FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Food and Drug Administration
Office of Regulatory Affairs
Office of Pharmaceutical Quality Operations
Division of Foreign Pharmaceutical Quality Inspections
12420 Parklawn Dr. Room 2038
Rockville, MD 20852

March 21, 2019

Mahanand Sarde
Assistant Vice President of Operations
Macleods Pharmaceuticals Limited
Survey 366 Plots 25-27, Premier Industrial Estate,
Kachigam, Daman, Daman, 396210 India

Reference: Inspection Date(s): January 21 – 25, 2019
Macleods Pharmaceuticals Limited

Location:
Survey 366 Plots 25-27, Premier Industrial Estate,
Kachigam, Daman, Daman, 396210 India

Dear Mahanand Sarde,

We are enclosing a copy of the establishment inspection report (EIR) for the inspection that the U.S. Food and Drug Administration (FDA) conducted at your premises on the referenced locale and date(s). When the Agency concludes that an inspection is "closed" under 21 CFR 20.64(d)(3), it will release a copy of the EIR to the inspected establishment. This procedure is applicable to EIRs for inspections completed on or after April 1, 1997.

The Agency continually works to make its regulatory process and activities more transparent to the regulated industry. Releasing this EIR to you is part of this effort. The copy being provided to you comprises the narrative portion of the report; it may reflect redactions made by the Agency in accordance with the Freedom of Information Act (FOIA) and 21 CFR Part 20. This, however, does not preclude you from requesting additional information under FOIA.

If there is any question about the released information, feel free to contact me at +1-240-402-0550.

For more information on the U.S. FDA, please visit our website at www.fda.gov.

Sincererly,

Kevin Gonzalez
Branch Director
Division of Foreign Pharmaceutical Quality Inspections

FEI: 3006363714

Enclosure: Establishment Inspection Report (EIR)

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Location: Moldova

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SUMMARY

This comprehensive Pre-Approval Inspection (PAI) of pharmaceutical drug manufacturer, Macleods Pharmaceuticals Limited was conducted under MARCS OP ID 115306. The inspection was conducted under CPGM 7346.832 (Pre-Approval Inspections). The inspection is reported under PAC code 46832 (NDA Pre-Approval Inspections/Methods Validation)

The objective of this inspection was the readiness for commercial manufacturing, conformance to the application, and data integrity audit for NDA-210796 (Dolutegravir, Lamivudine and Tenofovir disoproxil fumarate Tablets, 50/300/300mg) and NDA-210649 (Efavirenz, Lamivudine and Tenofovir disoproxil fumarate Tablets, 400/300/300mg). The TCM profile was covered during the current inspection.

The previous inspection conducted 05/22-29/2017 was classified VAI. A two (2) item FDA-483 was issued for the following: 1) Established laboratory control mechanisms are not followed; 2)

Employees engaged in the manufacture of a drug product lack the training required to perform their assigned functions.

During the current inspection a two (2) item FDA-483 was issued to Mr. Mahanand R. Sarde, Asst. Vice President, Operations for the following: 1) The responsibilities and procedures applicable to the quality control unit are not fully followed; 2) 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.

No refusals were encountered during the inspection and no samples were collected.

ADMINISTRATIVE DATA

Inspected firm:	Macleods Pharmaceuticals Limited
Location:	Survey 366 Plots 25-27, Premier Industrial Estate, Kachigam Daman, Daman, 396210 India
Phone:	260 2240125
FAX:	
Mailing address:	Survey 366 Plots 25-27, Premier Industrial Estate, Kachigam Daman, Daman, 396210 India
Email address:	
Dates of inspection:	1/21/2019-1/25/2019
Days in the facility:	5
Participants:	**Marcus A Ray, Investigator - Dedicated Drug Cadre**

On 01/21/2019, I, Investigator Marcus A. Ray was greeted by Mr. Lalit Mohan Patro, President, CQA & Engineering Services, who accompanied me from the hotel to the firm. Once I arrived at the firm I was greeted by the following individuals:

- Mahanand R. Sarde, Asst. Vice President, Operations
- Awdhesh Maheshwari, Sr. Vice President, Corporate Quality
- K.R. Jayaram, Vice President, Corporate QA
- K. Jagdish, Dy. General Manager, Engineering & Projects
- Vishal Anand, Asst. General Manager, Human Resources
- Sandeep Chomal, Dy. General Manager, Stores
- Nishat Ahmad, General Manager, QA
- S.B. Parhi, Dy. General Manager, Production
- Umesh Maniyar, Dy. General Manager, Quality Control
- P. Kusher Kumar, Sr. General Manager, Regulatory Affairs
- R.S. Diwan, Head, Operations

I presented my FDA credentials to Mr. Mahanand R. Sarde, Asst. Vice President, Operations, who identified himself as the most responsible person at the firm. An opening meeting was held with the listed individuals, which included but was not limited to a presentation of the firm's history and operations **(EXHIBIT-1)**. Dr. Sachin Yadaorao Bhagwate, Drug Inspector later joined the inspection. Dr. Bhagwate was present on 01/21/2019 and 01/25/2019. Mr. Girish J. Vaghela, Drug Inspector joined the inspection on 01/25/2019.

Note: Dates in documents collected from the firm and referenced in this report are in the format of dd/mm/yy. Dates listed in this report that do not reference documents are in the format of mm/dd/yyyy.

HISTORY

Macleods Pharmaceuticals Limited was incorporated in 1986. There are a total of six (6) facilities for drug products (formulation) and one facility for drug substance (API). Two of the other sites are also in Daman, one is in Palghar (Maharashtra), one is in Nalagarh (Himachal Pradesh), and one is in Ranipool (Sikkim). Also, the API facility is located in Sarigam (Gujarat).

The firm's corporate office is located at the following:

3rd Floor, Atlanta Arcade, Marol Church Road
Andheri (E), Mumbai, IN

The firm is also inspected by other agencies, including but not limited to WHO Geneva; MHRA; Germany Authority; MOH, Ukraine; MOH, Saudi Arabia; MCC, South Africa; MCAZ, Zimbabwe; TGA-Australia; and MOH, Malaysia.

The firm has more than 13,500 employees throughout its seven (7) locations. Additionally, this facility has approximately 609 employees. A breakdown of employees in each department was provided in the firm's presentation **(EXHIBIT-1, page 15)**. The firm's hours of operations are 9:00am-5:30pm (General Shift), 7:00am-3:00pm (1st Shift), 3:00pm-11:00pm (2nd Shift), 11:00pm-7:00am (3rd Shift).

The firm was previously inspected 05/22-29/2017 and a two (2) item FDA-483 was issued for the following: 1) Established laboratory control mechanisms are not followed; 2) Employees engaged in the manufacture of a drug product lack the training required to perform their assigned functions.

Changes since the previous inspection include the following:

- Serialization system/facility installed on bulk line for label with Optical Character Recognition System.
- Existing Raw material storage area expanded.
- New underground water storage tank created for raw water and soft water.

Changes to personnel since the previous inspection include the following:

- Mr. Nishat Ahmad has replaced Mr. K. K. Koshe as Head Quality
- Dr. Umesh Maniyar has been promoted as Head QC
- Mr. K. Jagdish has replaced Mr. S. Rane as Head, Engineering
- Mr. Vishal Anand joined as Asst. General Manager, Human Resources

The US agent for the firm is:
Andrej Gasperlin, President
AB Pharmaceuticals, LLC
17471 Highland Way Drive
Chesterfield, MO 63005

Any post-inspectional correspondence should be addressed to:
Mahanand Sarde, Assistant Vice President, Operations
Macleods Pharmaceuticals Ltd.
Plot No. 25-27, Survey Number 366
Premier Industrial Estate
Kachigam, Daman 396 210 (U.T.), India

INTERSTATE (I.S.) COMMERCE

The firm manufactures and ships approximately 13.5% of finished drug products to the United States.

JURISDICTION (PRODUCTS MANUFACTURED AND/OR DISTRIBUTED)

Macleods Pharmaceuticals Limited is a drug manufacturer of finished drug products, such as tablets and capsules. A list of drug products distributed to the United States market was provided **(EXHIBIT-1, pages 22-23)**. Additionally, a list of pending applications was provided. **(EXHIBIT-1, page 25)**

This inspection focused on the pre-approval products, NDA-210796 (Dolutegravir, Lamivudine and Tenofovir disoproxil fumarate Tablets, 50/300/300mg) and NDA-210649 (Efavirenz, Lamivudine and Tenofovir disoproxil fumarate Tablets, 400/300/300mg).

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

An Organizational Chart was provided. **(EXHIBIT-1, page 12)**

Dr. R. Agarwal, Managing Director oversees Macleods Pharmaceuticals Limited. Dr. Agarwal was not present during the inspection and holds his position at the corporate office.

The following personnel were present during the inspection and provided information:

Mr. Mahanand Sarde, Assistant Vice President, Operations; Mr. Sarde is responsible for the overall operations of the facility.

Mr. Lalit M. Patro, President, CQA & Engineering Services; Responsible for the overall Quality System and engineering services. Mr. Patro reports to Dr. R. Agarwal, Managing Director.

Mr. Rajendra S. Diwan; Head, Operation; Responsible for operational activity. Mr. Diwan Reports to Dr. R. Agarwal, Managing Director.

Mr. Awadhesh Maheshwari, Sr. Vice President, Corporate Quality; Responsible for Quality System and Regulatory Affair. Mr. Maheshwari reports to Mr. Lalit M. Patro, President, CQA & Engineering Services.

Mr. K.R. Jayaram; Vice President, Corporate QA; Responsible for Corporate Quality System. Mr. Jayaram reports to Mr. A. Maheshwari, Sr. Vice President, Corporate Quality.

Mr. K. Jagdish, Dy. General Manager, Engineering & Projects; Responsible for site engineering related activity. MR. Jagdish reports to Mr. Lalit M. Patro, President, CQA & Engineering Services.

Mr. Vishal Anand, Asst. General Manager, Human Resources; Responsible for personal and administrative activity. Mr. Anand reports to Mr. S. Nanda, President-HR.

Mr. Sandeep Chomal; Dy. General Manager, Stores; Responsible for site materials management and warehouse related activity. Mr. Chomal reports to Mr. R. S. Diwan, Head, Operation.

Mr. Nishat Ahmad, General Manager, QA; Responsible for Quality Systems. Mr. Ahmad reports to Mr. K.R. Jayaram, Vice President, Corporate QA.

Mr. Umesh Maniyar, Dy. General Manager, Quality Control; Responsible for site Quality Control. Mr. Maniyar reports to Mr. K.R. Jayaram, Vice President, Corporate QA.

FIRM'S TRAINING PROGRAM

I reviewed the SOP titled, "Training of Personnel", SOP No: QAD/003-15, Effective Date: Dec 2018.

Employees retrieve training via induction training, on-the-job training (OJT), and scheduled trainings. GMP trainings are conducted annually. I reviewed the training records of Operators AP and CS. Additionally, Analysts are qualified on specific functions such as, but not limited to dissolution, assay, and GC. I verified the training of Analysts, DC and JB.

Currently, the firm uses a paper-based tracking system for training. A software-based, Pharmaceutical Learning Management System (PLMS), will be implemented mid-February 2019.

No deficiencies were observed.

MANUFACTURING/DESIGN OPERATIONS

The current inspection of this pharmaceutical manufacturer, Macleods Pharmaceuticals Limited, was conducted under MARCS OP ID 115306. The objective of this inspection was the readiness for commercial manufacturing, conformance to the application, and data integrity audit for NDA-210796 (Dolutegravir, Lamivudine and Tenofovir disoproxil fumarate Tablets, 50/300/300mg) and NDA-210649 (Efavirenz, Lamivudine and Tenofovir disoproxil fumarate Tablets, 400/300/300mg).

In terms of the products subject to this inspection Macleods Pharmaceuticals Limited is responsible for the manufacture of finished dosage forms, testing of raw materials, stability testing, and release testing.

Manufacturing for NDA-210649 and NDA-210796 occurs in the Phase III building. The manufacturing flowcharts for each PAI product was provided **(EXHIBIT-2)**. The process flow occurs in two (2) parts due to both PAI products being a bilayer product.

The process flow of NDA-210649, Efavirenz 400mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets was described as such:

(Efavirenz Part)

Dispensing → Rechecking of Weights → Sifting of Raw Material → Dry Mixing → Granulation → Wet Milling → Drying → Sifting & Milling → Pre-lubrication & Lubrication

(Lamivudine and Tenofovir Disoproxil Fumarate Part)
Dispensing → Rechecking of Weights → Sifting of Raw Material → Dry Mixing → Granulation → Wet Milling → Drying → Sifting & Milling → Pre-lubrication & Lubrication

After the two (2) parts of the process flow are complete the next stages include: compression of both parts → coating → inspection → packing

Additionally, the process flow of NDA-210796, Dolutegravir Sodium 50mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets was described as such:

(Dolutegravir Part)
Dispensing → Rechecking of Weights → Sifting of Raw Material → Dry Mixing → Granulation → Wet Milling → Drying → Sifting & Milling → Pre-lubrication & Lubrication

(Lamivudine and Tenofovir Disoproxil Fumarate Part)
Dispensing → Rechecking of Weights → Sifting of Raw Material → Dry Mixing → Granulation → Wet Milling → Drying → Sifting & Milling → Pre-lubrication & Lubrication

After the two (2) parts of the process flow are complete the next stages include: compression of both parts → coating → inspection → packing

PRE-APPROVAL INSPECTION

The current facility is intended to be used as an alternate manufacturing site for finished dosage forms, testing of raw materials and finished dosage forms, stability testing. Three (3) batches of NDA-210796 and NDA-210649 were previously manufactured, tested, and placed on stability at the firm's Himachal Pradesh site (FEI: 3007517881).

Pre-approval coverage for the two (2) products were performed as part of this inspection:

- NDA-210796, Dolutegravir, Lamivudine and Tenofovir disoproxil fumarate Tablets, 50/300/300mg
- NDA-210649, Efavirenz, Lamivudine and Tenofovir disoproxil fumarate Tablets, 400/300/300mg

The proposed products are bi-layer drug products intended for treatment of HIV-1 infection in combination with other antiretroviral agents.

OBJECTIVE 1: READINESS FOR COMMERCIAL MANUFACTURING

As part of quality system review, the following items were reviewed: SOPs, training, rejections, corrective and preventative actions, out-of-specifications, change controls, retain/reserve sampling program, stability program, receipt and shipping procedures, and non-conformances.

There are adequate procedures in place for change controls, investigations, deviations, CAPAs, complaints, adverse events, and recalls.

Objective 1(a): Manufacturing and laboratory changes, investigations, and trends relating to the development of new drug substance and product manufacturing demonstrate that the establishment has appropriately assessed related issues.

There are written procedures in place for handling OOS, incidents, CAPAs, and deviations. The firm currently uses a paper-based system and log book to log and track the investigations. The firm plans to implement Trackwise for handling of the investigations by Q3 2019.

I reviewed the following SOPs:

- "Incident Reporting in Quality Control Laboratory", SOP No: QCD/098-07, Effective Date: Feb 2018
- "Handling of Laboratory Investigation", SOP No: QAD/033-19, Effective Date: Dec 2018
- "Corrective Action and Preventive Action", SOP No: QAD/063-04, Effective Date: Aug 2015
- "Handling of Deviations", SOP No: QAD/032-7, Effective Date: Dec 2018

Incident reports are applicable up to system suitability. After system suitability incidents are handled via OOS investigations.

I reviewed the following investigations:

Initiated Date	Classification Number	Product Name	Batch Number	Test	Short Description
25/08/18	OOS/104/18	Efavirenz, Lamivudine and Tenofovir Tablets (400mg/300 mg/300mg)	EED7801A EED7801B EED7801C	Assay	During analysis of Assay, Efavirenz was shown to be out of the specifications of 90-110%. The observed results were 148.1%, 147.6%, and 148.8%. The Analyst used the standard solution instead of sample solution for all three (3) samples. The sample

					solution was used and the samples were reanalyzed yielding the results within the specification. The Analyst received additional training as documented within the training record.
06/11/18	OOS/18/135	Dolutegravir Lamivudine and Tenofovir Disoproxil Fumarate Tablets	EDJ802A EDJ802B EDJ802C EDJ802D	Assay	During the analysis of stability sample it was noticed that the results did not comply with the specification limit of assay test (% label claim: 90% to 110.0%) for Dolutegravir. The results were 81.1%, 83/7%, 84.2%, 80.5%. The root cause was determined that the standard peak are obtained was on the higher side. An initial hypothesis was performed, the Analyst received additional training, and the repeat analysis was performed yielding the correct specification results (98.7%, 98.5%, 101.3%, 97.8%).
19/10/18	IR/1270/18	Dolutegravir Lamivudine and Tenofovir Disoproxil Fumarate Tablets	EDJ802	Assay	Absolute difference of % Assay was more than the established limit (NMT 2.0). The analysts was instructed to re-inject the same affected sample from the same vial at the end of the respective sequence after achieving system suitability criteria with bracketing standard.
17/11/18	EDJ802	Dolutegravir Lamivudine and Tenofovir Disoproxil		RSD	%RSD of replicate standard injection for Lamivudine (14.66%) and Tenofovir (14.64%) content did not meet the

		Fumarate Tablets			established limit (NMT 2.0). The Analyst was instructed to flush the system and purge all lines and repeat the analysis in next version of sequence. The system suitability and result were found to be satisfactory.

Objective 1(b): A sound and appropriate program for sampling, testing, and evaluation of components (including APIs), in-process materials, finished products, containers and closures for purposes of releasing materials or products has been established.

A facility diagram was provided. **(EXHIBIT-1, page 11).** The plot area is approximately 4236m^2 + 2160m^2. There are three (3) buildings (Phase I, Phase II, and Phase III) where production, packaging, receiving/storage of materials/components occur. The focus of this current inspection was building Phase II (Warehouse Area) and Phase III (Production Area). Phase I consists of manufacturing of sterile injectable products that are non-US customers.

On 01/21/2018, an initial walkthrough of the firm's warehouse, manufacturing/packaging, analytical and micro laboratory, and utilities area was conducted. The warehouse has separate quarantine and release areas. I observed that the temperature and humidity was being monitored throughout the facility. Through temperature mapping the firm identified where to put each device that displays the temperature and humidity. I verified the calibrations for each device were performed within the specified timeframe of six (6) months.

The warehouse is located in the Phase III building. Temperature/humidity is monitored throughout the warehouse. Calibrations on the temperature/humidity devices occur every six (6) months. I verified the calibration was performed for each device. The devices are placed in specific locations of the facility based on the mapping studies performed.

Incoming materials are verified against the documentation for items such as the correct product, quantity, expiration date, and approved vendor. After the incoming material is verified, the deduster is used and the weight is verified. The receipt is entered into the Electronic Resource Planning (ERP) system and a product code is assigned. I reviewed the following log books:

- "Balance Verification and Calibration Record", Book No. MPL/STR/BOOK/010/01
- "Balance Verification and Calibration Record", Book No. MPL/STR/BOOK/025/01

There are four (4) weight checks. The min and max weights are checked daily. Additionally, all four (4) weights are checked weekly.

Color coded labels are used to identify the status of the material. Black labels are used as a quarantine label, yellow labels are applied for materials under test, and green labels are used to indicate an approved status from QC. I observed a separate locked area for rejected material. A log is maintained for items that are moved into or out of the reject area. The area manager maintains the key for the reject area. Sampling is performed in a designated sampling booth by QC personnel. Once the results are analyzed and are found to meet the criteria it is released and approved by QC.

Raw materials are dispensed to manufacturing via the ERP system. Each raw material is assigned a specific code. This raw material code is verified with production to match the request of materials and batch record.

There is a sampling booth for the near infrared system (NIR) within the warehouse, which is used to determine the identity of raw materials. I reviewed the log book titled, "Sampling Booth (for NIR) Activity Log", MPL/QCD/BOOK/055/01. Additionally, the software used is Vision 4.0. I initially spoke with Mr. Gandhi, Dy. Manager to verify the privileges allowed, review audit trails, and verify the type of controls of the computer operating system. There are three (3) different user roles identified as Operator, Developer, and System Manager. I asked who has full administrative account access and I was informed only IT has this ability. I spoke with an IT personnel, Mr. Bhavin Rathod, Sr. Officer, who has the user role as System Manager. Mr. Rathod provided me with each user and user role **(EXHIBIT-3)**. I expressed my concern that there are multiple individuals with the "System Manager" role, which is the same as the IT Administrator. Additionally, there are no written procedures on the privileges of each user role. I was informed that the privileges of each user role have default settings and cannot be changed. Refer to **OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE, Observation #2**.

I observed the production areas appeared to be adequate size and design to perform the necessary operations. The facilities appeared to be maintained in an acceptable manner. I reviewed the flow of materials and personnel for the prevention of cross-contamination (raw materials, APIs, through finished products) using the facility diagrams as well as during the walkthrough of the manufacturing facilities and no objectionable conditions were observed.

Production performs in-process sampling every one (1) hour and QA performs sampling every two (2) hours. In-process checks consists of appearance, weight, hardness, friability, thickness disintegration time. I reviewed the in-process checks for both NDA-210796 and NDA-210649. Additionally, I reviewed the amounts used for sampling. I did not observe and objectionable conditions.

There are four (4) packaging lines. There is (1) packaging line for bottle packaging of products intended for the US market. Additionally, there is one (1) bottle line and two (2) lines for blister packaging, which are used to package products not intended for the US market. Prior to packaging, there is a 100% inspection of all capsules/tablets. The capsules/tablets are placed in the "Tablet/Capsule Storage Area" until packaging occurs. Bottles are cleaned with condensed air in the "Bottle Cleaning Area". In the case of tablets, packaging occurs as such:

Tablets placed in hopper and packaged into bottles → induction sealing → capping → secondary packaging (occurs in Phase III building) → weight of bottles verified with check weigher → labels affixed and verified → outsert placed on bottle cap → manually packaged into cardboard box.

The check weigher will reject any bottles that do not meet the weight criteria. A weight challenge is performed at the start and end of packaging. I reviewed the log book associated with the weight challenge and did not observe in discrepancies.

Only one (1) product is allowed on the packaging line during packaging operations. The packaging lines are cleared at the end of each packaging run to ensure no product and/or packaging material remains on the line. The line clearance is verified by the Operator and Supervisor. Labels are held under lock and key and only accessed by QA. Label and packaging material reconciliation checks are performed in the batch records.

Objective 1(c): The establishment has sufficient facility and equipment controls in place to prevent contamination of and by the application product (or API).

I verified that each piece of equipment identified for use in commercial manufacturing for NDA-210796 and NDA-210649 was on-site. I was provided with a list of the equipment intended to be used in commercial manufacturing and the qualification dates. **(EXHIBIT-4)**

I reviewed the SOP titled, "Performing of Equipment Validation (Equipment Qualification), SOP No: QAD/026-08, Effective Date: June 2018. New equipment is initially qualified, and a re-qualification occurs two (2) years after the initial qualification and every three (3) years thereafter.

I reviewed the following equipment qualifications:

- Rapid Mixer Granulator (Equipment No: EQ/PTF/003); "Performance Qualification", Report No: MPL/PTF/RPQ/003/00, Approved 15/03/14
- Rapid Mixer Granulator (Equipment No: EQ/PTF/003); "Requalification Protocol", Protocol No: MPL/QAD/PRQ/001/00, Report No: MPL/PTF/RRQ/003/00, Approved 26/03/16
- Fluid Bed Dryer (Equipment No: EQ/PTF/006); "Performance Qualification", Report No: MPL/PTF/RPQ/006/00, Approved 03/28/14
- Fluid Bed Dryer (Equipment No: EQ/PTF/006); "Requalification Protocol", Protocol No: MPL/QAD/PRQ/001/00, Report No: MPL/PTF/RRQ/006/00, Approved 02/04/16
- Compression Machine (Equipment No: EQ/PTF/225); "Performance Qualification", Report No: MPL/PTF/RPQ/225/00, Approved 30/08/16
- Compression Machine (Equipment No: EQ/PTF/225); "Requalification Protocol", Protocol No: MPL/QAD/PRQ/001/00, Report No: MPL/PTF/RRQ/225/00, Approved 18/08/18
- Granscoater 60" (Equipment No: EQ/PTF/028); "Performance Qualification", Report No: MPL/PTF/RPQ/028/00, Approved 07/02/14

- Granscoater 60" (Equipment No: EQ/PTF/028); "Requalification Protocol", Protocol No: MPL/QAD/PRQ/001/00, Report No: MPL/PTF/RRQ/028/01, Approved 04/02/16
- In-line Capper Machine (Equipment No: EQ/PTF/051; "Requalification Protocol", Repot No: MPL/PTF RRQ/051/00, Approved 02/05/16
- Tablet/Capsule Counter PP-12 (Equipment No: EQ/PTF/220; "Requalification Protocol", Report No: MPL/PTF/RRQ/220/00, Approved 08/01/18

Additionally, I reviewed the equipment log books associated with each major piece of equipment intended to be used in the commercial manufacturing of the PAI products.

I did not observe any deficiencies.

Water System

The reverse osmosis purified water system is located in Phase II building and provides purified water for manufacturing the in Phase III building. I reviewed the log book titled, "Logbook for Water Treatment Plant Phase II", MPL/UTI/BOOK/016/01. The firm monitors the pH, conductivity, TOC, microbial, and temperature of the purified water system. A sterilization is performed weekly. The temperature of the water is increased to 85°C or above and circulates the loop for one (1) hour and then drained.

The firm tracks/trends the test results on a quarterly and annual basis. I reviewed the hard copy reports for the annual water trend reports for 2018. Additionally, I reviewed the electronic Excel Spreadsheets used to track/trend the data. I did not observe any out of limit trends and/or excursions.

Cleaning Validation

I reviewed the following cleaning documents:

- "Cleaning Validation Report", Protocol Reference No. MPL/PTF/PCV/01, Rev. 00, Effective Date 21/12/17 for 300 L Bin Blender
- "Verification of Cleaning Process", MPL/PTF/PLV/03, Report No. MPL/PTF/RVC-ED7/00 **(EXHIBIT-5)**
- "Report for Verification of Cleaning Process", Report No. MPL/PTF/RVC-DJ/00 **(EXHIBIT-6)**
- "Procedure for Cleaning Validation Program", SOP No: QAD/074-06, Effective Date: Dec 2017
- "Cleaning of Equipments", SOP No: PRD/077-09, Effective Date: Aug 2018

When new products and/or new equipment are added in the manufacturing area a cleaning verification is performed. I reviewed the current cleaning verifications and SOPs. For each piece of

equipment there is an associated SOP on how to clean the equipment. Additionally, a cleaning checklist is in the batch manufacturing records (BMR) to ensure the proper cleanliness.

There are two (2) types of cleanings conducted and identified as Type A and Type B. Type A cleaning is initiated between batches of the same product. Type B cleaning is initiated during the change of different products. Swab and rinse samples are taken every ten (10) consecutive Type-B cleanings and every new product introduction in the facility. Currently, the firm has not had any swab and/or rinse failures.

Objective 1(d): Adequate procedures exist for change control; investigating failures, deviations, complaints, and adverse events; conducting recalls; and for reporting this information to FDA.

I reviewed the SOP titled, "Change Control", SOP No: QAD/030-16, Effective Date: Jan 2019. Additionally, I reviewed the following change controls:

Initiated Department	Change Control No.	Proposed Changes
QA	CCD/8475	Product Dolutegravir sodium 50mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets are to be manufactured at Daman, Unit-II facility. New BMR is to be prepared for exhibit batches.
QA	CCD/8561	New BPRs for Dolutegravir sodium 50mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets.
QA	CCD/8651	New BMR for Dolutegravir sodium 50mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets.
QA	CCD/8460	Efavirenz Lamivudine Tenofovir Disoproxil Fumarate Tablets 400/300/300mg intended to be manufactured at Damn, Unit II location.
QA	CCD/8417	New BPRs of Efavirenz Lamivudine Tenofovir Disoproxil Fumarate Tablets 400/300/300mg are to be prepared for packing of product for USA (stability) market.
QA	CCD/8943	New BMRs of Efavirenz Lamivudine Tenofovir Disoproxil Fumarate Tablets 400/300/300mg tablets with batch size.

No discrepancies were observed.

Limited coverage was given for complaints since the two (2) PAI products have not been commercially distributed. The firm has not been involved in any recalls since the last inspection. Refer to **RECALL PROCEDURES** section for additional information.

Objective 1(e): The feasibility of the proposed commercial process and manufacturing batch record, including instructions, processing parameters and process control measures, are scientifically and objectively justified. This objective is linked to the firm's process validation program.

Validation/Verification Studies

Currently, the facility has performed the process validation for one batch of each PAI product. The intention is to perform the process validation for three (3) batches of each PAI product. Once the process validations are performed for all three (3) batches the process validation will be approved pending acceptable results. I reviewed the following documents related to process validation:

- "Process Validation Protocol of Dolutegravir Sodium 50mg, Lamivudine 300mg, and Tenofovir Disoproxil Fumarate 300mg Tablets", Protocol No: MPL/PTF/PPV/DJ/01 **(EXHIBIT-7)**
- "Process Validation Report of Dolutegravir Sodium 50mg, Lamivudine 300mg, and Tenofovir Disoproxil Fumarate 300mg Tablets", Report No: MDL/PTF/RPV/DJ/01
- "Process Validation Protocol of Efavirenz 400mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets", Protocol No: MPL/PTF/PPV/ED7/00 **(EXHIBIT-8)**
- "Process Validation Report of Efavirenz 400mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets", Report No: MPL/PTF/RPV/ED7/00
- "Process Standardization and Validation", SOP No: QAD/025-16, Effective Date: Sep 2018

The process validation was verified against the manufacturing batch records to ensure the proper procedures were outlined. Additionally, samples are taken during each stage of the manufacturing process (granulation, compression, and coating) per protocol. I verified results of the analytical testing, such as assay, loss of drying (LOD), uniformity weight, hardness, thickness, friability, and disintegration time. No discrepancies were noted during the process validation during the first batch of each PAI product.

Hold Time Studies

I reviewed the following documents:

- "Hold Time Study of Dolutegravir Sodium 50mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets", Protocol No: MPL/PTF/PHT/DJ/01
- "Hold Time Study of Efavirenz 400mg, Lamivudine 300mg, and Tenofovir Disoproxil Fumarate 300mg Tablets", Protocol No: MPL/PTF/PHT/ED7/00

The hold time study was conducted for the binding and coating solutions carried out for 48 hours, lubricated blend and uncoated tablets carried out up to forty-five (45) days, and coated tablets carried

out up to 100 days. I reviewed the results of the analytical and microbial tests performed during the study. I did not observe any discrepancies.

OBJECTIVE 2: CONFORMANCE TO APPLICATION

During this current inspection I reviewed the CMC section of both NDAs and verified the API manufacturers, formulation, manufacturing methods, and analytical methods were consistent with the descriptions contained in the CMC section of both applications. Currently, there are no plans to scale-up commercial batches from manufactured exhibit/submission batches.

API Manufacturers

I verified the vendors for the API are the same as reported in the CMC section. I did not observe any other records indicating a different API manufacturer or quality from that described in the application.

I received a list of APIs/excipients and associated vendors used during the manufacturing of the exhibit batches and intended to be used for commercial manufacturing for NDAs 210649 and 210796. **(EXHIBIT-9)**

I reviewed the vendor information for the following APIs:

Name of API	Manufacturer	Approval Date
Lamivudine	Hetero Labs Limited	05/06/17
Lamivudine	Shanghai Desano Chemical Pharmaceutical	26/06/18
Efavirenz USP/HIS DMF Grade	Laurus Labs Limited	07/09/18

Note: Dates are in DD/MM/YY format

I did not observe any discrepancies.

Batch Record Review

I reviewed the submitted executed batch records and unexecuted Master batch records. To date the firm has manufactured two (2) batches for Dolutegravir Sodium 50mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets, Batch Numbers: EDJ801 and EDJ802. Batch Number EDJ802 was submitted to the Agency as the exhibit batch due to a change in the excipient, sodium starch glycolate. I reviewed the associated change control, CCD/8899, Date: 24/8/18.

Additionally, the firm has manufactured one (1) batch for Efavirenz 400mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets, Batch Number: EED7801.
I reviewed the following batch records:

- Batch Manufacturing Record, Dolutegravir Sodium 50mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets, Effective Date: 22/05/18, MFG Start Date: 24/05/18, MFG Completion Date: 09/06/18, Batch No: EDJ801, Batch Size: 280,000 Tablets
- **Batch Manufacturing Record, Dolutegravir Sodium 50mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets, Effective Date: 05/09/18, MFG Start Date: 10/09/18, MFG Completion Date: 17/09/18, Batch No: EDJ802, Batch Size: 280,000 Tablets
- **Batch Manufacturing Record, Efavirenz 400mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets, Effective Date: 12/05/18, MFG Start Date: 18/05/2018, MFG Completion Date: 29/05/2018, Batch No: EED7801, Batch Size: 140,000 Tablets
- **Batch Packaging Record, "Dolutegravir Sodium 50mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets, Effective Date: 04/06/18, Packaging Start Date: 08/06/18, Packaging Completion Date: 09/06/18, Batch No: EED7801A, Batch Size: 21,600 Tablets

I compared the batch records to those submitted to the Agency. I did not observe any discrepancies.

Note: **Denotes the exhibit batch records submitted to the Agency.

Stability Studies

The firm has written stability procedures. Stability testing is conducted as per product specific stability protocols and contains full details of the stability test requirements.
I received and reviewed the following documents:

- "Stability Protocol for Dolutegravir Sodium, Lamivudine and Tenofovir Disoproxil Fumarate Tablets (50mg/300mg/300mg), Protocol No: STA/FG-1589-00, Effective Date: Jun 2018
- "Stability Protocol for Efavirenz, Lamivudine and Tenofovir Disoproxil Fumarate Tablets (400mg/300mg/300mg), Protocol No: STA/FG-1587-00, Effective Date: Jun 2018
- "Procedure for Stability Programme", SOP No: QAD/096-01, Effective Date: Dec 2018
- Stability Summary Data Sheet for Batch Numbers: EDJ801A, EDJ801B, EDJ801C, EDJ801D, EDJ802A, EDJ802B, EDJ802C, EDJ802D
- Stability Summary Data Sheet for Batch Numbers: EED7801A, EED7801B, EED7801C

I observed the summary report for the 6-month time point for accelerated conditions of Dolutegravir Sodium, Lamivudine and Tenofovir Disoproxil Fumarate Tablets (50mg/300mg/300mg), Temperature: 40 +/- 2C, RH 75 +/- 5% for Batch No: EDJ0801B showed the study was started on 21st June 2018 and the withdrawal for the 6-month time point was documented as being performed on 12/12/2018. **Refer to GENERAL DISCUSSION WITH MANAGEMENT, Discussion Item #1.**

Stability samples are tracked with monthly stability planner/schedule and pulled for testing by the stability coordinator. There is a total of eight (8) stability chambers on-site and the chambers are continuously monitored and equipped with local audible alarms. I verified there are log books for

stability sample reconciliation, stability sample withdrawal, and for the opening and closing of the chambers.

Finished Product Testing

I reviewed the following documents:

- "Finished Product Specification (Release)", Dolutegravir Sodium, Lamivudine and Tenofovir Disoproxil Fumarate Tablets (50mg/ 300mg/ 300mg), Specification No: SPC/FG-1589-00
- "Finished Product Specification (Release)", Efavirenz, Lamivudine and Tenofovir Disoproxil Fumarate Tablets (400mg/300mg/ 300mg), Specification No: SPC/FG-1587-01

I verified the results of the finished product testing via analyst worksheets, electronic records, certificate of analysis, and batch manufacturing records. No discrepancies were observed during the review.

Analytical Methods

Mr. S. Senthilkumar, Validation, from the Mumbai R&D center provided information about the analytical methods. Analytical methods were developed at the firm's Mumbai site and transferred to the current facility.
I reviewed the following documents:

- "Analytical Method Validation Protocol for ID of Dolutegravir, Lamivudine, and Tenofovir Disoproxil Fumarate by TLC", Protocol No: IVP/2016/731/00
- "Analytical Method Validation Protocol for Assay of Dolutegravir, Lamivudine, and Tenofovir Disoproxil Fumarate", Protocol No: AVP/2016/728/00
- "Analytical Method Validation Report for Assay of Dolutegravir, Lamivudine, and Tenofovir Disoproxil Fumarate", Report No: AVR/2016/728/00
- Analytical Method Validation Protocol for Related Substances of Dolutegravir, Lamivudine, Tenofovir Disoproxil Fumarate", Protocol No: RVP/2016/727/00
- Analytical Method Validation Report for Related Substances of Dolutegravir, Lamivudine, Tenofovir Disoproxil Fumarate", Report No: RVR/2016/727/00
- Analytical Method Transfer Protocol and Report", Document Number: AMT/2018/052/00, Approved 14/05/2018

I did not observe any deficiencies.

Reference/Working Standards

I did not find any deficiencies with the handling and storage of HPLC reference and in-house working standards.

OBJECTIVE 3: DATA INTEGRITY AUDIT

The Analytical Laboratory is responsible for the testing of raw materials, packaging materials, in process, finished product and stability samples. The Analytical Laboratory is equipped with instruments to support the QC testing needs of the PAI products, such as HPLC, Gas Chromatographs (GC), Karl Fischer Titrator, FTIR, UV, Dissolution Apparatus. All laboratory equipment is identified with the equipment number and calibration labels. Each major piece of equipment has a log book containing sample test information and calibration/PM records. I verified the equipment in the laboratory was calibrated and the PM was performed within the specified timeframes.

While reviewing the "Daily Verification Record of Karl Fischer Factor", I observed blank controlled copies issued by QA were readily available to Analysts. Additionally, I observed there were four (4) blank pages titled, "Electronic Data Review Record of Standalone System, FRM/QCD/292/03 and sixteen (16) pages titled, "Daily Verification Record of Karl Fischer Factor, FRM/QCD/479/01. Refer to **OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE, Observation #1**.

The Microbiology Laboratory is responsible for conducting microbial test on raw materials, finished product, purified water samples, and environmental monitoring. The Microbiologists are responsible for entering data into MS Excel Spreadsheets to track/trend environmental monitoring data for quarterly trend reports. I spoke with Mr. Krishna Kumar Putnah, Manager-I, who showed me how to access the MS Excel documents. I was able to verify the Excel Spreadsheets required a passcode to access. Additionally, QC is responsible to entering data into the MS Excel Spreadsheets for the quarterly/annual reports.

The software Chromeleon 6.8 is used for HPLC and GC. The system is password protected. I reviewed the user types and privileges and IT is listed as the System Administrator. Additionally, I verified audit trails were enabled. The computer operating system does not allow individuals to change/time date function. Additionally, I reviewed the SOP titled, "User Management for Chromeleon Chromatographic Data Management System (CDMS)", SOP No: QCD/178-B, Effective Date: Jan 2019.

I reviewed the SOP titled, "Backup Procedure for Electronic Data', ITD/030-02, Effective Date: Nov 2018. Both daily and monthly (after the 15th of each month) backups are conducted and captured on tape cartridges that remain in the custody of the IT department. I reviewed the records and screenshots of the backups being performed and did not observe discrepancies.

I reviewed the electronic and hardcopy data of the firm's manufacturing and analytical records against the data submitted in the CMC section of the application. I verified the executed manufacturing batch records and the associated electronic and raw analytical data to support the exhibit batches, including the stability and dissolution profile studies submitted to the agency. I reviewed the firm's electronic chromatographic data, printed raw data, original test worksheets, and

analytical logbook entries. The data I reviewed was found to be complete and match the submitted data.

MANUFACTURING CODES

The batch numbering code consists an alpha-numeric code. The batch numbering code is explained as such:

EWXYZZ

Where E is used to denote the site, WX is a product code of two to three characters (the first character is the first letter of the product), Y is the last digit of the year manufactured, and ZZ is a sequential number (starting at 01) for the year that will expand to three digits at the 100th batch.

Example: EDJ802

E = Block Code
DJ = Product Code
8 = Year (2018)
02 = Second batch of same product

COMPLAINTS

I reviewed the SOP titled, "Handling of Complaints", SOP No: QAD/035-11, Effective Date: Jan 2019.

Limited coverage was given for this section since the two (2) PAI products have not been commercially distributed.

RECALL PROCEDURES

I reviewed SOP titled, "Product Recall", SOP No: QAD/035-11, Effective Date: Jan 2019.

The firm has not been involved in any recalls since the previous inspection. A mock recall is performed annually according to SOP QAD/035-11. I reviewed the mock recall approved on 22/08/2017. At the time of the mock recall the SOP titled, "Product Recall", SOP No. QAD/035-10, Effective Date: 26/10/16 was followed, which states a mock recall shall be performed every two (2) years.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

OBSERVATION 1

Specifically,

The responsibilities and procedures applicable to the quality control unit are not fully followed. Specifically, during the tour of the Analytical Laboratory on 01/21/2019 I observed unused copies of controlled documents in an unlocked drawer. The controlled documents included the following:

• Four (4) unused pages titled, "Electronic Data Review Record of Standalone System, FRM/QCD/292/03. The documents were released by QA to the QC Analytical Laboratory, signed and dated "Controlled Copy" on 04/01/19.

• Sixteen (16) unused pages titled, "Daily Verification Record of Karl Fischer Factor, FRM/QCD/479/01, The documents were released by QA to the QC Analytical Laboratory, signed and dated "Controlled Copy" on 28/12/18.

Reference: 21 CFR 211.22(d)

Supporting Evidence and Relevance: During the walkthrough of the Analytical Laboratory on 01/21/2018 I observed copies of four (4) unused pages titled, "Electronic Data Review Record of Standalone System, FRM/QCD/292/03 **(EXHIBIT-10)** and sixteen (16) unused pages titled, "Daily Verification Record of Karl Fischer Factor, FRM/QCD/479/01 **(EXHIBIT-11)**. These copies were located in an unlocked drawer where Analyst can obtain the copy without any documentation or tracking. I explained to the firm's Management the importance of not allowing controlled documents to be accessible to where there is no traceability to prevent errors and/or data integrity issues.

Discussion with Management: The firm's management acknowledged the observation and will submit a voluntary response within fifteen (15) business days.

OBSERVATION 2

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,

During the tour of the materials warehouse in Phase II, I observed identity testing of incoming raw materials, such as active pharmaceutical ingredients (API) and excipients is conducted via near infrared spectrophotometer (NIR). The software identified for NIR is Vision 4.0. I observed that your Dy. General Manager, QC has the role as System Manager. Furthermore, this is the same user role give to your IT department, who is the responsible Administrator for the system.

Reference: 21 CFR 211.68(b)

Supporting Evidence and Relevance: On 01/21/2019, during the walkthrough of the materials warehouse I observed there was an area to perform NIR testing on raw materials. The current software being used is Vision 4.0. I asked for a printout of the current users and privileges **(EXHIBIT-3)**. I was by IT personnel that only IT will have the role as System Manager. According to the list of current users and privileges Mr. Umesh Maniyar, Dy. General Manager, QC also has role as System Manager.

Discussion with Management: The firm's management acknowledged the observation and will submit a voluntary response within fifteen (15) business days.

REFUSALS

There were no refusals during the current inspection.

GENERAL DISCUSSION WITH MANAGEMENT

A closing meeting was held on 01/25/2019 and a two (2) item 483 was issued to the firm's management. A list of attendees was provided **(EXHIBIT-12)**. Additionally, the following item was verbally discussed:

Discussion Item #1: The summary report for the 6-month time point for accelerated conditions of Dolutegravir Sodium, Lamivudine and Tenofovir Disoproxil Fumarate Tablets (50mg/300mg/300mg), Temperature: 40 +/- 2C, RH 75 +/- 5% for Batch No: EDJ0801B showed the study was started on 21st June 2018 and the withdrawal for the 6-month time point was documented as being performed on 12/12/2018. The withdrawal date of 12/12/2018 was a typographical error and should have been listed as 21/12/2018. I reviewed the Stability Study schedule and found the correct date of withdrawal was 21/12/2018.

ADDITIONAL INFORMATION

There is no additional information to report at this time.

SAMPLES COLLECTED

No samples were collected.

VOLUNTARY CORRECTIONS

During the current inspection I verified the corrections to the firm's two (2) item 483 issued during the previous inspection conducted 05/22-29/2017. The previous inspectional observations included the following:

OBSERVATION 1

Established laboratory control mechanisms are not followed.

Specifically,

1.) Planned deviation PDR/509 allowed dissolution baths (EQ/QCD/002, EQ/QCD/076, EQ/QCD/083) that were not in a calibrated state to be used to test and disposition finished drug products. A total of 425 batches were tested before the instruments were returned to a calibrated state.
2.) Crospovidone USP reference standard, lot H0I211, was observed on 05/23/2017 to be incorrectly stored. The label on the bottle indicates to store the material in a desiccator once removed from its hermetic bag. The material was observed without its hermetic bag and stored in a refrigerator and not in a desiccator.
Correction:

1.) The SOP titled, Calibration of Measuring and Test Equipment", SOP No: QCD/082-10, Effective Date: Jul 2017, Section 4.11 was updated. Currently, the SOP states "if any instrument calibration date is due put the instrument status under calibration and do not use".
2.) During my tour of the Analytical Laboratory I did not observe any discrepancies with the use/storage of working/reference standards.

OBSERVATION 2:

Employees engaged in the manufacture of a drug product lack the training required to perform their assigned functions.

Specifically,

on 05/18/2017, training on SOP PTF/019-02 for the cleaning and operation of the Gansons vibratory sifter was given to employee VT. The employee answered 60% of the evaluation questions correctly. According to the firm's SOP QAD/003-11 on training, an employee must have a minimum 80%

correct on a written evaluation to demonstrate effective training. A score below 80% requires re-training. Because the evaluation had been scored incorrectly, no re-training was given to the employee.

Correction:

The firm now uses a four (4) part verification system to ensure the employee assessments are properly reviewed. Additionally, the firm is planning to implement a new software training program, Pharmaceutical Learning Management System (PLMS) by mid-February 2019.

I did not observe any discrepancies during my review of the training records.

EXHIBITS COLLECTED

EXHIBIT-1 Presentation, 30 pages
EXHIBIT-2 Manufacturing Process Flow, 12 pages
EXHIBIT-3 List of Users/User Roles for software, Vision 4.0, 1 page
EXHIBIT-4 Equipment List, 4 pages
EXHIBIT-5 Verification of Cleaning Process, MPL/PTF/PLV/03, Report No. MPL/PTF/RVC-ED7/00, 18 pages
EXHIBIT-6 Report for Verification of Cleaning Process, Report No. MPL/PTF/RVC-DJ/00, 18 pages
EXHIBIT-7 Process Validation Report of Dolutegravir Sodium 50mg, Lamivudine 300mg, and Tenofovir Disoproxil Fumarate 300mg Tablets, Report No: MDL/PTF/RPV/DJ/01, 35 pages
EXHIBIT-8 Process Validation Report of Efavirenz 400mg, Lamivudine 300mg and Tenofovir Disoproxil Fumarate 300mg Tablets, Report No: MPL/PTF/RPV/ED7/00, 34 pages
EXHIBIT-9 Approved Vendor List, 38 pages
EXHIBIT-10 Unused pages titled, "Electronic Data Review Record of Standalone System, FRM/QCD/292/03, 1 page
EXHIBIT-11 Unused pages titled, "Daily Verification Record of Karl Fischer Factor, FRM/QCD/479/01, 1 page
EXHIBIT-12 List of attendees for closing meeting on 01/25/2019, 1 page

ATTACHMENTS

- FDA FORM 483, "INSPECTIONAL OBSERVATIONS", issued on 01/25/2019, 3 pages
- Initial Field Recommendation, 2 pages

Marcus Ray -S

Digitally signed by Marcus Ray -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Marcus Ray -S, 0.9.2342.19200300.100.1.1=2001597816
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