captured, or not at all. It took three attempts to collect all of the

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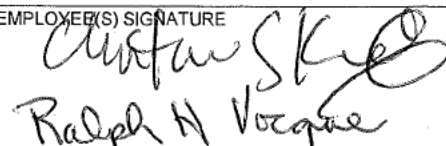
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requested photos and during the second attempt we directly observed one of your employees capturing photos using his cellular telephone despite your instruction to us that we were not allowed to have cellular phones in that area.

You did not provide us with adequate subject matter experts regarding SAP user levels and permissions, SAP qualifications/validations, label issuance and control, and ^{(b) (4)} water system qualifications. In all of these instances you provided us with staff who either were not qualified to answer questions related to the topics discussed, or would just repeat our words/repeat a procedure, which demonstrated the person's lack of knowledge about the subject.

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