DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	6/14/2024-6/26/2024*
	FEI NUMBER 3010453141

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Pramod Kumar Singh, Head of (b) (4) Operations - India and Africa

FIRM NAME	STREET ADDRESS
Mylan Laboratories Limited	(FDF-3) Plot Nos. 11, 12, 13, Indore SEZ, Pharma Zone, Phase II, Sector III
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Pithampur, District Dhar, Madhya Pradesh, 454775 India	(b) (4) Drug Products Manufacturer

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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:
FACILITY AND EQUIPMENT SYSTEM

OBSERVATION 1

Equipment and utensils are not cleaned at appropriate intervals to prevent that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

You failed to adequately clean and maintain your non-dedicated equipment used for drug products manufacturing. For example,

A. On 14-Jun-2024, I observed white to off-white (b) (4) materials on (b) (4) HEPA filter chamber and the (b) (4) Duct of (b) (4) ID: (b) (4) located in Block (b) (4) (b) (4) while this equipment was in Type A cleaning status. This non-dedicated (b) (4) is used in the manufacturing of the following (b) (4) drug products:

a. (b) (4) Tablets (b) (4) mg (b) (4) mg (b) (4) mg
b. (b) (4) Tablets (b) (4) mg (b) (4) mg (b) (4)
c. (b) (4) Tablets (b) (4) mg (b) (4) mg (b) (4) mg (b) (4)

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d. (b) (4) Tablets (b) (4) mg (b) (4) mg (b) (4) mg (b) (4) (b) (4)

On 17-Jun-2024, (b) (4) swab samples were collected from different locations of (b) (4) Duct of (b) (4) ID: (b) (4) and analyzed by HPLC to identify the presence of drug substances of the previously manufactured drug products. Test data revealed the presence of drug substances of the above listed drug product indicating a potential for drug products cross-contamination that were manufactured using this (b) (4) Swab test results are tabulated as follows:

Table 1

(b) (4)

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(b) (4)

Furthermore, the swab samples testing showed numerous unknown peaks randomly eluting at different retention times in all (b) (4) swab samples tested by HPLC. These unknown peaks were not identified and accounted for in the above table. The highest result obtained for the unknown peaks was (b) (4) PPM. There is a potential for the swab test results to be even higher than the reported result in table 1 considering not the entire (b) (4) residues could be collected from the areas swabbed due to large quantity of (b) (4) residues that was present in the areas swabbed.

Upon becoming aware of the potential for carryover and cross-contamination issues based on swab samples test results on 18-Jun-2024, your firm reported no Field Alert to the agency within three (3) working days.

B. Your firm considered acceptance limits of NMT (b) (4) PPM for (b) (4) NMT (b) (4) PPM for (b) (4) and NMT (b) (4) PPM for (b) (4) while reporting the swab sample test results (refer to Table 1). However, your minimum acceptance criteria as per the cleaning validation (CV) matrix (CV ID: MLLFD3/CVMAT/GEN/04/24/01) is NMT (b) (4) PPM for (b) (4) (b) (4) NMT (b) (4) PPM for (b) (4) and NMT (b) (4) PPM for (b) (4) Based on these validated acceptance limits, there is a potential for the carryover and cross-contamination of drug products manufactured using your non-dedicated (b) (4) ID: (b) (4) Your Quality Unit provided no justification for considering higher acceptance limits that undermines the obtained swab sample test results specifically for (b) (4) Furthermore, there is no procedure established for calculating equipment specific swab sample test result while your cleaning validation is based on equipment train (all equipment) that are used in the manufacturing of a given product that includes large number of equipment and the results calculated are based on total surface area of all equipment.

C. Your manual Type C (product changeover) equipment cleaning procedure is deficient. For example,

there is no cleaning of (b) (4) HEPA filter chamber and (b) (4) Duct performed upon Type C cleaning of (b) (4) Additionally, there is no verification of cleanliness of (b) (4) Duct performed since their installation several years ago. Your firm's (b) (4) of which the oldest (b) (4) (ID: (b) (4)) was installed on 04-Mar-2013 and the newest (b) (4) (ID: (b) (4)) was installed on 21-Jun-2019. Per your Quality Unit, none of the (b) (4) have been cleaned in the (b) (4) Duct areas since their installation.

D. Standard Test Procedures (STPs) used for swab samples analyses are deficient. For example, but not limited to:

1. Per your protocol and report for periodic monitoring of cleaning procedure, (b) (4) is the worst to clean drug substance from the equipment surfaces. Your STP No.: IPPTLE013-02, Name of Product: (b) (4) Effective date: 10-Feb-2014 established for the detection of (b) (4) drug substance does not assure the accuracy of swab sample test results. This STP refers to sonicating swab sample for (b) (4) in test tube containing (b) (4) ml of (b) (4) On 17-Jun-2024, I observed (b) (4) ml of (b) (4) was not sufficient to dip the entire swab stick head into (b) (4) solvent. The (b) (4) ml of (b) (4) dipped only about 40% of swab stick head while the other approximately 60% that also contained (b) (4) materials upon swabbing from (b) (4) ID: (b) (4) was not extracted completely into the solution due to inadequacies in your test procedure for swab test sample solution preparation. There is a potential that the actual results for swab samples (b) (4) and (b) (4) could potentially be much higher than the reported results for (b) (4) (refer to **Table 1**) and unknown impurities than the reported results.

Subsequently, there is no assurance over the reliability of your analytical test method validation (Report No.: MVR-TLET-RD-013/00, Approval date: 25-Nov-2009) pertaining to swab sample analysis for the detection of (b) (4) drug substance considering the swab head was not dipped completely into (b) (4) ml (b) (4) to ensure extraction of (b) (4) drug substance from the surface areas of swab head.

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2. Your STP No.: IPPASL066-01, Name of Product: (b) (4) Effective date: 21-Nov-2013 does not assure the accuracy of swab sample test results. This STP refers to sonicating swab sample for (b) (4) in test tube containing (b) (4) ml of (b) (4) Addition of (b) (4) ml (b) (4) indicated only about 60% of swab head could be dipped and thereby there is a potential for incomplete extraction of (b) (4) materials into the solution and the results obtained will not be a true reflection of the amount (PPM) of actives and impurities present in the equipment swabbed.

3. Your STP No.: IPPNVP073-01, Name of Product: (b) (4) Effective date: 28-Feb-2024 does not assure the accuracy of swab sample test results. This STP refers to sonicating swab sample for (b) (4) in test tube containing (b) (4) ml of (b) (4) Addition of (b) (4) ml indicated only about 60% of swab head could be dipped and thereby there is a potential for incomplete extraction of (b) (4) materials into the solution and the results obtained will not be a true reflection of the amount (PPM) of actives and impurities present in the equipment swabbed.

4. Your STP No.: IPPLAC302-00, Name of Product: (b) (4) Effective date: 18-Jul-2023 does not assure the accuracy of swab sample test results. This STP refers to collecting the swab samples into (b) (4) **ml test tube** containing accurately (b) (4) **ml** of (b) (4) and sonicate for (b) (4) Your procedure does not take into consideration that (b) (4) ml test tube is inadequate to contain (b) (4) ml solution (b) (4) + weight of a swab stick. There is a potential that swab test solution will spill outside of the test tube and as such (b) (4) of the solution is practically impossible for the same volume of the test tube. This may lead to unreliable swab sample test results. On 19-Jun-2024, per my request your QC Unit simulated swab test sample solution by using (b) (4) ml test tube instead of using (b) (4) ml test tube. Even though they used higher volume (b) (4) ml) of test tube than the specified in the test method (IPPLAC302-00), they were unable to (b) (4) ml solution due to insufficient space in the test tube and the inconvenience of swab stick being longer than (b) (4) ml test tube with no lid to close it.

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Based on the above listed inadequacies in your STPs and the practices of your QC Analysts while performing swab samples testing, there is a potential for getting unreliable test results on the lower side of the acceptance limits that may not trigger quality event (laboratory incident) leading to recleaning of the equipment upon investigation. Also, there is a potential for deficiencies in your analytical method cleaning validation leading to unreliable test results and carryover and/or cross-contamination risks among different drug products that are manufactured using non-dedicated equipment at your site.

E. Your Type A (batch to batch) equipment cleaning is deficient. For example, per your procedure SOP-000563943, Titled: Operation & cleaning of (b) (4) Model-(b) (4) Version: 16.0, section 6.10.4 requires removing any (b) (4) that may be present from the machine with the help of (b) (4) Further, the (b) (4) must be removed from (b) (4) bowl by (b) (4) per section 6.10.5. Your Production Operator stated the procedure was followed and (b) (4) residues were removed using (b) (4) (b) (4) was used to remove (b) (4) material from the equipment. However, on 14-Jun-2024, I observed thick accumulation of the (b) (4) materials in product contact areas for (b) (4) ID: (b) (4) while this equipment was in Type A clean status. This equipment was awaiting to be used in the campaign manufacturing of product (b) (4) (b) (4) Tablets (b) (4) mg (b) (4) mg (b) (4) mg, batch number (b) (4)

QUALITY SYSTEM

OBSERVATION 2

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

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Specifically,

Your investigations of out-of-specification (OOS) results were inadequate because they lacked scientific rationale for root cause determinations. For example,

A. Laboratory Investigation PR ID: 3455440, Date Opened: 28-Mar-2024, Product: (b) (4) Tablets (b) (4) mg, Stability timepoint: Long Term (LT) (25°C/60%RH) at 18 months for batch (b) (4) and at 3 months for batch (b) (4) LT (25°C/60%RH), Issue: OOS/OOT results observed for Dissolution profile test by HPLC, Final classification: Unconfirmed OOS, Specification limits: (b) (4) (b) (4) Not less than (b) (4)%.

Table 2

Batch. No. (b) (4)	**Stability Timepoint: 18 Month(s)/ 25°C±2°C/60%±5%RH** (b) (4) (b) (4)
Batch. No. (b) (4)	**Stability Timepoint: 3 Month(s)/ 25°C±2°C/60%±5%RH** (b) (4) (b) (4)

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(b) (4)

Your QC Analyst aborted HPLC sample set sequence upon finding OOS and OOT dissolution test results for batch numbers (b) (4) (OOS result) and (b) (4) (OOT result). In the same sample set sequence, dissolution test samples of batches (b) (4) (LT at 18 months), and (b) (4) (LT at 3 months) were not analyzed upon finding failing results. The following issues were observed:

1. Test sample vials pertaining batches (b) (4) and (b) (4) were not injected into the HPLC based on the OOS and OOT test results of batches (b) (4) and (b) (4) There was no justification provided for aborting sample set sequence in attempt to not test batches (b) (4) and (b) (4) Your QC unit disposed original test solutions and reperformed dissolution test for batches (b) (4) and (b) (4) without any justification while the Phase 1 investigation revealed no laboratory error.
2. Your Phase 1 (laboratory) and Phase 2A (manufacturing) investigations determined no root cause. During the experimental studies conducted under Phase 2B investigation, your Quality Unit determined the root cause being improper (b) (4) of (b) (4) in dissolution media. However, per your dissolution test procedure number: INPNSD301-03, Effective date: 03-Mar-2023 dissolution media required to be (b) (4) This was followed by (b) (4)

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The verification of laboratory raw test data worksheet revealed no discrepancy in [(b) (4)] of dissolution media. This was indicative of the [(b) (4)] was [(b) (4)] properly in the dissolution media. The QC Analyst that worked on the dissolution test solution preparation stated that the dissolution media was prepared according to the test procedure (INPNSD301-03). However, the root cause for this investigation to suggest improper [(b) (4)] of [(b) (4)] was not justified.

3. During the experimental testing at Phase 2B investigation, your Quality Unit disregarded the leftover of about [(b) (4)] dissolution media. There was no reverification of dissolution media [(b) (4)] performed along with no assessment was conducted to evaluate the impact of variations in [(b) (4)] on the dissolution profile of [(b) (4)] Tablets [(b) (4)] mg.
4. There was no justification provided to conclude the root cause being improper [(b) (4)] of [(b) (4)] in dissolution media while the test results of unit [(b) (4)] were within limits at [(b) (4)] dissolution time point and unit [(b) (4)] were within limits at [(b) (4)] dissolution time point for batch [(b) (4)] Also, for batch [(b) (4)] unit [(b) (4)] were within specification limit at [(b) (4)] [(b) (4)] dissolution time point. Both the batches were tested using the same stock of dissolution media.
5. Your dissolution test procedure (INPNSD301-03) for [(b) (4)] Tablets is deficient. There is no mention of the amount of dissolution media that must be [(b) (4)] at [(b) (4)] [(b) (4)] dissolution timepoints (refer to **OBSERVATION 3B**)

B. Laboratory Investigation PR ID: 3354171, Date Opened: 08-Dec-2023, Product: [(b) (4)] [(b) (4)] mg Capsules, Batch No.: [(b) (4)] Type of Analyses: Assay by HPLC, Issue: OOT result was observed for Assay, Result: [(b) (4)]%, OOT limit: NLT [(b) (4)]% and NMT [(b) (4)]%, Stage: Finished Product.

Your Phase 1 (laboratory) investigation identified no root causes and the results of re-injection, re-fill, re-dilution, re-stirring confirmed to the original OOT test result. There were no manufacturing issues identified during the Phase 2A investigation. The experimental studies performed under Phase 2B investigation ruled-out the possibility of any issues with standard preparation. However, you performed

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retest analysis for Assay and Content Uniformity (CU) using new sample under Phase 2B investigation. I observed the following issues under Phase 2B investigation:

1. Upon obtaining the failing (OOS) test result for CU test for Unit (b) (4) QC Analyst aborted the sample set sequence at Unit (b) (4) due to HPLC column leakage.

Table 3

(b) (4)

The reinjected, re-fill, and re-diluted test results for Unit (b) (4) were comparable with original results. The results of Unit (b) (4) were observed (b) (4) % and (b) (4) % for re-injection and re-fill. Your firm initiated no separate laboratory incident to investigate the failing (OOS) results obtained for CU test. The OOS test results for CU test were invalidated stating instrument (HPLC ID: QCD571) error due to column leakage during this analysis. However, there was no message relating to column leakage was found in the Empower 3 audit trail for HPLC ID: QCD571.

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2. There was no OOS investigation conducted to justify comparable results to the original result for Unit (b) (4) during the original analysis and reinjection, re-fill, and re-diluted analyses while the results of (b) (4) (Unit (b) (4) and (b) (4) (Unit (b) (4) samples to Unit (b) (4) were within specification limit.

3. There was no explanation provided for not reporting Unit (b) (4) tests results in the initial run and its correlation to OOS results obtained for Unit (b) (4) in re-injection and re-fill. Furthermore, the chromatographic data of retest was not verified and signed by analytical QA.

4. Your Quality Unit conducted testing into compliance by retesting for the second time using new samples and changed HPLC equipment from HPLC ID: QCD571 to HPLC ID: QCD496. This retest analysis gave favorable (passing) results for CU and confirmed OOT result for Assay based on which your firm released the batch into the market.

C. Laboratory Investigation PR ID: 2970698, Date Opened: 19-Nov-2022, Product: (b) (4) Tablets (b) (4) mg, Batch No.: (b) (4) Type of Analyses: Dissolution by HPLC, Issue: (b) (4) timepoint for Unit (b) (4) was (b) (4)% against the acceptance criteria of (b) (4)% to (b) (4)%. Result: Unit (b) (4) not complying to (b) (4) stage criteria. Stage: Finished Product.

This OOS investigation was deficient to identify test method deficiencies. For example, dissolution test procedure (INPNSD301-03) for testing (b) (4) Tablets was deficient. There is no mention of the amount of dissolution media that must be (b) (4) at (b) (4) dissolution timepoints (refer to **OBSERVATION 3B**).

D. Your procedure SOP-000463175, Titled: LABORATORY INVESTIGATION REPORT (LIR), Version: 12.0 pertaining to investigation of OOS, OOT, and atypical result(s) is deficient. There is no requirement in your current practices to charge confirmed OOT batch of finished product on the stability to monitor the batch throughout the shelf life of product to ensure the product would remain within the

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approved specification limit.

LABORATORY CONTROL SYSTEM

OBSERVATION 3

Laboratory controls do not include the establishment of scientifically sound and appropriate 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,

A. Your standard test procedures (STPs) pertaining to testing of drug products and equipment cleaning swab samples of shared (non-dedicated) equipment are inadequate and it does not assure the reliability of the test data generated using these STPs. For examples,

1. Your equipment cleaning swab samples testing procedure STP No.: IPPTLE013-02, Name of Product: (b) (4) Effective date: 10-Feb-2014 established for the detection of (b) (4) drug substance is not in line with your analytical method validation (AMV) (Report No.: MVR-TLET-RD-013/00, Approval date: 25-Nov-2009) for the referenced STP No.: IPPTLE013-02. Per this procedure, injection volume for swab sample test solution, system suitability standard solutions, swab blank, and bracketing standard injections into HPLC is (b) (4) **µl**. However, your AMV refers to (b) (4) **µl** as injection volume. Thereby, it appeared that your firm has been deviating for over a decade while conducting swab samples analyses that is in deviation of your analytical method validation for equipment cleaning swab samples testing.

2. Your Dissolution by HPLC test procedures is deficient to ensure reliability of test results for the following reasons:

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a. In STP No.: FPPNSD301R-03 for testing (b) (4) Tablets (b) (4) mg, (b) (4) mg, (b) (4) mg, and (b) (4) mg (b) (4) there is no mention of the amount of dissolution media to be (b) (4) (b) (4) at (b) (4) dissolution timepoints. This procedure is used for testing finished products at release and stability samples at long term and accelerated stability conditions.
b. In STP No.: FPPNSD302R-04 for testing (b) (4) Tablets (b) (4) mg, (b) (4) mg, and (b) (4) mg (b) (4) (b) (4) there is no mention of the amount of dissolution media to be (b) (4) at (b) (4) (b) (4) dissolution timepoints. This procedure is used for testing finished products at release and stability samples at long term and accelerated stability conditions.

Subsequently, upon making request for the evaluation of analytical method validation (AMV) protocol and report, your firm could not provide AMV protocol and the report (FP-NSLDAD-DS-M, Approval date: 21-Sep-2009) provided has no mention of the amount of dissolution media to be (b) (4) (b) (4) at specified dissolution timepoints. Similar, deficiencies were noticed while verifying analytical method transfer (AMT) protocol (MTP/FDF-3/DP/20/047-00, Approval date: 11-Aug-2020), and report (MTR/FDF-3/DP/20/047-00, Approval date: 27-Nov-2020) pertaining to (b) (4) Tablets (b) (4) mg, (b) (4) mg, (b) (4) mg, and (b) (4) mg (b) (4) I observed similar deficiencies relating to validation and transfer of analytical test method for (b) (4) Tablets (b) (4) mg, (b) (4) mg, and (b) (4) mg (b) (4)

Furthermore, there is no mention of the amount to be (b) (4) along with dissolution timepoints for the following (b) (4) drug products at the dissolution profile testing that was performed during the process validation:

(b) (4)

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DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	6/14/2024-6/26/2024*
	FEI NUMBER 3010453141

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Mr. Pramod Kumar Singh, Head of (b) (4) Operations - India and Africa

FIRM NAME	STREET ADDRESS
Mylan Laboratories Limited	(FDF-3) Plot Nos. 11, 12, 13, Indore SEZ, Pharma Zone, Phase II, Sector III
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Pithampur, District Dhar, Madhya Pradesh, 454775 India	(b) (4) Drug Products Manufacturer

(b) (4)

B. Your Quality Unit failed to provide a written and documented scientific justification to only sample (b) (4) "good tablets" from each container/pack after at least (b) (4) tablet reject was identified to be outside the acceptable range of weight according to your firm's SOP-000464236 titled, "OPERATION AND CLEANING PROCEDURE FOR THICKNESS SORTING MACHING – MAKE (b) (4)" under section 6.3.7.4. There is variability in the batch sizes for the smallest (b) (4) (b) (4) tablets) and the largest (b) (4) tablets) U.S. drug products manufactured at your facility.

OBSERVATION 4

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

Specifically,

Your Quality Unit lacks an oversight on the integrity of data pertaining to packaging material testing. For example,

A. Your QC Analysts potentially falsified testing data pertaining to (b) (4) identification test by Chemical Analysis. Per your STP No.: PMPFL001-08, Effective date: 19-Aug-2021, section 4.1.1, it takes about (b) (4) to complete the analysis. On 25-Jun-2024, your QC Analyst (b) (6) stated that he lost all (b) (4) samples relating to different batches post completion of weighing these samples using balance ID QCD 348. However, raw data worksheets for four (4) out of (b) (4) batches was found completed for (b) (4) identification test by Chemical Analysis. The evaluation of four (4) batches (b) (4) test data revealed that QC

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Analysts that claimed to have completed the analysis were not present in the firm to conduct identification analyses per STP No.: PMPFL001-08, section 4.1.1. The details relating to raw test data worksheets and biometric/attendance log for QC Analysts are as follows:

Table 4

Sr. No.:	Batch No.:	Weight taken (Date/Timestamp)	Time required to complete analysis	Analysts Initial: Attendance Log for In/Out (Date/Time)	Result reported as Complies by Analyst (Date)
1	(b) (4)	16-Jan-2024 (b) (4)	About (b) (4) (b) (4) (i.e. by (b) (4) around (b) (4) (b) (4) testing would have completed)	(b) (4), (b) (6)	(b) (6) 16/Jan/2024
2		16-Jan-2024 (b) (4)			
3		16-Jan-2024 (b) (4)			(b) (6) *Not initialed and dated
4		16-Jan-2024 (b) (4)			

** Analyst (b) (6) stated that he completed the analysis on 16-Jan-2024.*

Your Analysts (b) (6) provided no explanation about how they performed testing for four (4) out of (b) (4) batches for identification testing while per Analyst (b) (6) all (b) (4) samples were lost and none of it could be found. Thereby, it appeared that your Analysts potentially completed the raw data worksheet for the referenced batches (b) (4) by simply writing "Complies" followed by sign and date.

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Pithampur, District Dhar, Madhya Pradesh, 454775 India	(b) (4) Drug Products Manufacturer

B. On 24-Jun-2024, your Assistant Manager of QC deviated from procedure SOP-000565134, Titled: Good Quality Control Practices, Version: 38.0, section 6.9.1.23 relating to Good Documentation Practices (GDPs) by overwriting, and scrubbing the numbers by writing information on the approved controlled document in blue ink pen. This controlled document was titled "List for Packaging material Approved T.P. LIT", FORM -000564405, Signed and dated under Prepared By, Reviewed By, and Approved By on 01-Jun-2024. This document contained (b) (4) serial numbers pertaining to unique Material Code (M. Code) assigned to different materials. Per QC Manager, serial numbers are followed to locate T.P. LIT (Transparency Literature) and accordingly packaging material's "Printing" verification test is performed each time the material is received. However, "List for Packaging material Approved T.P. LIT" document contained incorrect information pertaining to Material Code being assigned to a different material and the same serial number was assigned to multiple materials. For example, serial number (b) (4) was assigned to two (2) different materials named LIT (b) (4) and LIT (b) (4) TAB (b) (4) MG (b) (4) However, per "List for Packaging material Approved T.P. LIT" serial number (b) (4) was assigned to material LIT (b) (4) only.

Furthermore, the evaluation of packaging material raw data worksheet revealed the information pertaining "Printing" test specification limit was pre-printed and your QC Analyst were simply required to write "Confirm". There is a potential for inadequacies in conducting this test due to the practices of simply writing "Confirm" on the worksheet based on the fact that two (2) different materials were assigned the same serial number and the transparency literature if would have been referred while conducting "Printing" test to by your QC Analyst this issue would have been identified and the test would not have confirmed to the specification limit.

OBSERVATION 5

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,

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A. Your Quality Unit failed to identify and investigate at least two (2) quality events relating to "Auditing Breached" documented on the audit trail for the (b) (4) (Equipment ID: (b) (4)) for (b) (4) audit trail review on (b) (4) as required for SOP-003059163 titled, "PROCEDURE FOR OPERATION AND CALIBRATION OF PARTICLE SIZE ANALYZER" under section 6.22 (b) (4) database review) and section 6.23 (Audit Trail Review), respectively.

B. Two (2) personnel of Quality Assurance (QA) for your firm appears to have "full" administration access to at least (b) (4) equipment/instruments within the Quality Control (QC) Laboratory with at least (b) (4) of the equipment/instruments with an audit trail.

PRODUCTION SYSTEM

OBSERVATION 6

Actual yield and percentages of theoretical yield are not determined at the conclusion of each appropriate phase of manufacturing and processing of the drug product.

Specifically,

Your Quality Unit failed to calculate and document the yield percentages of (b) (4) packaging batches for the U.S. Market. There are approximately (b) (4) batches for the U.S. Market for which the percent yields were not calculated, documented, and reviewed for any potential issues with the specific and separate packaging operation of each batch.

***DATES OF INSPECTION**

6/14/2024(Fri), 6/17/2024(Mon), 6/18/2024(Tue), 6/19/2024(Wed), 6/20/2024(Thu), 6/21/2024(Fri), 6/24/2024(Mon), 6/25/2024(Tue), 6/26/2024(Wed)

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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