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

| DISTRICT OFFICE ADDRESS AND PHONE NUMBER | DATE(S) OF INSPECTION |
|---|---|
| US Food & Drug Administration, CDER/Inspection Assessment Branch<br>White Oak Building 51, Room 4235, 10903 New Hampshire Avenue Silver Spring, MD 20993, Attn: Mr. Concepcion (Coki) Cruz; Telephone 001-301-796-3254; FAX: 001-301-847-8738; E-MAIL: cderosiab@fda.hhs.gov<br>Industry Information: www.fda.gov/oc/industry | January 24, 2017-February 1, 2017 |
| | FEI NUMBER<br>3007720135 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Sanjeev Sethi, Chief Scientific Officer

| FIRM NAME | STREET ADDRESS |
|---|---|
| Mylan Laboratories Limited | Plot No. 31, 32, 33 & 34-A ANRICH Industrial Estate |
| CITY, STATE AND ZIP CODE | TYPE OF ESTABLISHMENT INSPECTED |
| Bollaram, Jinnaram Mandal, Medak District 502 325, Telangana | Control Testing Laboratory |

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

Observation 1

Appropriate controls are not exercised over computers or related systems. Input to and output from the computer and related systems, records and data are not checked for accuracy. Furthermore, there is a failure to maintain a backup file of data entered into the computer or related system. Specifically,

A) Validation activities have not been performed for the network infrastructure and servers used to store electronic chromatographic data for the Empower 2 and Empower 3 systems. The Empower 2 system is used in the active pharmaceutical ingredient (API) analytical method validation laboratory. The Empower 3 system is used in the (b) (4) solid dosage analytical method validation laboratory. Furthermore, a site specific procedure describing the validation of computerized systems for the method validation laboratory did not exist. In addition, a risk assessment for the Empower chromatographic acquisition software system has not been performed. Several message center data events related to the performance of the Empower system network were also observed during the inspection.

B) A procedure has not been established describing the process of backing up electronic message center data for the Empower 2 and Empower 3 systems. The message center data provides status information and error messages associated with the chromatography hardware and network.
Regarding this, there were discrepancies regarding the back-up processes for the message center data in the API and the (b) (4) solid dosage method validation laboratories. The Empower 3 system used in the (b) (4) solid dosage analytical method validation laboratory was historically backing up and saving the data for the message center. However, the Empower 2 system used in the active pharmaceutical ingredient (API) analytical method validation laboratory started to back up the data in December 2016 and did not retain any message center data generated prior to December 20, 2016. The message center data for the API analytical method validation laboratory generated prior to December 20, 2016 was not available because it was automatically being purged (deleted) from the Empower system after (b) (4)

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| | | Daniel J. Roberts, Investigator<br>Liming Zhang, Investigator | 02/01/2017 |

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C) A procedure and process has not been established to periodically review and evaluate the electronic message center data generated for the Empower 2 and Empower 3 systems.
Regarding this, the following message center errors and events that occurred between June 1, 2016 and January 24, 2017 were not reviewed and evaluated by the Quality Unit for the Empower 3 system used in the (b) (4) solid dosage analytical method validation laboratory: 158 Data File Checksum Errors, 54 Ethernet Cable Disconnect events, 20 Project Integrity Failures (representing 15 actual events), and 200 Instrument Failures.

D) Between June 2016 and December 2016, there were 32 instances involving (b) (4) different chemists from the Active Pharmaceutical Ingredient Analytical Validation laboratory logging into the Empower 2 system and running samples including method validations under a shared user name "GUEST" and password. Based on this practice, there is no traceability to the chemist who actually ran the analysis on the system.

E) On January 31, 2017, we discovered 147 object run files located on the local hard drive for Ultra-Violet/Visible (UV-Vis) Shimadzu spectrophotometer instrument AVL064 that was located inside the finished dosage analytical method validation laboratory and used for the validation of residue, dissolution, (b) (4) assay, identification, and assay methods. In addition, these run files located on the local hard drive, which includes the back-up of these run files, could be deleted from the computerized system.
On February 1, 2017, during review of the electronic data for (UV-Vis) Shimadzu spectrophotometer instrument AVL064, we discovered that UV-Vis Scan ID SAMPLE_15838.spc was acquired on June 9, 2014 at 3:41pm and stored on the local hard drive. This UV-Vis scan corresponded to the same time frame and sample spectra for Analytical Method Validation for Determination of Dissolution of (b) (4) in (b) (4) (b) (4) Tablets by UV Protocol MVP (b) (4) MT-DS-001/01. However, UV-Vis Scan ID SAMPLE_15838.spc was not retained and included in the raw data package for this analytical method validation. The UV-Vis scan raw data associated with this Analytical Method Validation was retained for scans acquired on June 9, 2014 at 4:59pm, 5:05pm and 5:10pm. There was no documentation available discussing why this UV-Vis Scan ID SAMPLE_15838.spc that was acquired on June 9, 2014 at 3:41pm was not retained and excluded from the analytical method validation.

Observation 2
Laboratory records do not include complete data derived from all tests, examinations and assay necessary to assure

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compliance with established specifications and standards. Specifically,

A) Raw data is missing for the following seven (7) active pharmaceutical ingredient (API) analytical method validations:

- (b) (4) Assay, Report Number PC/AD/MV/(b) (4) 002 dated 2004
- (b) (4) Residual Solvents, Report Number PC/AD/MV/(b) (4) /001 dated 2004
- (b) (4) USP (b) (4), Related Substances, Report Number KPM09057.00 dated 2003
- (b) (4) Assay, Report Number KPM09056.00 dated 2003
- Forced Degradation, Report Number AD/DS/035 dated 2004
- (b) (4) USP (b) (4) Residual Solvents, Report Number KPM09020.00 dated 2002
- USP (b) (4) Content, Report Number KPM09055.00 dated 2003

The methods cited above were included in drug (b) (4) submitted to the Agency. Based on the lack of raw data, there is no evidence that the methods are appropriately validated and suitable for use.

B) On January 24, 2017, during a walk-through of the solid (b) (4) dosage method validation laboratory, we observed two (2) weighing printouts ripped and discarded in the trash bin located inside the weighing area.
The first weighing printout that was discarded contained a recorded value of (b) (4) grams with an unknown date and time. This weight printout was discarded during the preparation of (b) (4) diluent on January 21, 2017 that was used for Assay Test for Forced Degradation Study (b) (4) and (b) (4) Test Method ETD-T-AY-01/09 (Method-(b) (4)). The corresponding weight printout contained in this Test Method ETD-T-AY-01/09 (Method-(b) (4)) data was (b) (4) grams dated January 21, 2017 at 12:09.
The second weighing printout that was discarded contained a recorded value of (b) (4) grams dated January 21, 2017 at 10:12. This weight printout was discarded during the preparation of (b) (4) mobile phase on January 21, 2017 that was used for Dissolution Accuracy for (b) (4) (b) (4) Tablets Test Method ASTP-ECT-T-DS-02/00. The corresponding weight printout contained in this Test Method ASTP-ECT-T-DS-02/00 data was (b) (4) grams dated January 21, 2017 at 10:13.
Furthermore, the top load balance AVL042 Sartorius Model GPA 5202 that was used for these measurements was not password protected to prevent unauthorized access to the instrument settings including date and time. Based on the lack of appropriate controls, analysts have the ability to make modify or manipulate such settings. In addition, these weight printouts were being attached in the analytical data packets without a signature overlapping the weight printout and data packet sheet.

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Observation 3
Drug products are not stored under appropriate conditions of temperature so that their identity, strength, quality, and purity are not affected. Specifically,

Prior to September 2016, bioequivalence samples manufactured at the (b) (4) facility were being sent from the manufacturing facility to the Mylan R&D facility for temporary storage and then subsequently transferred to the (b) (4) facility to conduct bioequivalence studies. On January 27, 2017, we performed a walk-through of the bioequivalence sample storage area and observed that the (b) (4) tablets label stated that the sample should be stored at controlled room temperature (20-25°C). However, the temperature monitoring limit specified for this storage area was NMT 27°C.

Observation 4
The responsibilities and procedures applicable to the quality control unit are not in writing. Specifically,

Prior to November 30, 2016, there was no procedure established discussing the handling of product samples received from manufacturing sites including the receipt, storage, issuance and destruction of product samples. Prior to the implementation of this procedure, bioequivalence study and investigation product samples from manufacturing sites were received and handled at this facility.

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