

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
--	---

CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile 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 WE OBSERVED:

OBSERVATION 1

The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed.

Specifically, procedure for change control does not include adequate instructions for changes to fully executed protocols, handling of incidents and out of trends procedures are not followed.

For example,

- A) The change control (b) (4) procedure does not have any instructions for handling changes to protocols. Additionally, I observed that the reports do not include all information for the intended protocol.

For example,

- 1) The (b) (4) % submission batch protocol (Doc. No: (b) (4) has two revisions. The revisions were conducted after the execution.

Protocol Revision information			
Ver.	Approval date	Change	Date of Mfg of batches
01	08 Jun 2020	Original protocol	June 2020-July 2020
02	25 Sept 2020	Product specification changes	June 2020-July 2020
03	23 Jan 2021	To in line with (b) (4) (b) (4)	June 2020-July 2020

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X	DATE ISSUED 10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
--	---

CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer
---	--

According to the process validation procedure of drug products, the submission/exhibit batches manufactured would be considered the process validation batches, if no changes for scale occur after approval. The process validation protocol changes to the specification allow the products tested for viscosity to go from failing to passing for viscosity.

2) The (b) (4) % submission batch report (Doc. RP- (b) (4) fails to include all batches manufactured



(b) (4) does not include a reference to the placebo batch or the first process validation batch.

3) The placebo batch (b) (4) executed to determine failure for viscosity does not have a batch number a (b) (4) Procedure for Trial/Confirmatory/Pre-Validation of Drug Product (b) (4) nor the Allotment of Location Code and Batch Number (b) (4) (b) (4) The identification number for the placebo batch is (b) (4) which the requirements as described in the procedures. Additionally, the batch numbering system does not have a record for the executed placebo batch.

B) The handling of incidents procedure is not followed.
For example,

1) Incident 200374932 for major visual defects in (b) (4) batch (b) (4) was not initiated within (b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11:38:37 X	DATE ISSUED 10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
--	---

CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer
---	--

The handling of incidents procedure section 5.1.3 states (b) (4)
(b) (4) The limit for major visual defects is Not more than (NMT) (b) (4) %.

On 06/23/2021, the visual inspection for (b) (4) batch (b) (4) was initiated. The visual inspection conducted was observed to have a break between 06/26/2021 and 06/29/2021. Incident 200374932 states that during the inspection on 06/26/2021, "the number of rejections due to black particles was trending to exceed (b) (4) %." The results for major critical defects for black particles was approximately (b) (4) % (Limit: NMT (b) (4) %).

The initiation date for Incident 200374932 was 02-Jul-2021. The incident description includes critical and major visual inspection failures. However, there are three reports bearing the same incident number (200374932). The reports were separated for critical, major and minor defect. The SAP system does not include a reference for the minor defects.

- 2) The management of pharmacopoeia updates procedure (b) (4) was not followed for the (b) (4) USP test method No. MET-CFTO-010781. Section 5.6.9 of management of pharmacopoeia updates procedure states, "If the updates published in the official pharmacopoeia/supplements, not implemented after the effective date of publication, the same shall be routed through current version of (b) (4) titled 'Handling of Incidents.'" The (b) (4) USP test method states that the tests for (b) (4) impurities and enantiomeric purity reference the USP monograph. The United States Pharmacopoeia monograph for (b) (4) (b) (4) was updated in December 2019. The test method was not updated but used for the testing and release of (b) (4) drug substances tested in between June 2020 and August 2020. There is no incident for the failure to update the current method to the updated USP monograph.

OBSERVATION 2

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By 2001767329 Date Signed 10-29-2021 11 38 37 X	DATE ISSUED 10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer

Laboratory controls do not include the establishment of scientifically sound and appropriate specifications, sampling plans and test procedures designed to assure that components, in-process materials and drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically, the drug substance and drug product do not include scientifically sound specification, sampling plans and test methods.

The following examples are for the Drug product,

- B. The viscosity specification for (b) (4) % was changed due to the equipment not being capable of producing precise results. There were approximately eight consecutive in-process viscosity failures for three exhibit process validation submission batches (b) (4) of (b) (4) %. The method was not validated prior to testing being conducted. The method feasibility study conducted does not support the equipment to be unable to produce results. The justification provided for the change in specification is not adequate.
- C. The particle matter visible and subvisible test method is not scientifically sound. The test procedure makes reference to USP <771> for visible particles and <778> for subvisible particles. There is no method description (i.e. instructions) included in USP <771> for the testing for visible particles.

Incident 2003656855 is for the abnormal results for the (b) (4) measurement for particulate matter by light obscuration for (b) (4) % exhibit batch (b) (4). The result for particle size greater than (b) (4) um specification is the average of (b) (4) measurement to be not more than (b) (4) particles per mL. The (b) (4) measurement was (b) (4).

- D. The related substances test method has the sample temperature of (b) (4) °C and a relative standard deviation of (b) (4) % for system suitability which are not supported by scientifically sound data. The method validation was conducted at (b) (4) °C and changed to (b) (4) °C, there was no change control or justification provided for the change. The test method was used for the release of all drug products. The Analytical method validation (b) (4) and validation of analytical test procedures for related substances by liquid chromatography (WI (b) (4) QC-0038) procedures require the acceptance

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X	DATE ISSUED 10/29/2021

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Krishna Venkatesh , Head Sterile	
FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer

criteria be the same as the system suitability in the test method the procedures were not followed. The acceptance criteria (b) (4)

(b) (4) is include in the test method used for validation.

The method validation, transfer and sample analysis were all conducted using (b) (4)

(b) (4) There is no deviation written for the failure to follow test metho

There is no scientifically sound data to support the system suitability requirement is adequate.

E. The test method for (b) (4) % and (b) (4) (b) (4) % system suitability for Assay, Preservative Content and Related Substances do not include the

(b) (4)

During the preservative contest by HPLC analysis for (b) (4) % exhibit batch (b) (4) an incident (200352321) was opened for the system suitability failure (Result (b) (4) %). There was a discrepancy between the test method and the record of analysis template worksheet. The test method system suitability requirement documented was NMT (b) (4) % and the record of analysis template was NMT (b) (4) . The correction for the incident was to correct the record of analysis to match

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X	DATE ISSUED 10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer

the test method. The correction is not scientifically sound as the method validation system suitability validated is NMT (b)(4) %.

F. Visual inspection for particulate matter for (b)(4) % and (b)(4) % (b)(4) was performed by (b)(4). You failed to provide evidence demonstrating that selecting (b)(4) samples from a theoretical batch size of (b)(4) is adequate to detect particulate matter. "Procedure for visual inspection of filled and sealed containers by using visual inspection hood", SOP-FT09-PR-0095, effective July 16, 2021, was updated to change the sampling amount from (b)(4) bottles. You failed to provide scientific evidence demonstrating that your current (b)(4) representative to detect particulate matter of your theoretical batch size.

The following example is for the Drug substance,

G. The test method for (b)(4) USP (Test Method. MET-CFTO-010781) references the current USP for enantiomeric purity. The test method was verified, however changes observed include difference in system suitability relative standard deviation (RSD) and chromatographic conditions.



(b)(4) sensitivity solution and additional system suitability requirements of signal to noise ratio.

OBSERVATION 3

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By 2001767329 Date Signed 10-29-2021 11 38 37 X	DATE ISSUED 10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
--	---

CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer
---	--

Specifically, you failed to provide scientific justification demonstrating that samples collected for your environmental monitoring process represent the greatest risk of microbial contamination.

4) "Re-evaluation for viable monitoring sites of (b)(4) was conducted on October 24, 2019. You failed to provide a robust scientific justification explaining why areas inside (b)(4) (Equipment ID: 2604824) that could negatively impact aseptically filled product are not sampled for viable monitoring.

1) (b)(4) ID:2604824 (b)(4) (b)(4) never been evaluated for microbial growth. The material of construction for the (b)(4) (b)(4) Adequacy of your (b)(4) (b)(4) and cleaning suitability of the (b)(4) is unknown.

2) (b)(4) Your current rationale for not conducting surface monitoring for (b)(4) (b)(4) You failed to provide a robust scientific justification for not conducting viable monitoring as the (b)(4)

3) Difficult to clean surfaces identified by your production operators have never been evaluated for environmental monitoring. Examples of difficult to clean areas are: area between the (b)(4) Per your Manager Quality Assurance, during viable monitoring evaluation for the (b)(4) air visualization studies were not analyzed to determine sampling locations. Add (b)(4), operators involved in cleaning of the (b)(4) line were not interviewed to evaluate difficult to clean surfaces.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	DATE ISSUED 10/29/2021 Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X
---------------------------------	---	---

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
--	---

CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer
---	--

- 5) You failed to perform a risk evaluation for not conducting viable personnel monitoring for aseptic filling operators who participate in aseptic filling. Aseptic processing personnel qualification for the Grade C area consist of individual participating in a media fill (SOP-FT09-PR-0133). During participation, viable monitoring for personnel is not conducted. You failed to perform an assessment of the human flora recoveries and impact of your environmental state of control for your Grade C area. Examples of atypical and opportunistic pathogens recovered from active and settle plates from room (b) (4) include: *Gardnerella vaginalis*, *Dermococcus nishinomyaensis*, *Staphylococcus haemolyticus*, and *Kocuria varians*. Atypical and opportunistic pathogen recoveries from the Grade C area are not investigated unless alert and action levels are observed. Furthermore (b) (4) integrity testing is not conducted for, (b) (4) (b) (4) used by aseptic filling operators. The rationale for not being conducted was not provided.
- 6) Viable monitoring selection for Grade C filling room (b) (4) was evaluated via document "FT9PRPQP087-00", effective December 22, 2017. Re-evaluation of the sampling locations with respect to personnel movement and equipment has not been conducted. On October 18, 2021, during media fill simulation for batch (b) (4) the following area are not evaluated for viable monitoring:
- H. Human-Machine Interface (HMI serial number: (b) (4) Operators were observed frequently touching the HMI during production simulation. A scientific justification why the HMI is not monitored was not provided.
 - I. Personnel movement was observed between the bottle filling area near the (b) (4) and the (b) (4) stand located on the (b) (4) Rational justification detailing why the area is not assessed was not provided.

Your environmental monitoring process is not robust to assure adequate process controls for aseptically filled products.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By 2001767329 Date Signed 10-29-2021 11 38 37 X	DATE ISSUED 10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Krishna Venkatesh , Head Sterile	
FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer

OBSERVATION 4

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include adequate validation of the aseptic and sterilization process.

Specifically, your current equipment qualification process is inadequate in assuring suitable (b) (4) (b) (4) monitoring of the room and (b) (4) and (b) (4) You failed to provide assurance that your current process controls are adequate for aseptic filling.

- 4) You failed to adequately validate your (b) (4) cycle for (b) (4) equipment ID, 2604824. The equipment is used in aseptic filling of: (b) (4) (b) (4) %, and (b) (4) %, (b) (4) and (b) (4) (b) (4) % (b) (4) Initial (b) (4) approved via document "4029771_PTD_CD_Report_V1.0" on Ju 2017. Initial (b) (4) study, worst-case load configuration was challenged against a total of (b) (4) and (b) (4) (b) (4) (b) (4) is conducted using (b) (4) During (b) (4) (b) (4) nged the validated load configuration without assessing (b) (4) You failed to evaluate potential obstruction of (b) (4) against newly added items. Examples of changes made include:

Table listing addition and changes in the (b) (4)
(b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	DATE ISSUED 10/29/2021 Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER

12420 Parklawn Drive, Room 2032
Rockville, MD 20857

DATE(S) OF INSPECTION

10/18/2021-10/29/2021*

FEI NUMBER

3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Krishna Venkatesh , Head Sterile

FIRM NAME

Dr. Reddy's Laboratories Ltd.

STREET ADDRESS

Plot No Plto P9, Phase Iii - Vsez

CITY, STATE, ZIP CODE, COUNTRY

Duvvada, Andhra Pradesh, 530046 India

TYPE ESTABLISHMENT INSPECTED

Sterile Manufacturer

(b) (4)



**SEE REVERSE
OF THIS PAGE**

EMPLOYEE(S) SIGNATURE

Rita K Kabaso, Investigator
Nancy M Espinal, Investigator

Rita K Kabaso
Investigator
Signed By 2001767329
Date Signed 10-29-2021
11 38 37

X

DATE ISSUED

10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
--	---

CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer
---	--

(b) (4)

After location changes you failed to validate your new load configuration to confirm the adequacy of your (b) (4). Additionally, failed to provide a scientific justification why validation has not been conducted.

During (b) (4) development studies, initial qualification, and requalification, you failed to place a BI and CI in the groove of the (b) (4). This is the (b) (4) packaging product contact surface. You failed to evaluate the adequacy of your (b) (4) process. Furthermore, the microbial environment for the (b) (4) is unknown.

Your (b) (4) failed to provide assurance that your (b) (4) s adequately (b) (4) and is free of viable microorganisms.

- 5) You failed to adequately assess (b) (4) conditions for (b) (4) (Equipment ID: 2604824). (b) (4) was executed via protocol "VALPR-FT09-000567" dated Sept (b) (4) are placed at the (b) (4). The (b) (4) of the HEPA filters. You failed to evaluate the (b) (4). You failed to provide a justification containing scientific evidence that your (b) (4) process is robust to detect (b) (4) conditions at the (b) (4) during filling. (b) (4) storage conditions for (b) (4) % and (b) (4) % (b) (4) is (b) (4) °C.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	DATE ISSUED 10/29/2021 Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer

(b) (4) conditions during product filling of (b) (4) is unknown as the design suitability of your (b) (4) does not capture (b) (4)

(b) (4) for Grade C room (b) (4) executed via protocol "ET09PRPQP087-00" dated November 11, 2017, is inadequate. You failed to evaluate (b) (4) (2033497-I08-00) against the (b) (4) placed in the room. Additionally, you failed to evaluate the operation conditions of the room during (b) (4). During (b) (4) out of calibration date (b) (4) were used. Justifica use of the out of calibration date (b) (4) was inadequate.

6) You failed to adequately challenge your (b) (4) Equipment ID: 2602558) utilized to (b) (4) items used on your (b) (4) (Equipment ID: 2604824). (b) (4) distribution studies were conducted January 10, 2014, via document (b) (4) "002-00". During (b) (4) was identified as a (b) (4). You f (b) (4) d on the (b) (4) (PR-L-22-03). The design (b) (4) pattern of the (b) (4) rack due to items being (b) (4) and items suspending on (b) (4). You failed to evaluate the (b) (4) direction against the maximum load configuration to assure uniform (b) (4).

7) You failed to establish an adequate frequency replacement for your (b) (4) fitted to your (b) (4) ID:2604824. The (b) (4) is fitted with (b) (4) used to transfer (b) (4)

(b) (4) Prior to installation, a risk assessment was conducted, however, you failed to evaluate compatibility of (b) (4) material of construction with respect to frequent use of (b) (4). Deterioration of (b) (4) and potential negative impact of (b) (4) integrity is unknown.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	DATE ISSUED 10/29/2021 Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer

OBSERVATION 5

Establishment of the reliability of the component supplier's report of analyses is deficient in that the test results are not appropriately validated at appropriate intervals.

Specifically, results are taken from the manufacturer certificate of analysis without validating the test results at an appropriate interval.

Your procedures do include the requirement for full testing (Reduced Testing Procedure for Raw Materials and Packaging Materials (SOP-(b)(4) QC-0094) at a specified interval however, the Sampling and Testing of Raw Materials (SOP (b)(4) QC-0113) and Sampling and Testing of Packaging Materials (SOP (b)(4) QC-0115) procedures allow for test results to be taken from the manufacturer's certificate of analysis because of the non-availability of in-house testing facility. There is no quality assurance check point to assure that results taken from the manufacturer certificate of analysis are validated at an appropriate interval.

Your firm manufactures drug products sterile injectable and has applications for sterile (b)(4). The Reduced Testing Procedure for Raw Materials and Packaging Materials section 2.2 states "Reduced testing isn't applicable for submission batches/regulatory filing batches. All input materials such as APIs/Excipients/solvents, packaging materials, etc. used in those batches shall be tested for complete analysis as per DRL specifications." The following materials used in the manufacture of submission batches were not fully tested:

(b)(4)



SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11:38:37 X	DATE ISSUED 10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
--	---

CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer
---	--



In the last two (b) (4) (b) (4) (b) (4) (b) (4) have been used in the manufacture of approximately (b) (4) commercial sterile drug products. The sterile drug products were packaged and shipped to the United States and are within expiry.

OBSERVATION 6

The accuracy, specificity and reproducibility of test methods have not been established and documented. Specifically, not all the drug substance and drug product test methods have been appropriately established or documented.

For example,

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By 2001767329 Date Signed 10-29-2021 11 38 37 X _____	DATE ISSUED 10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer

- C) (b) (4) test method may not have documents for method verification, validation, or transfer include but are not limited to;
- a. Viscosity Profile (As a function of (b) (4))
 - b. Particulate matter for sub-visible particles by light obscuration
- D) Spectroscopic identification test has not been verified for (b) (4) USP (Drug Substance).

OBSERVATION 7

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically, investigations into atypical recoveries in your Grade C room are not conducted. Per the Microbiology Head of Department, investigations are only conducted for pathogenic, alert, and excursion recoveries. Per your "Microbial Identification Program", "SOP (b) (4) QC-0123" (b) (4) identified as objectionable microorganism will be investigated. You failed to provide a scientific justification why atypical recoveries in the Grade C area are not investigated. The following organisms were recovered from room (b) (4) where (b) (4) is located: *Gardnerella vaginalis*, *Past pneumotropica*, and *Bacillus badius*.

Additionally, investigations into any unexplained discrepancies was not thoroughly conducted to identify appropriate root cause and implement adequate corrective and preventative actions. For example,

- 8) Investigation into Incident 200355767 initiated on August 27, 2020, is inadequate. Your investigation fails to evaluate contamination arising from the number of personnel observing compounding of (b) (4) injection (b) (4) mg/(b) (4) nL batch (b) (4). Your active air sample in compounding room (b) (4) recovered: *staphylococcus sallivarius*, *Tothis dentocariosa*,

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	DATE ISSUED 10/29/2021 Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer

micrococcus lutes and *Rothis mucilaginosa*. The possible root causes identified are: improper handling of media plates during transfer, and the increase of personnel in the compounding room compared to routine production. You failed to establish the number of personnel adequate for your compounding room. You failed to evaluate previous recoveries to ensure your compounding room was not exhibiting environmental warning trends.

- 9) You failed to establish an adequate corrective and preventative action for failure of your quality personnel in evaluating critical maintenance breakdown conducted on the (b) (4) Incident 200355914 initiated September 6, 2020, regarding viable microbial excursion in the (b) (4) was attributed to maintenance being performed after (b) (4) % (b) (4) had already been executed. The potential root cause into the excursion was the pressure differential fluctuations prior to product filling. Your corrective action was to update work instruction "WI-FT09-PR-0016" to include an impact assessment section. Environmental trending was not conducted to ensure your clean room was not trending out of environmental control. A scientific justification was not provided for the investigation inadequacies.
- 10) You failed to implement an adequate corrective and preventative action regarding Incident 200358029. On October 2, 2020, during (b) (4) (b) (4) mg/vial batch (b) (4) Alert recov (b) (4) area. The identify (b) (4) use was operator error. During cleaning, the (b) (4) and the operator forgot to (b) (4) fo (b) (b) (4) (b) (4) You failed to provide technical knowledge justifying the a (b) (4) during cleaning. Your corrective action was to revise "SOP-FT09-PR-0015", (b) (4) ented December 23, 2020 (82 days from incident date). You failed to implement an adequate corrective action to assure that your production employees are knowledgeable in their job functions and can adequately perform their duties in a manner that would not negatively impact aseptically filled products.
- 11) Incident 200361222 initiated on November 27, 2020 was not thoroughly investigated to assure your environment was in a state of control after fungal recovery. On November 21, 2021, during filling of (b) (4) Injection (b) (4) mg/mL batch (b) (4) settle plate (b) (4) in your Grade C filling room recovered *Curvuleria lunata*. Your corr (b) (4) on was to pe orm

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	DATE ISSUED 10/29/2021 Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
--	---

CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer
---	--

cleaning and conduct settle plate monitoring for the room. You failed to provide a scientific justification detailing a reason why surface and active air monitoring was not conducted. You failed to provide assurance that your clean room was brought back to established operating conditions.

OBSERVATION 8

The control systems necessary to prevent contamination or mix-ups are deficient.

Specifically, you failed to establish detailed instructions for performing (b) (4) cleaning when using Water for Injection (WFI). Prior to (b) (4) and after batch filling, (b) (4) 2604824, is cleaned by obtaining (b) (4) in a (b) (4) bucket from the (b) (4) room (b) (4). The WFI amount used for cleaning the equipment is (b) (4) ning is conducted by dipping a li (b) (4) wipe into the (b) (4) bucket and conducting overlapping strokes. Per your cleaning operator, the WFI water in the (b) (4) bucket is changed when the water becomes visually dirty. Scientific knowledge demonstrating the adequacy of your cleaning method is unknown. You have not assessed potential cross contamination from the operators (b) (4) onto your equipment. In addition, qualification of your (b) (4) is lacking.

The effectiveness of your cleaning process and (b) (4) is inadequate in removing potential microbes that could negatively impact your aseptically filled product.

***DATES OF INSPECTION**

10/18/2021(Mon), 10/19/2021(Tue), 10/20/2021(Wed), 10/21/2021(Thu), 10/22/2021(Fri), 10/25/2021(Mon), 10/26/2021(Tue), 10/27/2021(Wed), 10/28/2021(Thu), 10/29/2021(Fri)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By: 2001767329 Date Signed: 10-29-2021 11 38 37 X	DATE ISSUED 10/29/2021

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 12420 Parklawn Drive, Room 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 10/18/2021-10/29/2021*
	FEI NUMBER 3006549835

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Krishna Venkatesh , Head Sterile

FIRM NAME Dr. Reddy's Laboratories Ltd.	STREET ADDRESS Plot No Plto P9, Phase Iii - Vsez
--	---

CITY, STATE, ZIP CODE, COUNTRY Duvvada, Andhra Pradesh, 530046 India	TYPE ESTABLISHMENT INSPECTED Sterile Manufacturer
---	--

X Nancy M Espinal
Investigator
Signed By: 2001865749
Date Signed: 10-29-2021 11:39:20

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Rita K Kabaso, Investigator Nancy M Espinal, Investigator	Rita K Kabaso Investigator Signed By: 2001767329 Date Signed 10-29-2021 11 38 37 X	DATE ISSUED 10/29/2021