U.S. FOOD & DRUG ADMINISTRATION

DEPARTMENT OF HEALTH & HUMAN SERVICES

US Food & Drug Administration
Center for Biologics Evaluation & Research
Office of Compliance & Biologics Quality
Division of Manufacturing & Product Quality

Establishment Inspection Report

Catalent Maryland, Inc.
7555 Harmans Rd
Harmans, MD 21077

FEI Number: 3015434301

Inspection Dates: March 6-10, 2023

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1 SUMMARY

This section written by VM.

The authors (inspectors) of this report are Viviana Matta, with initials "VM"; Grace Forsythia Igot, with initials "GFI"; Kevin Matthews, with initials "KM"; Sukyoung Sohn, with initials "SS"; and Emmanuel Adu-Gyamfi, with initials "EA". The author of each section written will be identified by the person's initials.

A pre-license inspection (PLI) of Catalent Maryland, Inc. located in Harmans, MD, was conducted by team members of CBER in support of Biologics License Application (BLA) STN 125781/0 submitted by Sarepta Therapeutics, Inc. for the product delandistrogene moxeparvovec, an adeno-associated virus (AAV) vector-based gene therapy to treat the proximate cause of Duchene Muscular Dystrophy

The inspection was conducted in accordance with Compliance Program Guidance Manual-45 Biological Drug Products 7345.848. The equivalent of a Level 1 inspection was performed under Product Code 57N (Human Cell and Gene Therapies (e.g., Cell Therapies, Vectors, Genetically Modified Cells)) and Program Code 41848A (Pre-License Inspection-Somatic Cell and Gene Therapy). The inspection included coverage of all manufacturing areas associated with receipt, production, testing, storage and distribution of the drug substance and related quality systems, in addition, evaluation of the quality systems, production systems, facilities and equipment systems, packaging and labeling systems, material systems and laboratory control systems.

The last inspection of Catalent Maryland, Inc. facility by the FDA was conducted from 01/18/2023 to 01/24/2023 as part of the OBPO Branch FY' 2023 Workplan. The inspection covered the manufacturing operations of the licensed product, Zolgensma DSI, and the firm's investigation and corrective actions related to the cross-contamination of one lot of SRP9001 (Sarepta drug substance) with the AstraZenca COVID vaccine viral vector. The inspection included coverage of the Quality, Laboratory Control, Facilities/Equipment and Materials Systems. No FDA Form-483, Inspectional Observations, was issued. The inspection was classified as No Action Indicated (NAI).

At the conclusion of this inspection, an FDA Form-483 (**Attachment 2**) containing two observations was issued and discussed with the firm's management on March 10, 2023. The observations are summarized as follows: the Quality Unit failed to ensure the integrity and effectiveness of the Quality Management System and to address issues that have the potential to impact the integrity of the product. The FDA Form-483 was issued and discussed with Mr. Joe Torres, Vice President of Operations. All FDA correspondences, including the FMD-145, should be addressed to Mr. Joe Torres, Vice President of Operations, at the address below.

2 ADMINISTRATIVE DATA

This section written by VM

Firm Name and Address

Catalent Maryland, Inc.

7555 Harmans Rd

Harmans, MD 21077

Phone: 1-410-975-4050

Email: joe.torres@catalent.com

FEI Number: 3015434301

Hours of Operation

Administrative hours are 8:00am to 5:00pm.

FDA Inspection Team Members

The inspection team was comprised of CBER staff.

Lead inspector – Viviana Matta, Consumer Safety Officer (CSO), OCBQ/DMPQ/B2

Inspector – Grace Forsythia Igot, Biological Reviewer, OCBQ/DMPQ/B2

Inspector – Kevin Matthews, CSO, OCBQ/DMPQ/B3

Inspector - Sukyoung Sohn, Biologist, OTP/OGT/DGT1/GTB1

Inspector - Emmanuel Adu-Gyamfi, Biologist, OTP/OGT/DGT1/GTB1

Dates of Inspection: 03/06/2023-03/10/2023. All inspectors were present all days of the inspection.

Presentation of Credentials

We (VM, GFI, KM, SS and EA) presented our FDA credentials to Mr. Joe Torres, Vice President on 03/06/2023 and issued the FDA 482 Form, Notice of Inspection (**Attachment 1**).

Persons Interviewed

A list of all individuals interviewed during this inspection and their area(s) of expertise is submitted as **Exhibit VM-1**.

Refusals

No refusals were encountered during the inspection; the firm was cooperative and professional.

Correspondence Should Be Sent To:

Mr. Joe Torres, Vice President of Operations

Catalent Maryland, Inc.

7555 Harmans Rd

Harmans, MD 21077

3 HISTORY of BUSINESS

This section written by VM

Paragon was founded in 1990 at University of Maryland (UMD) BioPark in Baltimore, MD. In May 2019, Catalent Inc. acquired Paragon. In September 2019, Paragon Biosciences Inc., was renamed Catalent Maryland, Inc. The principal executive offices are located at 14 Schoolhouse Road, Somerset, New Jersey. Catalent continues to operate as a contract manufacturer of clinical and commercial cell and gene therapy products, and of COVID vaccine drug substance. Operations of this site include cell bank manufacturing, bulk production, aseptic filling, inspection & packaging, and quality control testing.

The following major changes took place after the previous inspection:

- Ms. Christine Bouril appointed Director of Environmental Health and Services
- Mr. Jeff Lukowski terminated as Senior Director of Supply Chain
- Implementation of the inventory management system, (b) (4)

4 INTERSTATE COMMERCE

This section written by VM

Catalent is a CMO that manufactures delandistrogene moxeparvovec drug substance under pending BLA STN 125781/0. The drug substance is shipped to Catalent Pharma Solutions Paragon (BioPark) located at 801 West Baltimore St., Suite 105, Baltimore, MD 21201. The drug product is intended for marketing in the US. The firm also manufacutures the drug substance intermediate (DSI) for the licensed product, Zolgensma.

5 MANUFACTURING OVERVIEW

This section written by VM

Delandistrogene moxeparvovec drug substance is manufactured by (b) (4)

The (b) (4) drug substance manufacturing process includes the following unit operations:

(b) (4)

The (b) (4) drug substance (b) (4) process includes the following unit operations:

(b) (4)

The Manufacturing unit is responsible for all manufacturing operations and the Quality unit is responsible for all testing and material release.

6 FACILITY OVERVIEW

This section written by VM

All access to the GMP manufacturing rooms is limited to authorized and trained personnel. Entrance into the rooms is controlled by key card access. Building (b) (4) consists (b) (4)

Areas used for manufacture of delandistrogene moxeparvovec are delineated on the table below:

(b) (4)

Suites (b) (4) are dedicated for the manufacture of delandistrogene moxeparvovec. Supporting areas such as (b) (4), warehouses, cold storage and QC testing labs are shared.

All suites have the same room classification (ISO (b) (4) and equipment design. A list of equipment and square footage for each suite is submitted as **Exhibit VM-3**. Open operations include (b) (4) These operations are performed within a Biosafety Cabinet (BSC) qualified for ISO (b) (4) conditions. All other operations are closed and performed using single use materials. Hallways within the manufacturing suites area are classified as ISO (b) (4)

No objectionable conditions were noted.

7 QUALITY SYSTEMS

This section written by GFI

The firm's quality systems policy is delineated in CPS-QP-1001: *Corporate Quality Manual*, effective 12/06/2020. This document is a single foundational harmonized approach for Quality Management System (QMS) that provides GMP quality controls integrated with elements of Quality management, Quality Assurance, and the use of Quality by Design and risk management tools. Catalent's QMS comprises the set of interrelated and interacting quality systems used to direct and control how quality policies and standards are implemented. These interrelated systems are as follows: Facilities and Equipment System, Production System, Material System, Packaging and Labeling System, and Laboratory Control System. For each system, they are supported by subsystems: quality documentation (document control, electronic systems, and control of records), responsibilities of management and all employees (review, internal communication, and responsibilities as a unit), resources (HR, training, and facility), product realization (design and development, change control, quality by design, customer related processes such as requirements and communication, purchasing process, qualification, purchasing information, and verification of purchased product), and measurement, analysis and improvement (internal audits, control of non-conforming products, continuous improvements, corrective actions/ preventative actions).

I requested a copy of the firm's quality systems policy and reviewed the document. No objectionable conditions were noted.

7.1 Change Control

This section written by GFI

The Standard Operating Procedure (SOP) for the handling of change controls, 05.0174: *Change Control Management in* (b) (4) *,* effective 01/28/2022, was requested. Per the procedure, a Change Control Review board (CCRB) will have recurring meetings to review all change proposals. Change control is initiated through opening a new Change Control REC (record) in (b) (4) by the "Change Owner". Several fields are documented in the record including a short description, assigned to, due date, department, reason for change, scheduled start date, classification, and type and other details specific to the change control.

A risk analysis is included and a Subject Matter Expert (SME) in each area identifies the risk involved in the change. After consulting with all impacted areas (including assessor/approver matrix), the "Change Owner," and impacted department assessors will determine action items to complete the change. A child record is created for each type of action item which includes details of the action such as a short description, who the action is assigned for completion, the due date the action needs to be completed and the department, and other details for the action item. The Change Owner adds the for the approval panel and a separate QA approver. Once the SME approvers have approved, the QA approver will be notified for a final review and closure of the record. If additional action items are need and the QA rejects the closure, the record is moved back to final review.

Once the QA reviewer approves the action items and the change control, the record is sent to client representatives for approval. Once the client is satisfied with the change control, they will sign and date the record for approval. The change owner will perform "Route for closure" activities and move the record state to "Closed- Done." Extension requests can be created for child record (except for changes initiated from regulatory or customer commitments) and will need QA approval.

I reviewed their SOP for handling change controls and no objectionable conditions were noted.

7.2 Deviation Management

This section written by VM

The firm's standard operating procedure for handling of deviations, 05.0240: Deviation Management in (b) (4), effective 5/26/2022, was reviewed. The firm uses (b) (4) electronic software system for deviation management. I requested a list of deviations for the past two years. Based on impact, the deviations were classified as Critical, Major or Minor. The firm's standard operating procedure for handling Corrective and Preventive Actions (CAPAs), 05.1266: CAPA Management in (b) (4), effective 03/01/2023, was reviewed. CAPAs are tracked in the (b) (4) system from creation to implementation and approval. Effectiveness checks are created for CAPAs where the expected change in outcome may be measured and is expected to have a predictable or correlated change.

No objectionable conditions were noted.

The firm's standard operating procedure delineating trending of deviations, 02.0029: Trending of Deviations, effective 08/25/2020, was reviewed. A trend report is required to be generated within (b) (4) of the end of the review period. Once all trends are identified, Quality Systems summarizes the trends in a report. The standard operating procedure requires all trends to be identified, as agreed upon the Quality Unit and the department's subject matter expert, the data supporting each trend and the corrective actions identified for each trend. Upon final approval, all the corrective actions should have associated CAPAs to be tracked for completion. I requested the most recent trend report. (b) (6), (b) (7)(C) explained trend reports were generated (b) (4) during 2021; nonetheless, for 2022 the trend report was generated for the (b) (4) and would not be due until after (b) (4) from the end of 2022.

I reviewed quarter 4 trend reports for all suites associated with the manufacture of delandistrogene moxeparvovec drug substance:

- (b) (4) and (b) (4) Trend Report: Harmans Suite (b) (4) Environmental Monitoring, October 2022-December 2022, approved 02/28/2023
- (b) (4) and (b) (4) Trend Report: Harmans Suite (b) (4) Environmental Monitoring, October 2022-December 2022, approved 02/28/2023
- (b) (4) and (b) (4) Trend Report: Harmans Suite (b) (4) Environmental Monitoring, October 2022-December 2022, approved 02/28/2023
- (b) (4) and (b) (4) Trend Report: Harmans Suite (b) (4) Environmental Monitoring, October 2022-December 2022, approved 03/05/2023

The reports did not contain the CAPAs identified for each trend. Refer to **Objectionable Conditions and Management's Response** (Observation 2) section of this establishment inspection report.

7.3 Out-of-Specification (OOS)

This section written by VM

The firm's standard operating procedure for handling of out of specification results is 03.0044: *Laboratory Investigations*, effective 12/17/2021. Out of specification investigations are tracked in (b) (4). A laboratory investigation is initiated (Phase I) and if no laboratory cause is identified, a Phase II investigation is initiated to identify potential product issues. Phase II investigations, deviations, were initiated adequately when no laboratory cause was identified and when an identified out of specification result was determined valid.

No objectionable conditions were noted.

This section written by EA/SS

We (EA/SS) reviewed two OOS results associated with (b) (4) testing on the (b) (4) samples reported to the firm by (b) (4). The two deviations were related to cross contamination of the test sample by (b) (4). They were both classified as critical, and the details are summarized below:

Deviation #347686: On 03/26/2021, the firm received a notification from (b) (4) that the (b) (4) made in the Suite (b) (4) failed the (b) (4) test performed using (b) (4). The deviation investigation was initiated on 4/22/2021, and written notification was sent to Sarepta on 04/23/2021. Catalent conducted investigational testing on the (b) (4) sample and the subsequent (b) (4) for the presence of the (b) (4) using a (b) (4) method. Manufacturing of the (b) (4) for the client (b) (4) was launched in this facility (Suit (b) (4) and Suit (b) (4) for the (b) (4) process) in October 2020. The (b) (4) testing confirmed contamination of the (b) (4) in the (b) (4) sample and the subsequent (b) (4).

The main root causes were assessed to be: 1) lack of understanding of enhanced requirements to decontaminate the (b) (4) direct and indirect contact equipment during technical transfer, 2) usage of shared non-product contact equipment and shared (b) (4) from the (b) (4) manufacturing areas, 3) the leak during the (b) (4) of the (b) (4) (deviation 314674), and 4) insufficient restriction of personnel movement.

Critical CAPAs associated with this event were implemented on 05/16/2021, and effectiveness check was open on 03/11/2022. The contaminated lot was rejected, and manufacturing of the (b) (4) at this facility was terminated as of 01/01/2022.

Detailed information on this deviation was previously obtained by ORA during the inspection in November 2021, and the firm sent the final investigation report to the FDA on 04/04/2022. ORA classified the inspection in November 2021 as voluntary action indicated (VAI). No objectionable conditions were noted.

Deviation #566826/ Lab investigation report (LIR) #566398: On 07/11/2022, the firm was notified by that the) made in the Suite failed the test: On 07/26/2022, a confirmatory test result on was communicated to the firm. The laboratory investigation report (LIR) was open on 07/27/2022, and the deviation was open on 7/28/2022. The LIR was closed on 09/06/2022, and the root cause was not determined.

According to the deviation report, there is no indication of a systemic or ongoing contamination with (b) (4) material. There have been (b) (4) samples tested from April 2022 to August 2022 with confirmed negative results (b) (4) However, as of 03/10/2023, the exact root cause was not identified. The deviation record is closed.

We (EA/SS) interviewed several of the SMEs associated with the deviation. The probable cause of this deviation may be due to sharing of common (b) (4) in the storage (b) (4). Because common (b) (4) were used, there is remote possibility that the (b) (4) used to hold the (b) (4) sample prior to shipping to (b) (4) may hve been contaminated. As a corrective action, procedures have been implemented to decontaminate (b) (4) prior to using them to hold samples (this is part of their CAPAs

There has not been any other occurrence of reported (b) (4) test failure due to cross-contamination according to firm. The affected lot has been rejected even though the (b) (4) tested showed negative results. The VP of Quality confirmed that all testing has been paused and the company is going to dispose of any remaining (b) (4) samples by 04/30/2023 and also confirmed that no other incidence has occurred since this deviation. We (EA/SS) requested for and reviewed the full list of manufactured in-process lots (b) (4) lots), rejected lots, and reasons for rejection and confirmed that no additional (b) (4) related OOS has occurred.

Two CAPAs are summarized as follows:

- CAPA 651923: decontamination of sample containers and racks with a (b) (4) contact time with (b) (4) after removing the samples from the rack
- CAPA 651934: remove and/or permanently segregate all (b) (4) samples (including (b) (4) from other Client samples at this facility. (b) (4) decontamination of all storage locations (b) (4) that once contained (b) (4) samples

An effectiveness check will be performed with an initial review date of 04/30/2023 to confirm CAPAs generated are in place and in use. No objectionable conditions were noted.

No objectionable findings are noted.

7.4 Document Control

This section written by GFI

To create a new document, the author/document owner logs into (b) (4) and creates/drafts a new document using the applicable new document template. An approval workflow is initiated where an approver from each functional department is assigned to review the new document. Revision of existing documents complete the same steps and ensure changes are being tracked as edits are being made. Once the document is finalized and the approval workflow is complete, the author will send the document to the client for review via the firm's Client SharePoint site. Training needs and assignments are identified, approved by all affected departments including the author's department management, and undergo a training plan risk assessment. Once all tasks on (b) (4) is approved and completed, a release date will be set, and the document is approved and signed by all respective departments. Review dates are automatically set to (b) (4) from the effective date and a periodic review task will be assigned on (b) (4). All users can print controlled documents and forms from the (b) (4) system. (b) (4) documents will expire (b) (4) after it is printed, opened, or saved.

Original hard copies of controlled document, records, reports, and completed logbooks are submitted to the Document Archive through a QA/Document Control (DC)/Archivist where the submission is documented in a Document Receipt Log logbook. Access to the Document Archive is done through a request Form1 from SOP 02.0015 *Request for Copies of Master Documents from Quality Assurance/Document Control* or via an email to the Archivist staff. Once the request is processed, QA/DC/ Archivist will maintain and record transaction details including the name of the requester, check out date, and date

the document is returned through an electronic log. It is also the responsibility of the QA/DC/Archivist for retrieving and destroying records and documenting the destruction through a Document Destruction Log with a witness to verify the destruction.

The following standard operating procedures associated with document control were requested and reviewed:

- 05.1116: Document Lifecyle in (b) (4) for Users, effective 12/20/2022
- 02.0066: Records Retention, Archival and Retrieval, effective 05/18/2020

The firm's procedures for creating, revising, maintaining, assessing and printing controlled documents appears acceptable and no objectionable conditions were noted.

7.5 Batch Record Review and Release

This section written by VM

Batch record review and release is documented in form FRM-0073, effective 04/07/2022, and this form is included as part of the batch record. The form requires the batch record is adequately completed, process lot genealogy attached, QC testing is within specification, attached environmental monitoring report, certificates of analysis are approved and all pertinent investigations and change controls are approved and sent to the client.

I reviewed batch production record for (b) (4) SRP-9001 (b) (4) Drug Substance Lot (b) (4), approved by the quality unit 03/06/2023. The corresponding (b) (4) lot for the aforementioned drug substance lot is (b) (4). The (b) (4) section of the batch production record requires (b) (4) preparation. The batch production record required Complete (b) (4) preparation with part number (b) (4); however, the operator documented using part number (b) (4) on 03/23/2022.

The operator first cited a deviation to address the change and then cancelled it to reference open change control (b) (4). I asked Senior Manager for QA Disposition, Vandana Yadav, why the batch record had been approved when the change control was still open and she answered batch records may be approved with open change controls as long as there is no impact to the product. I explained this is not what FRM-0073 delineates and it is a deviation from the procedure. Refer to **Objectionable Conditions and Management's Response** (Observation 2) section of this establishment inspection report.

7.6 Training

This section written by GFI

The firm's standard operating procedures pertaining to training of personnel, 05.0057: *Training Program*, effective 02/24/2023, and 05.1023: *Creation, Assignment, and Periodic Review of Training*, effective 10/13/2022, were requested and reviewed. The procedure states that management under compliance training will identify each personnel's training requirements and any overdue training should be escalated to management for action and should only be extended for unexpected absences. Training for revised SOPs, Work Instructions (WI), or other controlled GMP documents must be completed before they are used in production. In addition, training and refresher trainings must be successfully completed prior to executing any production tasks. Low risk trainings consist of "awareness" and "understanding trainings" that may need an assessment after each training. High Risk trainings consists of On-The-Job Training (OJT) where competency is assessed through skills demonstrations. Training may also be delivered through Instructor-Led Courses (ILC) or computer-based Training (CBT). Management of the training profiles, tracking, and assignment of the trainings for each personnel are executed through the firm's Learning Management System (LMS).

I requested training credentials for four employees from Manufacturing and QC Micro:

- (b) (6), (b) (7)(C) (Associate I, Manufacturing)
- (Associate I, Manufacturing)
- (Lead Scientist, QC Micro)
- (Senior Scientist, QC Micro)

During the review, I verified that all credentials contained completed training on Good Manufacturing Practices (Core), Good Documentation Practices, Gowning, Personnel Flow and Behaviors in the GMP Manufacturing Clean Rooms, and Introduction to Logbooks. There were no objectionable conditions noted for employee training credentials and training curriculum.

7.7 Quality Agreements

This section written by GFI

Procedures for the firm's handling of quality agreements are delineated in standard operating procedure 02.0036: Quality Agreements, effective 03/29/2021. The SOP provides the process of initiating, approving, and maintaining Quality Agreements at

Catalent. A list of contract testing laboratories and their quality agreements was requested for review.

Quality Agreements for Contracted Testing Laboratories

(b) (4)

I noted the Quality Agreement between Paragon Bioservices, Inc and (b) (4) listed only (b) (4) locations: (b) (4) and did not include other locations. I interviewed Daniel Varas – Senior Manager of Supplier Quality to get clarification. He provided a CAPA QCA #596902 that amends the QA to a new Global QA that includes all locations.

Quality Agreements for Shipping and storage:

(b) (4)

Quality Agreements for Suppliers (Direct Product Contact Consumable):

(b) (4)

The firm's procedures for quality agreements and all quality agreements with the firm's contracted organizations listed above were reviewed and no objectionable conditions were noted.

7.8 Annual Product Review

This section written by VM

The firm's standard operating procedure delineating annual product reviews, 02.1028: *Periodic Product Quality Review (PPQR)*, effective 12/21/2021, was reviewed. No changes to annual product reports were noted since last inspection.

No objectionable conditions were noted.

7.9 Internal Audit Procedure

This section written by GFI

The firm's procedure for internal auditing is delineated in standard operating procedure 02.0051: *Internal Audit Management on* (b) (4) , effective 04/18/2022. The procedure describes that the Quality department will target to publish audit schedules prior to the (b) (4) of the (b) (4). Each respective audit will cover one of the following six elements:

- Quality System
- Facilities and Equipment: Buildings, facilities, utilities, process equipment and validation
- Materials management, rejection of materials, storage, and distribution
- Production Operations: Production and in-process controls
- Product Finishing: Quality Assurance labeling and product disposition
- Laboratory Controls: Quality Control operations (analytical & microbiology), method qualification and validation

Audits will be scheduled, prepared, and planned by a lead auditor (Quality) and managed within (b) (4) under an audit record and its associated child records. An opening meeting will be held with the audit team and management of the respective areas to be audited to discuss audit scope and responsibilities, key contact personnel, and schedule details. During the audit, the lead auditor and audit teams shall observe

operations to assess compliance with written procedures and CGMPs. Audit Team shall discuss any events and/or non-compliance with personnel as they are found. The audit Team shall review documentation applicable to the audited area for compliance. An audit is concluded with a close out meeting with the functional area director or manager and quality management. Upon completion of the audit, the lead auditor establishes audit critical dates in (b) (4) and within 30 calendar days from the audit completion date. The document was reviewed and there were no objectionable conditions noted.

A copy of the 2022 Internal Audit schedule was requested and reviewed. The schedule listed all six areas to be audited per their SOP and their target audit dates for 2022. I noted the document did not include when the previous audit was performed and this was discussed with management. No objectionable conditions were noted.

7.10 BPDR/Recall/Complaints/Adverse Events

This section written by VM

No changes impacting the handling of Biologic Product Deviation Reports (BPDRs), recalls, product complaints, and adverse events were reported since the last inspection.

8 MATERIALS AND WAREHOUSE

8.1 Inventory System and Sampling

This section is written by VM

The following standard operating procedures associated with materials management were reviewed:

- 05.0032: *Request, Issuance and Return of Released GMP Materials*, effective 02/08/2023
- 05:0065: *Transfer of Manufactured Products to Materials Control*, effective 02/08/2023
- 05.0264: *Materials Control Space Management*, effective 02/08/2023
- 05.1048: *Material Planning and Allocation*, effective 02/04/2023
- 05.1074: *Movement of Materials Between Sites*, effective 02/04/2023

- 05.0267: *Sampling of GMP Material*, effective 02/08/2023
- Work Instruction 0087: *Inventory Transfer* (b) (4), effective 02/04/2023

The firm currently utilizes (b) (4) warehouse spaces: (b) (4) warehouses are located in the Harmans campus subject of this inspection. (b) (4) is an intermediate warehouse with primarily released materials storage of temperature-controlled materials. (b) (4) is utilized in the same capacity as (b) (4) and is under expansion. On 03/06/2023, we (VM, GFI, KM, SS and EA) performed a walkthrough of (b) (4) warehouse. On 03/07/2023, we (VM, GFI and KM) performed a walkthrough of (b) (4) warehouse. Both warehouses utilize the (b) (4) inventory management system. Access is controlled by keycard and keys for equipment and restricted storage areas. The key to access lockbox containing keys corresponding to drug substance (b) (4) is not maintained in a secure location inside the warehouse and issuance of keys in the lockbox is not limited to authorized personnel, and this was discussed with management (**Discussion Item VM-1**).

The (b) (4) storage site is located in (b) (4). There are (b) (4) warehouses used at (b) (4) is only used by Catalent and Catalent employees are on-site. (b) (4) is only used for (b) (4) storage at this time; however, this will be a future site for (b) (4). At (b) (4) calibrations were verified for controlled temperature storage equipment which include the following temperatures: (b) (4) is primarily used for materials to be used at (b) (4). The warehouse is also an intermediate warehouse with longer term storage of temperature-controlled materials.

All materials are received at the appropriate warehouse, shipped for sampling at (b) (4) (if applicable), sampled at (b) (4) and shipped back to the appropriate warehouse. Materials are shipped back (if applicable) to (b) (4) when a picklist is created. All inventory among the warehouses is maintained and controlled in the (b) (4) system. Supply Chain Process Maps are submitted as **Exhibit VM-4**. Although materials were identified to be stored at the appropriate temperatures, there is no standard operating procedure designating specific identified locations for temperature-controlled materials personnel (**Discussion Item VM-2**).

No objectionable conditions were noted.

8.2 Supplier Qualification

This section is written by GFI

A copy of the firm's supplier's qualification procedure, SOP 02.0033: *Supplier Qualification Procedure*, effective 11/22/2022, was reviewed. Under this protocol, each supplier undergoes a risk assessment using their protocol, CPS-GQP-5265: *Global Supplier Quality Risk Assessment*s. Supplier Risk Assessments are done under (b) (4) Workbook CPS-GQP-5265-F01 Supplier Risk Assessment Tool. This form must be approved by the Supplier Quality manager or designee and a Quality Compliance Assessment (QCA) is created as a child record. Supplier qualifications SOP was reviewed and there are no objectionable findings.

I discussed with management my concern with no effective date on the risk assessment tool and recommended validation of the workbook. The validation for the worksheet was reviewed and firm confirmed that their Workbook manager (b) (4) will be notified to add an effective on the form.

8.3 Raw Materials

This section is written by VM

The following SOP pertinent to raw material management were reviewed:

- 05.0265: *Incoming GMP Material Processing*, effective 02/08/2025

The following direct for production raw material was selected for review: Poloxamer 188, with manufacturer lot (b) (4). Raw material was processed per SOP.

No objectionable conditions were noted.

9 PRODUCTION AND PROCESS CONTROLS

This section is written by VM

9.1 (b) (4)

The delandistrogene moxeparvovec drug substance manufacturing process includes a total of unit operations. The entire delandistrogene moxeparvovec

manufacturing process utilizes single-use equipment technology. Open operations include (b) (4) . These operations are performed within a Biosafety Cabinet (BSC) qualified for ISO (b) (4) conditions in an ISO (b) (4) background. Hallways outside of suites are classified as ISO (b) (4) On 03/07/23, I observed through a glass window the (b) (4) process in Suite (b) (4) Production Room with ISO (b) (4) room classification for Sarepta Lot # (b) (4) . At least (b) (4) operators were engaged in the step and a quality unit person and supervisor participate as needed.

No objectionable conditions were noted.

9.2 Changeover and Line Clearance

This section written by VM

The facility is a multi-product facility and includes warehousing, materials control, facilities engineering, manufacturing operations, quality control, quality assurance, validation, and administration. Only manufacturing operations for (b) (4) can be performed in a room and suites utilized for the manufacture of delandistrogene moxeparvovec drug substance are dedicated. (b) (4) Rooms (b) (4) supports manufacture of all (b) (4) but may only be used for (b) (4) . Major process equipment, utilized in the drug substance manufacturing, has been installed and qualified throughout the manufacturing suites supporting the product manufacturing process.

An introduction procedure is followed if new equipment is added. The site utilizes single-use, disposable product contact consumables, where possible, for drug substance operations. The cleaning of equipment is done to ensure that cross-contamination is prevented according to the standard operating procedures mentioned in the facility cleaning section of this establishment inspection report. In addition, the laboratories have defined and segregated areas for testing.

Area clearance is performed to ensure manufacturing area is ready for the next processes as delineated in standard operating procedure, 05.0250: Clearance and Room Status Tagging, effective 28Feb2023. Room status tagging is used to provide a clear status indicator for each individual manufacturing space.

No objectionable conditions were noted.

10 FACILITIES

10.1 Environmental Monitoring Qualification, Routine Monitoring and HVAC

This section written by VM

The Environmental Monitoring (EM) program consists of routine viable and non-viable particulate air sampling and viable surface sampling. Grade (b) (4) and Grade (b) (4) areas are sampled (b) (4). Grade (b) (4) and Grade (b) (4) are sampled (b) (4) when active and (b) (4) when in use. EM sampling frequencies, action limits for non-viable particulates and microbiological levels (in operation) are delineated in standard operating procedure 03.1005: *Environmental Monitoring System – BWI*, effective 23Jan2023.

Data from the qualification studies was evaluated to determine the sampling locations and the operating limits for the routine environmental monitoring program. Procedures are in place to define the requirements to investigate EM excursions and to implement corrective and preventive actions when required. Per standard operating procedure 02.0029: Trending of Deviations, effective 08/25/2020, EM data is periodically trended.

I reviewed (b) (4) trend reports for all suites associated with the manufacture of delandistrogene moxeparvovec drug substance:

- (b) (4) and (b) (4) Trend Report: Harmans Suite (b) (4) Environmental Monitoring, October 2022-December 2022, approved 02/28/2023
- (b) (4) and (b) (4) Trend Report: Harmans Suite (b) (4) Environmental Monitoring, October 2022-December 2022, approved 02/28/2023
- (b) (4) and (b) (4) Trend Report: Harmans Suite (b) (4) Environmental Monitoring, October 2022-December 2022, approved 02/28/2023
- (b) (4) and (b) (4) Trend Report: Harmans Suite (b) (4) Environmental Monitoring, October 2022-December 2022, approved 03/05/2023

The reports did not contain the CAPAs identified for each trend. Refer to **Objectionable Conditions and Management's Response** (Observation 2) section of this establishment inspection report.

10.2 Facility Cleaning

This section written by VM

The standard operating procedures for cleaning of the facility and equipment, 04.0042: *Cleaning of the GMP Manufacturing Clean Rooms*, effective 02/08/2023, and 05.0043:

Biological Safety Cabinet Monitoring and Cleaning, effective 12/08/2022, were reviewed.

The disinfectants selected for use are supported with the following disinfectant studies:

- Final Report MWP-22-029: *Disinfectant Efficacy Surface Challenge Testing with* (b) (4) *for Catalent Maryland, Inc.*, approved 03/05/2023
- MWP-19-019: *Disinfectant Efficacy Surface Challenge Testing for Catalent Maryland, Inc.*, approved 05/22/2020.

According to corporate policy, CPS-QS-3080: *Disinfectants and other Antimicrobial Chemical Agents (formerly* (b) (4) *)*, effective 23Jul2019, environmental monitoring isolates are selected for use in the disinfectant efficacy studies. Strain selection is defined in QCTD-0108-B-PRO: *Selection of In-House Isolates for Growth Promotion Testing at Harmans (BWI) site of Catalent Cell and Gene Therapy*, approved 03/15/2021.

Disinfectants are suitable for surfaces and environment. Disinfectant rotation and selection appear acceptable. Per CPS-QS-3080: *Disinfectants and other Antimicrobial Chemical Agents (formerly* (b) (4) , effective 23Jul2019., section 3.3.2.4.4, requires selection of environmental monitoring isolates for disinfectant efficacy studies; however, there is no requirement for re-assessment of disinfectant efficacy studies and this was discussed with management (**Discussion Item VM-3)**.

No objectionable conditions were noted regarding facility cleaning.

10.3 Preventive Maintenance and Calibration

This section written by VM

The standard operating procedure delineating equipment preventive maintenance and calibration, 09.1002: *Maintenance Program at BWI*, effective 02/20/2023, was reviewed.

The document delineates preparation of preventive maintenance plans, communication of actions and maintenance documentation. Calibration and preventive maintenance activities are recorded in (b) (4) electronic system. The firm has in place preventive maintenance plans and instruction for corrective maintenance orders.

I verified the calibration for (b) (4) with asset identification (b) (4) performed 03/01/2022. I also verified the calibration for the (b) (4) with asset identification (b) (4) performed 03/22/2021. No objectionable conditions were noted.

10.4 Water and Process Gasses

This section written by VM

I reviewed standard operating procedure, 03.1048: *WFI Sampling and Routine Monitoring*, effective 02/01/2023. This document describes the frequency, procedure, and required testing, and acceptable levels for the (b) (4) water for Injection system (b) (4) This system covers the BWI facility, including the maintenance areas and manufacturing levels. QC and QA is the responsible parties to maintain records for the WFI. Water for Injection (WFI) is used for (b) (4) . The firm is presently in compliance with (b) (4) standards based on the results from the most current (b) (4) and (b) (4) Trend Report provided during the inspection. (b) (4) all met acceptable criteria. However, there was a deviation that occurred in (b) (4) of the report, but the adulterated sample was found on the maintenance floor and had no association with the manufacturing suites.

I reviewed standard operating procedure 03.1053: *Gas Systems Monitoring Program*, effective 11/21/2022, (b) (4) I reviewed (b) (4) *Trend Report Harmans Bulk Gas Systems,* January 2021-December 2021, approved 07/06/2022.

No objectionable conditions were noted.

10.5 Computers/Automated Systems

This section written by VM

The firm utilizes the following electronic systems: (b) (4) was implemented in

March 2023. The implementation of (b) (4) . is documented in change control (b) (4), approved 01/30/2023.

The change control described the change and defined the actions taken to ensure transition to (b) (4) in a compliant manner, including QA validation and training rollout, and establishment of a "Go-Live" date. The change control included validation of the system which included the configuration, validation testing, data cutover, and deployment of Catalent's current (b) (4) System connected sub-systems. In addition, action 638289 was initiated for training of warehouse operators in relabeling operations for the transition.

No objectionable conditions were noted.

10.6 Pest Control

This section written by KM/VM

KM reviewed standard operating procedure 05.0289: *BWI Pest Control*, effective 01/18/2023. Per this document, pest sightings are reported to and handled by the facilities team. The firm has a licensed vendor that treats and controls all pest related issues and also conducts (b) (4) maintenance. All pest incidents must be reported on FRM-0285 in the pest logbook located at the front desk of the BWI facility. (b) (4) is responsible for contacting the approved vendor and setting up an appointment within (b) (4) will also further the process and close out the case once the issue had been resolved and the work order has been closed. The Environmental Health and Safety (EHS) staff collaborates with (b) (4) to ensures that no chemical used in the pest control process would affect safety and efficacy of the manufacturing area or air quality level. Management provided the quality agreement and last pest management service. Per the record, the last service was conducted in December 2022. Next (b) (4) maintenance is set for (b) (4) . No objectionable conditions were noted.

11 MAJOR PROCESS EQUIPMENT IQ/OQ/PQ

11.1 SRP-9001 (b) (4) Process

The site utilizes single-use, disposable product contact consumables, where possible, for drug substance operations. Major equipment used in the delandistrogene moxeparvovec manufacturing process include: Biological Safety Cabinets - (b) (4)

I requested for review the qualification for Biological Safety Cabinet with equipment identification (b) (4) .FR: *Final Report for Installation and Operational Qualification Protocol for* (b) (4) *Biological Safety Cabinet BSC-*(b) (4), approved 09/24/2020. All acceptance criteria were met and documented.

I requested for review the High Efficiency Particulate Air (HEPA) certification report for Biological Safety Cabinet with equipment identification BSC-(b) (4), approved 10/27/2022.

I requested for review the qualification of (b) (4) with equipment identification (b) (4) FR: *Final Report Requalification Test Plan for Temperature Controlled* (b) (4) , approved 02/11/2022. All acceptance criteria were met and documented.

I requested for review the qualification of (b) (4) with equipment identification (b) (4) .FR: *Final Report for the Installation and Operational Qualification Protocol for Material Control* (b) (4) , approved 09/22/2020. All acceptance criteria were met and documented.

No objectionable conditions were noted.

12 LABORATORY AND QUALITY CONTROL

12.1 Sample Control/Chain of Custody

This section written by EA

On 03/06/2023, the inspection team walkthrough the GMP warehouse led by a Senior Manager for compliance, and the QC Associate Director. Access to the warehouse was restricted and controlled by keycard. Incoming materials are offloaded at the dock, and

are checked for defects and damages. This warehouse is also used to store material under quarantine while being sampled and tested. Material handling is done by the material controls group (a subgroup of QA). Materials are received into the company's (b) (4) system. Labels are generated from this inventory management system. The company is in the process of transitioning from a QAD electronic data-based system to a more robust (b) (4) for inventory of materials and traceability. At the time of the inspection, some of the materials in the warehouse bore labels from the old QAD system. No objectionable conditions were noted.

Materials and Reagents used in the QC lab

After materials are delivered to the general warehouse, GMP-QC materials are sampled in room (b) (4) (which is badge accessed and airlocked) for testing through a third party. The test results are reviewed before the materials are released by QA for use. The use of QC materials and reagents are governed by the following SOPs:

- 03.0272: *Quality Control Laboratory Material management (v2, effective 04/15/2022)*
- 03.1043: *Qualification of Critical and Reference Materials (v1 effective 03/07/2023)*
- 03.0233: *Reference Material and Critical reagents Program (v3, effective 03/07/2023)*
- *03.1121: Qualification of* (b) (4) *(v0, effective Jun/17/2022)*

QC reference material

I requested for and reviewed the list of all reference materials used in the QC operations for Sarepta (b) (4)) product (SRP-9001). The respective client supplies the reference standard to be used for testing. Sarepta qualifies the assay reference and sends to Catalent. The reference is tested (Per SOP03.0233 v3) before use. No objectionable conditions were noted.

Other materials used in the QC lab

The use of all materials in the QC lab is governed per 03.0272 v2: Quality Control Lab Materials Control. Regular materials classified as non-critical are ordered through the (b) (4) system. QC personnel receives the materials upon ordering and enters them into the logbook in the QC lab. Non-critical QC reagents/materials (eg, (b) (4) etc) are neither sampled nor tested. The lots numbers assigned by the vendor are recorded on the experimental paper worksheet during experiment for tracking purposes. The QC lab manages the sourcing of such non-critical reagents from vendors. This SOP (03.0272 v2) provides instructions and description of procedure for ordering receiving,

inspection, labeling, handling, storage, review, and inventory management of QC lab materials based on the risk status of the material (i.e., Low risk, moderate risk, high risk). For high-risk materials such as compendial/client provided critical reagents performance trending is required. No objectionable conditions were noted.

Critical Reagents Management

Based on my interview with SMEs, the management of QC critical reagents is under the responsibility of the Critical Reagent Management team. Per 03.1043 v1: *Qualification of critical and reference materials,* critical reagents are defined as any reagent that has direct impact on the test procedure's accuracy or reproducibility. While the 03.1043 has instructions for material management including inspection, receiving labeling, expiry, it is unclear how reagents are classified as critical or otherwise. The SOP stipulates that new lots of critical reagents/materials must be qualified prior to use in cGMP activities. However, the SOP lacks a systematic or risk-based assessment approach for critical reagent classification. See **Discussion Item EA-1** for further details. The SME indicated that depending on the critical reagent, confirmatory ID testing and concentrations are tested by a third party. The test results are matched against the client supplied CoA. QA reviews the results and issues a release for its use. (b) (4) are managed separately via SOP *03.1121.* Although there is a lack of clear instructions on how to classify critical reagents, which was discussed with the firm (See **Discussion Item EA-1**), no objectionable conditions were noted.

Storage and organization

The procedure for receiving, documenting aliquoting, storage and release are stated under 03.233 v3: *Reference Materials and critical reagents Program*. Reagents are received and logged into inventory book. I inspected the Controlled Temperature Unit (CTU) (b) (4) are kept. I also inspected the CTU used for storage of critical reagents for Sarepta's (b) (4) program, CTU (b) (4) equipment and verified that the storage and tracking of critical reagents was documented in the inventory logbook . No objectionable conditions were noted.

(b) (4)

Material (b) (4) handling and disposition is governed by the 03.0095 v8, effective 08 Feb 2023: *Processing Raw material* (b) (4) *Samples of Client GMP Materials*. Briefly, material (b) (4) maintained in the facility can include (b) (4) . We (SS and EA) inspected and confirmed that the firm has adequate storage capacity for (b) (4) materials. We verified that (b) (4) samples were appropriately labeled (e. g., (b) (4) of (b) (4) samples were stored in CTU (b) (4)

(b) (4) storage). Instructions specified by the 03.0095 v8 are acceptable. No objectionable conditions were noted.

12.2 Test Methods

This section written by GFI

(b) (4) Testing at QC Micro Lab (Room (b) (4)

(b) (4)

The operator then proceeded to prepare the (b) (4) system for use and proceeded with sample preparations and (b) (4) sample testing. In addition, documentation of the operators and date, start and end times, equipment information, and sample information were recorded.

The following documents were requested and reviewed:

- 05.0066: *Aseptic Techniques Used for Processing in the Biological Safety Cabinet* (effective 11/25/2022)
- 03.0271: *Operation, Cleaning and Maintenance of QC Laboratory* (b) (4) (effective 08/11/2021)
- 03.0002: (b) (4) (effective 08/30/2022)
- 05.0043: *Biological Safety Cabinet Monitoring and Cleaning* (effective 12/08/2022)
- 05.0027: *Cleaning of Non-Product Contact Manufacturing Equipment* (effective 03/04/2019)
- Logbook (b) (4) for QC Fridge (b) (4)

The documents listed above were reviewed and I found no objectionable observation with how the firm conducts their cleaning and operation of BSC, (b) (4) , and non-contact equipment, (b) (4) testing, and aseptic techniques in the BSC. No objectionable conditions were noted.

12.3 Lab/Instrumentation/Logbooks

This section written by EA

Controlled temperature unit CTU Alarms

The company tracks and monitors all CTUs for temperature excursion per:

- 05.1068: *Equipment Alert and Alarm Management (v2, effective 03/08/2023)*
- 05.1098: *Environmental Monitoring Systems (EMS) Alert and Alarm Management (v11, effective 03/08/2023)*

CTU data is tracked and recorded using the database (b) (4) , which allows real time monitoring of all CTUs used for sample and reagent manaegment. I interviewed QC manager, who leads the QC team in managing system failures and temperature excursions. The QC manager confirmed that in the event of an excursion or an alarm, the EMS sends out notification in a form of text, email, and phone call to elicit timely response by the team. The instructions in the two SOPs I reviewed are appropriate.

Equipment Calibration

Regarding equipment calibration and management, I confirmed that QC equipment logbooks for selected number of QC equipment were up to date. These included the (b) (4) I inspected at the (b) (4) farm at Room (b) (4) equipment at the QC lab located at rooms (b) (4) . The calibration frequencies and general maintenance schedules of equipment are chronicled in the company's '(b) (4) database per 05.1086 v6 effective 10/06/2021 (Facilities and Engineering Operation of (b) (4) No objectionable conditions were noted.

12.4 Drug Substance Shipment Validation

This section written by SS

The drug substance (DS) is shipped from this facility (Catalent BWI) to the drug product (DP) manufacturing site, Catalent BioPark (801 West Baltimore, St., Suite 105, Baltimore, MD 21201). The shipping temperature is intended to be (b) (4) . The commercial packaging configuration for the DS is as follows:

- (b) (4)

I (SS) reviewed the SOP 05.1194: *Pack Out and Shipment of Product*, effective 11/28/2022. This SOP describes the procedures for shipment, storage, and receipt of (b) (4) DS with ID samples in designated shipping container for Sarepta. The SOP is adequate for their intended purpose with no objectionable findings noted.

I reviewed the DS shipping validation report, VAL-RPT-01757: *Shipping Qualification Summary Report for SRP-9001 Drug Substance*, effective 6/13/2022. The shipping validation is comprised of thermal operational qualification (OQ), transportation OQ, and performance qualification (PQ):

- (b) (4)

I reviewed the temperature data for thermal OQ and PQ. All the shipping temperatures complied with the predefined acceptance criterion of (b) (4). No objectionable conditions were noted in the temperature data and the shipping validation report.

13 CONTAMINATION CONTROL

13.1 Gowning

This section written by GFI

A copy of the firm's SOP on personnel gowning requirements and practices in the GMP clean rooms, 05.0055: *Gowning, Personnel Flow and Behaviors in the GMP Manufacturing Clean Rooms,* effective 03/28/2022, was reviewed with no objectionable concerns to their procedures. I observed through a glass window an inoculation process in Suite (b) (4) Production Room with Grade (b) (4) room classification. Operators (b) (4)

No objectionable conditions were noted.

13.2 Personnel, material, product, and waste flows

This section written by VM

I reviewed diagrams for the personnel, waste, equipment, and product flow.

- 55-GMP-DRA-0004: Waste Flow Building (b) (4) effective 08/25/2022
- 55-GMP-DRA-0005: Personnel Flow Building (b) (4) effective 08/25/2022
- 55-GMP-DRA-0006: Material Flow Building (b) (4) effective 08/25/2022
- 55-GMP-DRA-0010: Product Flow Building (b) (4) effective 08/25/2022

During the walkthrough and observation of production activities, I observed proper personnel, equipment, material, product, and waste flow with the firm's guides throughout the warehouse, QC, and manufacturing areas. I also noted appropriate

material movement of incoming and outgoing product and materials at the warehouse loading dock.

No objectionable conditions were noted regarding personnel, material, product, and waste flow.

14 ADDITIONAL INFORMATION

This section written by VM

The firm intends to engage in drug product fill and finish. At the time of the inspection an (b) (4) had been installed and was under qualification. The room in which the (b) (4) is located will be classified as Grade (b) (4) space. A power point of future capabilities and timeline is submitted as **Exhibit VM-5**.

15 OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

This section written by VM

During the close out meeting, the inspection team presented the "Form FDA 483, Inspectional Observations" (**Attachment 2**) to Mr. Joe Torres, Vice President of Operations. The list of individuals present during the close out meeting is submitted as **Exhibit VM-1**.

Observations listed on Form FDA-483

OBSERVATION 1

Your quality unit (QU) failed to ensure the integrity and effectiveness of the Quality Management system.

Specifically,

Change controls are not scientifically justified and do not include a sufficient analysis of the impact of the change by the Quality Unit as delineated in standard operating procedure 05.0174, Change Control Management in (b) (4) , effective 01/28/2022.

In 03/23/2022, SRP-9001 Lot # (b) (4) Preparation was prepared utilizing (b) (4) formula with part number (b) (4) rather than the part number listed in the bill of materials, (b) (4) , and the (b) (4) drug substance-batch record was signed off for

release by the quality unit on 03/06/2023. Change control (b) (4), covering the change, was not approved by the Quality Unit prior to release of the drug substance lot for further manufacturing.

Supporting evidence: 05.0174, Change Control Management in (b) (4), effective 01/28/2022, is submitted as **Exhibit VM-6**. Change control (b) (4), is submitted as **Exhibit VM-7**, and shows under change action (b) (4) the (b) (4) update. Change action (b) (4) for (b) (4) formula (b) (4) introduction shows completed 10/05/22; however, the Master Production Record (MPR) 0859 was not updated with the change. Approval record from customer for change control (b) (4) is submitted as **Exhibit VM-8**. Management stated on 03/25/2021 MPR.0859 was updated and (b) (4) (also mentioned as (b) (4)) was inadvertently removed. The timeline for the changes to the MPR is submitted as **Exhibit VM-9**. Batch production record for (b) (4) preparation of SRP-9001 (b) (4) Drug Substance with Lot # (b) (4) selected pages are submitted as **Exhibit VM-10**. FRM-0073 with Quality Unit approval of Lot # (b) (4) is submitted as **Exhibit VM-11**. (b) (4) drug substance lot # (b) (4) genealogy is submitted as **Exhibit VM-12**.

Discussion with management: Management agreed with the observation and promised corrections. Deviations and corrective actions were generated to address this concern during the inspection.

OBSERVATION 2

The Quality Unit failed to address issues that have the potential to impact the quality of the product.

Specifically,

The Quality Unit did not follow the SOP 02.0029: Trending of Deviations, to implement CAPAs to track completion of corrective actions that address deviation trend issues. There is no documented evidence that CAPAs were created to ensure completion of actions to address deviation trends that were identified in the most recent Deviation Trend Summary Report-Harmans (BWI) Facility, (b) (4) 2021, approved 03/01/2023. SOP 02.0029: Trending of Deviations, effective 25Aug2020, section 5.1.29, requires all corrective actions to address trend issues to have CAPAs created to track completion.

Supporting evidence: Deviation Trend Summary Report-Harmans (BWI) Facility, Quarter 4, 2021, approved 03/01/2023, is submitted as **Exhibit VM-13**. SOP 02.0029: Trending of Deviations, effective 25Aug2020, is submitted as **Exhibit VM-14**.

Discussion with management: Management agreed with the observation and promised corrections. Deviations and corrective actions were generated to address this concern during the inspection

16 GENERAL DISCUSSIONS WITH MANAGEMENT

This section written by GFI

Several items were also discussed with the firm's management team. The discussion items are as follows:

Discussion Item EA-1: I conveyed several concerns regarding the management and classification of critical reagents use per SOP 03.1043 v1 effective 03/07/2023 (qualification of critical and reference materials). The SOP did not provide clear instructions on how to designate a reagent as critical. I recommended that the SOP be revised to include clear guidance on how to classify reagents to ensure that reagents (such as the (b) (4)) are appropriately classified to support key in-process and release testing done at Catalent. In our discussion, I also recommended that the company implement a comprehensive procedure that can be relied on to classify and track all critical reagents used under cGMP assays in QC lab to ensure proper oversight.

This section written by VM

Discussion Item VM-1: I recommended that the key to access the lockbox containing keys corresponding to drug substance (b) (4) be maintained in a secure location inside the warehouse and that the issuance of keys in the lockbox be limited to authorized personnel.

Discussion Item VM-2: I recommended establishing an SOP designating specific identified storage locations for temperature-controlled materials.

Discussion Item VM-3: I recommended establishing timeframes for re-assessment of disinfectant efficacy studies.

17 ATTACHMENTS

Attachment 1: FDA Form 482, dated March 6, 2023

Attachment 2: FDA Form 483, dated March 10, 2023

18 EXHIBITS

Exhibit VM-1: List of personnel
Exhibit VM-2: List of drug substance lots
Exhibit VM-3: Manufacturing Suite Description
Exhibit VM-4: Supply Chain Process Maps
Exhibit VM-5: Product Fill Plan
Exhibit VM-6: SOP 05.0174, Change Control Management in (b) (4)
Exhibit VM-7: Change control (b) (4)
Exhibit VM-8: Approval record from customer for change control (b) (4)
Exhibit VM-9: Timeline for the changes to the MPR
Exhibit VM-10: Batch production record for Lot # (b) (4)
Exhibit VM-11: FRM-0073 with Quality Unit approval of Lot # (b) (4)
Exhibit VM-12: (b) (4) drug substance lot # (b) (4) genealogy
Exhibit VM-13: Deviation Trend Summary Report-Harmans Quarter 4
Exhibit VM-14: SOP 02.0029: Trending of Deviations
Exhibit VM-15: Portable drives with firm's documents (4)
Exhibit EA-1: (b) (4) SRP-9001 Critical Reagents

Viviana Matta -S

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Date: 2023.05.23 17:07:00 -04'00'

Viviana Matta, CSO, OCBQ/DMPQ/B2

Grace Forsythia A. Igot -S

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Grace Forsythia Igot, Biological Reviewer, OCBQ/DMPQ/B2

Kevin Matthews -S

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