

**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 5/14/2018-5/24/2018*
	FEI NUMBER 3008565058

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
Dr. Darshan Makhey, President - Global Quality

FIRM NAME Glenmark Pharmaceuticals Ltd	STREET ADDRESS Plot No. 2, Pharma Zone SEZ
CITY, STATE, ZIP CODE, COUNTRY Pithampur, Dhar, Madhya Pradesh, 454775 India	TYPE ESTABLISHMENT INSPECTED Finished Oral Solid Dosage 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:  
LABORATORY CONTROL SYSTEM**

**OBSERVATION 1**

The accuracy, sensitivity, specificity and reproducibility of test methods have not been established and documented.

Specifically,

Your firm's QC laboratory has not validated analytical methods used in the determination of active residue from equipment's used for processing of the following products:

- 1) (b) (4) Capsules USP (b) (4) mg & (b) (4) mg,
- 2) (b) (4) Tablets USP (b) (4) mg, (b) (4) mg, (b) (4) mg & (b) (4) mg,
- 3) (b) (4) Tablets,
- 4) (b) (4) Tablets,
- 5) (b) (4) Capsules USP (b) (4) mg, and
- 6) (b) (4) Tablets USP (b) (4) mg & (b) (4) mg

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Arsen Karapetyan, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Generic Drug User Fee Amendments (GDUFA)	Pratik S Upadhyay Generic Drug User Fee Amendments (GDUFA) Signed by Pratik S. Upadhyay - S Date Signed 05-24-2018 23:26:58 X	DATE ISSUED 5/24/2018

**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 5/14/2018-5/24/2018*
	FEI NUMBER 3008565058

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
Dr. Darshan Makhey, President - Global Quality

FIRM NAME Glenmark Pharmaceuticals Ltd	STREET ADDRESS Plot No. 2, Pharma Zone SEZ
CITY, STATE, ZIP CODE, COUNTRY Pithampur, Dhar, Madhya Pradesh, 454775 India	TYPE ESTABLISHMENT INSPECTED Finished Oral Solid Dosage Manufacturer

Your production unit has standalone non-dedicated manufacturing equipment that in absences of using a non-validated analytical test method (swab analysis by UPLC) for determining Type B equipment cleaning effectiveness creates a potential for carryover of active residues remained on the equipment leading to cross-contamination of the products manufactured using the same equipment.

Your firm in justification stated that the firm was considering Assay by HPLC method validation in substitution for equipment cleaning method by UPLC, whereas, both the methods and their sample and standard preparations are completely different. For example,

Assay by HPLC test method has tablets and/or capsules for the sample solution preparation whereas cleaning test method has swabbing stick(s) for the sample solution preparation. The concentration of sample and standard solution varies for both the test solutions.

**OBSERVATION 2**

Laboratory controls do not include the establishment of scientifically sound and appropriate sampling plans designed to assure that conform to appropriate standards of identity, strength, quality and purity.

Specifically,

Your SOP CM/QA034 "Sampling Methodology for (b)(4) is deficient in section 5.5 (b)(4) sample of (b)(4), subsection 5.5.2 indicates "The (b)(4) sample shall be collected as (b)(4) gram unless and otherwise mentioned in the sampling (b)(4) / process validation / batch production record. (b)(4) bags / Glass Bottles with stoppers shall be used for collecting the (b)(4) samples". For example,

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Arsen Karapetyan, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Generic Drug User Fee Amendments (GDUFA)	Pratik S Upadhyay Generic Drug User Fee Amendments (GDUFA) Signed by: Pratik S. Upadhyay -S Date Signed: 05-24-2018 23:26:58 X	DATE ISSUED 5/24/2018

**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 5/14/2018-5/24/2018*
	FEI NUMBER 3008565058

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
Dr. Darshan Makhey, President - Global Quality

FIRM NAME Glenmark Pharmaceuticals Ltd	STREET ADDRESS Plot No. 2, Pharma Zone SEZ
CITY, STATE, ZIP CODE, COUNTRY Pithampur, Dhar, Madhya Pradesh, 454775 India	TYPE ESTABLISHMENT INSPECTED Finished Oral Solid Dosage Manufacturer

-There is no mention of the sampling amount collected during unloading of the (b) (4) from (b) (4) locations. IPQA employee responsible for sample collection was unable to explain the sampling amount collected from each location. Additionally, there is no weighting tape indicating the weight of sample collected each time from different locations and the gross weight to make it to (b) (4) gram.

- The sampling instructions mentioned in your process validation and batch production records are deficient as there is mention of the glass bottle size and (b) (4) instructions for the samples collected from (b) (4) locations.

SOP CM/QA034, section 5.5 is used for (b) (4) sampling of the following products:

- (b) (4) Tablets USP (b) (4) mg & (b) (4) mg, and
- (b) (4) Tablets USP (b) (4) mg

**OBSERVATION 3**

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

Specifically,

- Your firm's QC unit did not investigate in to the issues of API peak seen in the blank injections during method validation for related substances by HPLC method. Additionally, system suitability (precision) standard injections (b) (4) ppm) peaks were not integrated (b) (4). The reintegration of these peaks changed the area of standards by over (b) (4) i.e. 30%.

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Arsen Karapetyan, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Generic Drug User Fee Amendments (GDUFA)	Pratik S Upadhyay Generic Drug User Fee Amendments (GDUFA) Signed by: Pratik S Upadhyay -S Date Signed: 05-24-2018 23:26:58 X	DATE ISSUED 5/24/2018

**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 5/14/2018-5/24/2018*
	FEI NUMBER 3008565058

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
Dr. Darshan Makhey, President - Global Quality

FIRM NAME Glenmark Pharmaceuticals Ltd	STREET ADDRESS Plot No. 2, Pharma Zone SEZ
CITY, STATE, ZIP CODE, COUNTRY Pithampur, Dhar, Madhya Pradesh, 454775 India	TYPE ESTABLISHMENT INSPECTED Finished Oral Solid Dosage Manufacturer

- In the past two years, your firm has initiated approximately sixteen (16) Incident reports related to power outages in your QC laboratories which occurred during testing of samples on HPLC and GC equipment. During our review of these incident reports, it was observed that “chromatographers” who processes data and Analytical Quality Assurance (AQA) reviewers who review processed data do not have the user privilege “Verify Incomplete Data in Raw Data Files” in Empower 3. For this reason, during the review of two such incidents during dissolution testing for finished products, the investigation by your firm determined that the interrupted sample injections were processed by chromatographers and showed that the sample did not run. However, during our review of electronic data in the QC laboratory, it was observed that QC managers and the system administrator have the user privilege to “Verify Incomplete Data in Raw Data Files”. Subsequently, we requested your manager to verify the incomplete data and reprocess the injection for both sample sets (two different incidents) and discovered that the injected samples did in fact run, the first incident with approximately (b) (4) minutes out of (b) (4) minutes, and the second with approximately (b) (4) minutes out of (b) (4) minutes, with both injections resulting in elution of the principal peak. After reprocessing the incomplete data, your firm performed rate of release calculations on the unreported processed injections, which appeared to be within specification. However, this discrepancy in your firm’s ability to review and investigate all electronic raw data is a significant gap in your Data Integrity procedures and practices reviewed during the current inspection.

**FACILITIES AND EQUIPMENT SYSTEM**

**OBSERVATION 4**

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Arsen Karapetyan, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Generic Drug User Fee Amendments (GDUFA)	Pratik S Upadhyay Generic Drug User Fee Amendments (GDUFA) Signed by: Pratik S Upadhyay -S Date Signed: 05-24-2018 23:26:58 X	DATE ISSUED 5/24/2018

**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 5/14/2018-5/24/2018*
	FEI NUMBER 3008565058

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
Dr. Darshan Makhey, President - Global Quality

FIRM NAME Glenmark Pharmaceuticals Ltd	STREET ADDRESS Plot No. 2, Pharma Zone SEZ
CITY, STATE, ZIP CODE, COUNTRY Pithampur, Dhar, Madhya Pradesh, 454775 India	TYPE ESTABLISHMENT INSPECTED Finished Oral Solid Dosage Manufacturer

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically,

Your firm's manufacturing equipment are not 21 CFR part 11 compliant. For example,

A) There are total (b) (4) standalone manufacturing equipment which are not equipped with HMI/PLC/SCADA system. There is no time stamped audit trail, data management, alarm management, archival and retrieval of records on these standalone manufacturing equipment.

These equipment includes but are not limited to (b) (4) and (b) (4) that are operated at (b) (4) speed per manufacturing instructions given in BMRs. However, there is no setting as (b) (4) on these equipment. Your production operator was unable to explain and show the equipment operating speed. This information was not clearly defined at the time of process validation that could significantly impact the quality of products manufactured for the U.S. market.

B) Your firm's total (b) (4) standalone production equipment has an inbuilt HMI system but none of these equipment have time stamped audit trail, data management, alarm management, archival and retrieval of records. These equipment includes but are not limited to (b) (4).

C) Your firm's total (b) (4) standalone production equipment has an inbuilt SCADA system but none of these equipment have time stamped audit trail, data management, alarm management, archival and retrieval of records. These equipment have capabilities for printing of audit trail report in real time for only critical process parameters which is complied with the BMRs.

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Arsen Karapetyan, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Generic Drug User Fee Amendments (GDUFA)	Pratik S Upadhyay Generic Drug User Fee Amendments (GDUFA) Signed by: Pratik S Upadhyay -S Date Signed: 05-24-2018 23:26:58 X	DATE ISSUED 5/24/2018

**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 5/14/2018-5/24/2018*
	FEI NUMBER 3008565058

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
Dr. Darshan Makhey, President - Global Quality

FIRM NAME Glenmark Pharmaceuticals Ltd	STREET ADDRESS Plot No. 2, Pharma Zone SEZ
CITY, STATE, ZIP CODE, COUNTRY Pithampur, Dhar, Madhya Pradesh, 454775 India	TYPE ESTABLISHMENT INSPECTED Finished Oral Solid Dosage Manufacturer

**QUALITY SYSTEM**

**OBSERVATION 5**

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

Specifically,

Your firm's Quality Unit has no adequate oversight on the raw data pertaining to production and QC laboratory. For example,

1) On 05/15/2018, we observed torn balance printouts, shredded documents, torn draft investigation reports, etc. Your firm's interim investigations pertaining to balance printouts confirmed that production employees dismantled printouts pertaining to balance number EPD292 on 05/10/2018 for the (b) (4) operation of (b) (4) tablets (b) (4) mg, batch number (b) (4) ((b) (4) of lot-(b) (4)).

Your firm's production employees deviated from SOP CQA 061 "Data lifecycle management" section 5.1.2 "Raw Data" and 5.1.3. "Metadata (data about data)" must be contemporaneously and accurately recorded by permanent means.

2) Your firm maintains a total of (b) (4) document destruction bins at various locations throughout the facility and the documents gets shredded using a shredder located in QA documentation cell and shredder area as per SOP CM/QA050 "Procedure for disposal of GMP documents by shredding". Your SOP CM/QA050 per ANNEXURE-III allows shredding of investigations reports (draft), records of supporting documents to change control, etc.

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Arsen Karapetyan, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Generic Drug User Fee Amendments (GDUFA)	Pratik S Upadhyay Generic Drug User Fee Amendments (GDUFA) Signed by: Pratik S. Upadhyay -S Date Signed: 05-24-2018 23:26:58 X	DATE ISSUED 5/24/2018

**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 5/14/2018-5/24/2018*
	FEI NUMBER 3008565058

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
Dr. Darshan Makhey, President - Global Quality

FIRM NAME Glenmark Pharmaceuticals Ltd	STREET ADDRESS Plot No. 2, Pharma Zone SEZ
CITY, STATE, ZIP CODE, COUNTRY Pithampur, Dhar, Madhya Pradesh, 454775 India	TYPE ESTABLISHMENT INSPECTED Finished Oral Solid Dosage Manufacturer

We observed entries for several investigations reports (draft) in your document disposal records that were shredded per SOP CM/QA050.

3) On 05/21/2018, we observed that your firm has no control over the issuance of qualification protocols and worksheets used for recording of equipment qualification activities. The equipment qualification protocols and worksheets are maintained on both production and QA computers and can be printed without seeking an approval from the QA department as it was evident for Compression ID: EPD264.

Your SOP CM/QA028 "Preparation and Approval of document" is deficient for the control over issuance and control of qualification documents.

**\*DATES OF INSPECTION**

5/14/2018(Mon), 5/15/2018(Tue), 5/16/2018(Wed), 5/18/2018(Fri), 5/21/2018(Mon), 5/22/2018(Tue), 5/23/2018(Wed), 5/24/2018(Thu)

X Arsen Karapetyan  
Investigator - Dedicated Drug Cadre  
Signed By: Arsen Karapetyan -S  
Date Signed: 05-24-2018 23:28:07

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Arsen Karapetyan, Investigator - Dedicated Drug Cadre Pratik S Upadhyay, Generic Drug User Fee Amendments (GDUFA)	Pratik S Upadhyay Generic Drug User Fee Amendments (GDUFA) Signed By: Pratik S Upadhyay -S Date Signed: 05-24-2018 23:26:58 X	DATE ISSUED 5/24/2018