FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

Date: 14 June 2021

To: [redacted], Staff Director, Office of Biological Products Operations (OBPO) Division 2, Team Biologics

From: [redacted], NE Investigator, OBPO
[redacted], Senior Advisor, OBPO
[redacted], Senior Advisor, OBPO
[redacted], Chemist, CBER/OCBQ

Subject: Investigation of Emergent Manufacturing Operations Baltimore LLC; Investigation Dates: 2-10 June 2021

FEI: 3015448605

eNSpect Op ID: 200634

Responsible Firm: Emergent Manufacturing Operations Baltimore LLC
5901 East Lombard St.
Baltimore, MD 21224

I, [redacted], collated this document which was authored by the investigation team. Each section is indicated with the initials of the author that wrote the text as follows:

[redacted]

Endorsement:
This operation was initiated as a pre-production inspection to review the firm's implementation of corrections to the FDA 483 issued at the close of the inspection that occurred 12-20 April 2021 and to determine the firm's readiness to resume manufacturing of the COVID-19 vaccine drug substance described in EUA 027205 filed by applicant Janssen Biotech Inc. On 25 May 2021, a regulatory meeting related to the findings from the April inspection was held with the firm.

While on-site, the firm provided an updated timeline to indicate a new date of readiness stated as June 26th, therefore the inspection was converted to an investigation and modified the objectives to include batch record review of selected executed batches of COVID-19 vaccine drug substance. The team reviewed 14 batch records to identify the most significant concerns documented in the batch records (and associated records) of previously manufactured drug substance batches.

At the conclusion of the investigation, the team shared ten discussion items with firm management. The firm indicated they would respond to the investigational findings in writing.

Routing: OBPO/Division 1 Compliance Branch

Cc: CBER/OCBQ
[redacted], Director, Team Biologics Staff

BACKGROUND AND INTRODUCTION

[redacted] This pre-production inspection of Emergent Manufacturing Operations Baltimore LLC (referred to as "EMOB") was initiated to review the firm's implementation of corrections to the previous 483 issued on 20 April 2021 and determine the firm's readiness to resume manufacturing of the COVID-19 vaccine drug substance described in EUA 027205 filed by applicant Janssen Biotech Inc. While on-site, the firm provided an updated time-line to indicate a new date of readiness stated as June 26th, therefore the inspection was converted to an investigation and modified the objectives to include batch record review of selected executed batches of COVID-19 vaccine drug substance.

The firm's corrective actions and readiness date of June 7 was described in the firm's written response to the 483, dated 30 April 2021, and verbally in the regulatory meeting held on 25 May 2021.

In addition to the above goals of the investigation, the team also reviewed fourteen batch records to identify the most significant concerns documented in the batch records (and associated records) of previously manufactured drug substance batches.

ADMINISTRATIVE INFORMATION

[redacted] On 28 May 2021, I pre-announced the investigation by calling multiple

representatives of the firm and leaving voicemail when no one answered initially. I received a call back from Mr. Ed Elmore – Senior Director of Quality who provided answers to the COVID-19 preventative measures in place at the firm and in the region. During this call I also requested that all documents relevant to the firm's 483 response dated 30 April 2021 and the firm's presentation made during the regulatory meeting on 25 May 2021 be prepared for review on the morning of June 2nd. Mr. Elmore stated he would arrange for preparation of these materials.

On 2 June 2021, the investigation team [redacted] arrived at the firm and presented our credentials and issued an FDA482 Notice of Inspection to Ms. Mary Oates – Senior Vice President Global Quality (**attachment #1**) who identified herself as the most responsible person on site for the firm. A copy of the 482 is presented in **attachment #1**. Upon my question, Ms. Oates stated the firm's legal identification and organization has not changed from the previously reported data in April 2021.

A copy of the firm's corporate registration documents (dated 2010) from the state of Delaware are provided in **exhibit #**[redacted]

On 4 June 2021, an FDA482 was issued to [redacted] with Janssen Pharmaceuticals Inc. and the investigation team [redacted] presented credentials to [redacted] who identified himself as the most responsible person on-site for Janssen. A copy of the 482 is presented in **attachment #2.**

On 7 June 2021, FDA482 notice of inspection forms were re-issued to both [redacted] and Ms. Oates with the addition of CSO [redacted] who joined the team to assist with the review of individual batch records (refer to **attachments #3 and #4**).

During the opening meeting on 2 June 2021, Mr. Edward "Ed" Elmore provided an opening presentation to summarize the current state of the facility and operations with slides that are presented in **exhibit #**[redacted]

During the close-out meeting on 10 June 2021, the investigation team verbally discussed ten items with the firm management as described in the General Discussion with management section below. A form FDA483 was not issued due to the operation being converted to an investigation.

REVIEW OF CORRECTIVE ACTIONS

[redacted] During this investigation, we reviewed the firm's corrective actions from selected portions of the firm's written response as follows. The Observation number from the April 2021 inspection is referenced and the corrective action proposed in the firm's

response is numbered and paraphrased. Each observation has more than one corrective action proposed but the numbering below only indicates the observation. The coverage related to each corrective action is indicated with the investigators initials in each case.

Observation #1-1.3
Newly initiated J&J drug substance batches will undergo independent third-party certification by [redacted] prior to release, including a review of any site investigation to confirm adequacy of the investigation and root cause analysis.

[redacted] Coverage:
As a follow up to corrective actions noted by Emergent Manufacturing Operations Baltimore (EMOB) in the response to the 483 issued on 20 April 2021, I discussed and reviewed documents associated with the enhanced oversight by Janssen, in addition to batch release and the role of [redacted] regarding batch certification. The information gained from discussions and the review of documents relating to these topics are summarized in the following sections.

Janssen Enhanced Oversight
Janssen has >70 people dedicated to production oversight at EMOB either as an onsite technical Person-in-Plant (PIP, ≥ 30 people) directly observing the operations in the facility or working in a QA capacity as a Quality Person-in-Plant (QPIP) reviewing batch records, deviations reports and investigations, batch release certification etc., in addition to providing resources regarding CGMP and process quality. I [redacted] was provided the oversight plan entitled "Janssen Oversight Plan and Procedure for the Manufacture of [redacted] at Emergent BioSolutions Bayview Facility Baltimore, Maryland". The plan details Janssen's oversight model which includes the following aspects:

1. Janssen will exercise increased oversight and final sign-off of the manufacture of its [redacted] Drug Substance at Emergent Bayview. This will include Janssen's final decision on the disposition of all batches manufactured and final approval/sign-off of all critical GMP systems and processes.
2. Janssen will supervise all critical activities related to Janssen products in Emergent Areas [redacted] in addition to shared areas where Janssen products are processed (e.g. [redacted] etc.).
3. Janssen will provide direction with full 24/7 on-the-floor coverage for all Janssen critical manufacturing operations, plus expanded presence in other GMP areas to assure procedure adherence and prevention of non-conformance.
4. Janssen will support and engage in daily governance of operational execution of Janssen products.

The plan indicated that Janssen will have access to all areas of the facility, data, trending, and any information to provide oversight. Janssen personnel will have access to verify, through actual observation of production to ensure Emergent staff adhere to approved written procedures. Janssen personnel will be notified immediately of any manufacturing deviations and any manufacturing changes for its [redacted] drug substance. Janssen will conduct a review of batch records and underlying data and associated discrepancies of drug substance manufactured at EMOB.

During my discussions with [redacted], who serves as Janssen's Senior Director of Quality onsite at EMOB, he indicated that Janssen's oversight will operate alongside of the existing EMOB's Quality System and that the technical PIPs will document their observations of critical process operations on oversight forms. During the Drug Substance batch certification, including the batch record review and approval process, Janssen Quality will consolidate and review these oversight forms ensuring the appropriate procedures were followed and any issues or events observed have been appropriately addressed and closed. [redacted] indicated that this plan was implemented 15 April 2021. I asked which lots were initiated and/or were in-progress at the time this plan was implemented, and I was provided with the following list:

Area	Lot #	Status/Stage on 15Apr2021
[redacted]		

[redacted] indicated that the oversight aspect of the plan was implemented for some of these batches; however, the batch release certification process (using the oversight forms) has not yet occurred since there were batches that were initiated prior to or were already in progress at the time the oversight plan was implemented and thus do not have the complete documentation to perform the batch certification as defined in the plan. Additionally, there has not been any initiation of new batches after implementation of the plan. Thus, the batch certification process will be fully implemented for the newly initiated batches.

The plan also outlined mechanisms of governance between Janssen and EMOB, having daily/weekly operational management meetings to act as a mechanism for discussion and escalation in the event of a disagreement in operational areas, batch record review etc. These operational meetings include but not limited to, shift changes, deviation/CAPA management, batch record management and review, batch and raw

material planning etc. Issues that are not resolved during these meetings are escalated to a Daily Management Pulse meeting for resolution. Additionally, there are Monthly Oversight Governance meetings that can be assembled as needed and be used to track and trend the execution performance of EMOB under Janssen oversight. These meetings also serve to provide as an escalation point for all issues and disputes not able to be resolved in operational meetings.

I [redacted] came across an example of the type of information discussed in the Daily Management Pulse meetings during my discussion with [redacted], from the Engineering group at EMOB, regarding deviations relating to excursions of dissolved oxygen in the bioreactor stages. He noted that trending data of the operating parameters for bioreactors are discussed daily between EMOB and Janssen in these Daily Pulse meetings. I was provided with slides that included this type of data that was presented at a Pulse meeting that took place 17 March 2021 in which bioreactor trending data for GMP [redacted] and GMP [redacted] batches were presented and discussed.

[redacted] Coverage:
On 4 June 2021, I discussed the role of [redacted] and Janssen in monitoring the effectiveness of enhancements with [redacted] Senior Director, Global Quality Engineering. [redacted] provided me with a document entitled Oversight of Production Suite, Warehouse and QC Laboratories – Personnel and Material Flow (effective 5/19/2021), which outlines [redacted] role in providing oversight of new procedural and process revisions for material and people flow through the facility, as well as ensuring that there is proper documentation and training for these activities. [redacted] also provided me with a copy of the Movement of Material and Waste for Areas [redacted] and [redacted] checklist that will be used for this oversight.

[redacted] also provided me with the Consulting Agreement between Emergent and [redacted] When I asked about the relationship between [redacted] and Janssen, he stated that there are no agreements between them. I also asked to meet someone from [redacted] and on the same day, [redacted] from [redacted] introduced himself to me and provided me with his business card.

I asked [redacted] about the relationship between Janssen and Emergent, and he provided me with the quality agreement dated 11/23/2020. I asked him if there was any new agreements, and he provided me with a copy of a document entitled "Janssen Oversight Plan and Procedures for the Manufacture of [redacted] at the Emergent BioSolutions Bayview Facility Baltimore, Maryland" dated as approved on 5/26/2021. This document includes four (4) areas of oversight by Janssen: increased oversight and final sign-off of manufacturing, supervision of all critical activities, providing direction with full 24/7 on-the-floor coverage, and supporting and engaging in daily governance of operational execution. The oversight also includes

having Janssen technical and quality personnel in the plant.

Batch Record Approval, Final Batch Release and Batch Certification Process

[redacted] Coverage:

I [redacted] discussed the batch record approval, final batch release and batch certification process with [redacted], QA Manger for Raw Materials and was provided with the following SOPs:

- SOP000285v8.0 "Quality Assurance and Manufacturing Review of Manufacturing Records" (effective 9/27/2019)
- SOP002288v16.0 "Product Release Program" (effective 30 March 2021)

[redacted], who is involved in the final batch release review process indicated that there have not been any major changes to the batch record approval and batch release process since this was discussed in detail during the site visit from 9-12 February 2021. The batch record approval and batch release are consecutive processes, with batch record approval being initiated as the first step in the overall process. As per SOP000285v8.0, the executed batch record undergoes review by a manufacturing reviewer and a QA reviewer. This process is initiated after completion of manufacturing process and begins with the submission of the executed Batch Production Record (BPR) to a qualified reviewer or a Manufacturing manager for review. EMOB has a separate group within production, that are solely responsible for reviewing the batch record and this group does not participate in production. The manufacturing reviewer completes the manufacturing portion of the Batch Record Review Checklist [redacted] Each module of the batch record including the buffer and media preparation modules has this checklist. After review by manufacturing, the batch record is then reviewed by Quality Assurance and also completes the Batch Record Review Checklist [redacted] initiated by the manufacturing reviewer.

The checklist requires initialing and dating of specific items that were checked in the batch record and has separate boxes to reference deviations and comments made in the batch record followed by signature lines for the Manufacturing Reviewer and QA reviewer.

Regarding the final batch release, I reviewed SOP002288v16.0 "Product Release Program" and discussed the process with [redacted]. The SOP defines the procedures for final disposition of a batch. To initiate final batch release, QA completes a Product Disposition Form. This SOP also covers procedures related to shipment of DS to an intermediate storage site, and Release For Further Processing (RFFP, Condition Release Memo), which involves the release of custody of DS to Janssen before final batch release. Several forms are required regarding shipment of DS to various sites from EMOB, depending on where the DS will be shipped and the status of the DS (Quarantine vs. Released). There are separate notification forms for shipment of DS to

the storage facility and forms for shipment of product to the filling facility. There are two versions of the form for shipment to the filling facility, depending on the disposition status (Quarantine vs. Released) of the lots being shipped to the filling facility.
I discussed the requirements for the RFFP or conditional release memo as the change of custody of the DS from EMOB can be performed before completion of final batch release. For the conditional release of DS, a risk assessment is performed and includes the following:

- All currently identified open deviations were assessed by Quality Assurance to determine if the events impact product disposition; deviations are as follows:
- All in process and release test results available to date were evaluated; no results, to date would impact product disposition.
- All relevant change controls were assessed to determine product impact; no change control impacts product disposition.
- A preliminary review of batch records confirms no process-related deviations impact product disposition.

These are noted in the memo to have been performed. The memo also includes the listing of the specific containers, lot numbers and a note of the status of the lots. The memo is signed off by both parties. I asked about the timing of the RFFP memo and when final batch release is completed. I was told that usually final batch release process is completed shortly after issuance of the RFFP memo. [redacted] indicated that the status of BDS remains in a "Quarantine" status in [redacted] until final batch release is completed, thus BDS will stay in a Quarantine status even when custody of BDS is transferred to Janssen if final batch release has not yet been completed.
I reviewed the revision history of SOP00228v16.0 and noted an inclusion in section 6.5 (change made 30 March 2021) that states to "ensure the review of all electronic batch data is completed. This will include the review of any equipment trend to ensure all Critical Process Parameters are met for batch release". This is also reflected in the Product Disposition checklist that includes "a verification that all electronic data has been reviewed including Trend data for equipment to ensure all Critical Process parameters are met for batch release".

The initiation of final batch release process can occur simultaneously or just after issuance of the RFFP memo. If there is issuance of an RFFP memo prior to full batch release, this information is captured in the Product Disposition Checklist. In my discussions with [redacted] in regard to the revision history, I inquired about the addition of the electronic batch data review and he indicated that Janssen wanted the review of the electronic data for equipment to be included in the checklist for final batch disposition.

[redacted] Oversight- Batch Certification
[redacted] Coverage:

I was provided with the protocol "Batch Record Review Protocol for Janssen Bulk Vaccine (COVID-19) Emergent BioSolutions Baltimore Bayview Facility, Baltimore, Maryland" which was noted as effective 19 May 2021. This protocol outlines the role and evaluation process of [redacted] group regarding batch record review. Noted in this protocol, as a remedial action to a 483 issued 20 April 2021, EMOB agreed to include participation of a third-party [redacted] in certain reviews, oversight, and facilitation of remedial activities. Among these activities, [redacted] is to participate in the certification of batch records related to the production and testing of Janssen COVID-19 batches manufactured at the Facility. Additionally, certain oversight activities are being conducted by [redacted] under a separate protocol entitled "Oversight of Production Suite, Warehouse and QC Laboratories-Personnel and Material Flow, Emergent BioSolutions Baltimore, Bayview Facility, Baltimore, MD, Effective as of 18 May 2021". The results and outputs from the activities conducted under the Oversight Protocol will be considered and incorporated as part of the Batch Certification Process.

As per the Batch Record Review protocol, [redacted] will review batch records for Janssen Bulk Vaccine (COVID-19) batches that are manufactured, tested, and planned for release or use in further manufacturing of finished vaccines. The review will include key aspects of the manufacturing and testing process, associated records, data, and information related to Bulk Vaccine Batches, from the bill of materials for ingredients and components staged for production of the bulk, in-process or finished Bulk Vaccine Batch through packaging and labeling and bulk release. Upon completion of the review by [redacted] of each Bulk Vaccine Batch Record, [redacted] will issue a written document "Certification Letter" to EMOB to show evidence of review and satisfaction as appropriate.

I [redacted] discussed with [redacted], [redacted] epresentative on site, about the role of [redacted] in providing oversight at EMOB. The role of [redacted] with regards to observation of production is limited to only ancillary actions to production involving areas that include warehousing and material movement, raw materials, QC sampling and testing, weigh and dispense activities, and waste removal. Regarding the batch record review, currently, [redacted] acts as a facilitator in the interaction between Janssen and EMOB with respect to reviews of the batch record and does perform batch record review in association with EMOB by assisting in making changes and identifying issues or deficiencies per EMOB's SOP. In the future, [redacted] will be involved in doing a separate independent review of the batch record involved with final batch disposition.

[redacted] Coverage:
On 4 June 2021, I also discussed the role of [redacted] in batch certification with [redacted]. [redacted] provided me with a copy of the Batch Record Review Protocol for Janssen Bulk Vaccine (COVID 19) (effective 19 May 2021), which outlines [redacted] role in certification of J&J drug substance batches. [redacted] also provided me with

a copy of the Batch Review Checklist. During my review of the protocol, I noted that it includes a Model Certification Letter as attachment A. I also noted that the protocol and Model Certification Letter include mention of review of the adequacy of deviation and investigations. I was not able to view any complete Certification Letters as the certification process had not yet been performed for any batches at the time of the investigation.

Observation #1-1.4
Emergent has initiated a new deviation 3100012594 to document an additional comprehensive investigation of the OOS result originally investigated under deviation 3100012112. Additional CAPAs with associated target dates will be initiated upon completion of this investigation.

[redacted] Coverage:
On 3 June 2021, I discussed deviation 3100012594 with [redacted], Director, Quality Assurance. [redacted] stated that this new deviation was initiated as a supplement to the investigation conducted under deviation 3100012112. We discussed EMOB's progress on the following CAPAs described in the deviation:

Personnel Flow and Showering

- Modify signage for all production areas to accurately classify them as "viral": [redacted] stated that this CAPA (1100003410) was still in process and due in June 2021.
- Update SOP001516 to eliminate showering requirements given that Bayview is now a single virus facility and to prohibit associates from working in a viral area (based on the new signage) and entering Weigh and Dispense on the same working day: see my discussion under Observation 4 below.

Gowning Practices for Weigh and Dispense

- Area [redacted] has been decontaminated and decommissioned, including access limitation, material removal and [redacted] did not discuss the decontamination and decommissioning of Area [redacted] (as described in RPT055966) with [redacted]
- The Area [redacted] locker room is no longer in use: [redacted] stated that his locker room is no longer in use, but I was unable to verify this status during the investigation.
- SOP001516 and SOP044383 will be updated to require Weigh and Dispense associates to enter the Weigh and Dispense [redacted] in street clothes and dedicated plant shoes, where they will don the appropriate gowning: [redacted] stated that operators now enter the Weigh and Dispense area via the [redacted] in street clothes and change into a plant uniform but I was not able to

verify these SOP changes during the investigation. This corrective action will need to be verified when the firm is in production.

- Update SOP001516 to require Weigh and Dispense associates to store dedicated plant shoes in the warehouse in the vicinity of the Weigh and Dispense room: [redacted] stated that this CAPA (1100003411) was in process and due in June 2021.

Training

- Integrated and instructor-led training related to routine activities, such as gowning, waste handling, cleaning and disinfection will be provided: [redacted] provided me with the slides and records for the following trainings during our discussion:
  - TRN040737 v1.0, A Holistic Approach to Contamination Control
  - TRN040743 v1.0, Bayview Cleaning and Sanitization
  - TRN040744 v1.0, Bayview QC Raw Material Sampling
  - TRN040745 v1.0, Bayview QC Internal Testing Sample Transport
  - TRN040749 v2.0, Bayview Warehouse Cleaning
  - TRN040750 v1.0, Bayview Waste Disposal in the Quality Control Laboratories
  - TRN040754 v1.0, Bayview Material Waste & Flow and Special Medical Waste
  - TRN040759 v1.0, Bayview Weigh Dispense

  [redacted] further stated that TRN040751 v1.0, Bayview Operation of the Decontamination [redacted] was still in process and due in June 2021.

  During discussion of the trainings with [redacted], I noted that there is no mention of how to determine the [redacted] contact time for the [redacted] disinfection steps. I further noted that some areas where this step is done there are no clocks. [redacted] provided me with a copy of the revised material and waste flow SOP (SOP001518, version 17.0, effective 6/1/2021) and showed me that it states in section 6.1.3 on page 4 all of the acceptable ways to determine this time. I suggested that these options be included in the applicable trainings as a training enhancement (see **Discussion Item #3**).

  During the discussion of these training with [redacted], I noted that there were duplicate entries for some employees suggesting that they had taken the same training twice. I discussed the record for training TRN040744 with [redacted] on 3 June 2021, and he explained that this instructor led training was given due to the employees having some confusion on several points. However, the managers listed in the training record only need to take the training once. I

discussed the duplications I noted for the "read and acknowledge" trainings with Mr. Elmore on the same day, and he explained that in situations where an employee completed one of these trainings in a short amount of time, they were asked to repeat the training to ensure they actually read the document. He noted that this was intentional and part of addressing the training feedback EMOB received during the April 2021 inspection.

On 4 June 2021, I had a follow-up discussion of these trainings records with [redacted] who explained to me that for some of the instructor led trainings (TRN040737 and TRN040754; see **exhibits #[redacted] and [redacted]** the instructors did not always use sign-in sheets and therefore did not always track who attended each training. Therefore, during the recording of attendance of the trainings, the instructors used their memory to document which employees attended. [redacted] further stated that this gap led to the duplications I observed, and when I stated that this would also lead to no ability of EMOB to confirm who attended these training (even if they were listed only once), he agreed (see **Discussion Item #3**). [redacted] stated that EMOB had opened a deviation due to this issue (3100013030; opened on 4 June 2021) and planned to address it via a CAPA to perform knowledge checks that would require someone to have attended the training in order to pass.

- Instructor-led training will be provided on GMP principles, microbial contamination prevention and viral containment: [redacted] provided me with the slides and records for TRN040727 v1.0, FDA Inspection Review and Remediation. I noted the same duplicate training record issue described above for this training (see **exhibit #[redacted]** and **Discussion Item #3**).
- Viral containment education will be included in the [redacted] training for Bayview facility personnel: [redacted] stated that this CAPA (1100003412) was in process and due in July 2021.
- PLN040854, "Viral Contamination Control Strategy" will be updated to include the defined training necessary to ensure employees understand the necessary controls and their role in viral containment: I did not address this CAPA during the investigation. This CAPA will need to be verified when the firm is in production.

Waste Movement Practices

- SOP044335, "Removal of Special Medical Waste from Manufacturing Areas," was created to establish robust controls relating to the removal of [redacted] waste. Personnel will receive instructor-led training on this SOP: see discussion under Observation 3 below.

- The entire facility will be cleaned and disinfected to remove any virus that may be present: see discussion under Observation 2 below.
- Per the firm's FDA483 response, the Weigh and Dispense [redacted] has been enlarged to allow for entry of materials on pallets or dollies, avoiding contact with the floor. During the walkthrough of 2 June 2021, I observed that the [redacted] for Weigh and Dispense were switched (versus the [redacted]). [redacted] explained that this was done under a change control and due to the room that was previously the [redacted] being larger than the room that was previously the [redacted]. On the same day. [redacted], Sr Director, Quality, provide me with the relevant change control (2100006389). During my review of the change control, I noted that it included records of training on the new personnel flow and that this training record had the same duplicate training record issue described above (see **exhibit #**[redacted] and **Discussion Item #3**).
- An [redacted] to provide dedicated egress for waste has been installed: I observed this [redacted] during the walkthrough of 2 June 2021.
- Waste flows have been revised as shown in SOP001518 (material and waste flows) and SOP044365 (QC waste flow) to ensure that waste does not cross paths with materials or personnel involved in manufacturing operations: [redacted] provided me with a copy of the material flow form [redacted] version 1.0, effective 5/22/2021) and waste flow for Areas [redacted] form [redacted] version 1.0, effective 5/22/2021). I did not collect the form showing the QC waste flow during the investigation.

Material Transfer Gowning

- SOP001516 has been updated to clarify the requirements for material transfer gowning and degowning: [redacted] provided me with a copy of the revised SOP (SOP001516, version 25.0, effective 6/1/2021) and identified that the gowning requirements were modified in sections 6.4.1.1 and 6.4.2.1 on page 7, and section 6.4.3.1 on page 8 to reflect removal and discarding of gowning materials.

Handling of Viral Stock and Cell Bank

- Update SOP001516, "Personnel Flow and Gowning Procedure for Production Envelope," will be updated to state that double gloves will be required when handling viral material, which will be decontaminated, removed and replaced before performing any additional activities: see my discussion under Observation 4 below.
- New [redacted] will be purchased and dedicated to Client [redacted] Existing gloves will be discarded: On 4 June 2021, [redacted] provided me with a purchase order

for new [redacted] I was not able to verify that the existing [redacted] were discarded during the investigation.

Facility Cleaning

- The entire facility will be cleaned and disinfected to remove any virus that may be present: see my discussion under Observation 2 below.
- The cleaning program was assessed. As a result, cleaning SOPs SOP000392, "Cleaning Program for controlled Areas [redacted] SOP041886, "Area [redacted] and Weigh and Dispense EMOB Cleaning Program for Controlled Areas" and SOP044245, "Warehouse Cleaning Procedure," were revised and training is being provided: [redacted] provided me with a copies of the revised SOPs and he highlighted the following revisions:
  - Area [redacted] and [redacted] Cleaning (SOP000392, version 15.0, effective 6/1/2021), addition of contact time and documentation of time, clarified how to clean, and added [redacted] after [redacted] application.
  - Area [redacted] and Weigh and Dispense Cleaning (SOP041886, version 5.0, effective 6/2/2021) addition of Weigh and Dispense to SOP and [redacted] after [redacted] application; and
  - Warehouse Cleaning (SOP44245, version 4.0, effective 6/2/2021); addition of freight elevator, identifying cleaning agent, added [redacted] cleaning of floors, changed [redacted] use from [redacted] to [redacted], and added a cleaning log.

Congestion in the Warehouses

- All materials in both the Bayview warehouse and the Central warehouse were evaluated according to an approved protocol to determine if they must be discarded based on risk of exposure to contamination: see my discussion under Observation 5 below.
- Both warehouses were cleaned and decontaminated: see my discussion under Observation 2 below.
- Materials that are transported from the Central warehouse to Bayview will be [redacted] before delivery to Bayview to ensure no contamination is present: see my discussion under Observation 2 below.
- A sampling booth is being constructed at the off-site warehouse to prevent the need to sample in the Bayview facility: see my discussion under Observation 3 below.

Congestion in Production

- A new SOP, SOP044405, "Bayview on the Floor Program" will be created to require routine checks throughout the facility. This includes walkthroughs of the manufacturing suites by the shift lead at the [redacted], [redacted] walkthroughs by the manufacturing manager, and [redacted] walkthroughs by site leadership team members. These will be performed using a checklist, which includes an evaluation of congestion in the area: see my discussion under Observation 2 below.
- Supplies will not be stored in the Area [redacted] and [redacted] downstream suites: I did not address this CAPA during the investigation.
- Two equivalent mechanisms of waste removal will be implemented to reduce the buildup of waste in the facility: see my discussion under Observation 3 below.

[redacted]

- SOP041748, "New Product Introduction," will be revised to require an evaluation of the volume of waste and determination of the appropriate waste removal processes: I did not address this CAPA during the investigation.
- SOP001510, "System Level Impact Assessment Process," will be revised to ensure decontamination [redacted] are no longer considered "no impact systems" and are appropriately classified and qualified: I did not address this CAPA during the investigation.
- The functionality of [redacted] will be demonstrated in accordance with a written protocol: see my discussion under Observation 3 below.
- The [redacted] decontamination cycle and [redacted] will be qualified: see my discussion under Observation 3 below.
- SOP000388, "Operation of the Decontamination [redacted] will be updated to describe how the bags containing the waste are to be placed into the [redacted] [redacted] to ensure there is adequate [redacted] Operators will be trained on this procedure before the [redacted] is used: see my discussion under Observation 3 below.
- PLN040854, "Viral Contamination Control Strategy" will be updated to reflect the use of both the [redacted] and [redacted] procedures as acceptable waste removal processes. Currently, the plan only recognizes the use of the [redacted] I did not address this CAPA during the investigation. This CAPA will need to be verified when the firm is in production.

[redacted]

- A [redacted] will be installed to transfer [redacted] directly from the [redacted] area to the production areas: I did not address this CAPA during the investigation. This CAPA will need to be verified when the firm is in production.

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

Raw Material Flow

- SOP044231 "Return of Unused Manufacturing Components and Materials" has been obsoleted, preventing return of materials from production to the warehouse: [redacted] provided me with a copy of this SOP (SOP044231, version 1.0, effective 2/21/2021) identified as being obsolete via watermark.
- PLN040854 "Viral Cross Contamination Control Strategy" will be updated to restrict material flows across areas designed for different products: I did not address this CAPA during the investigation. This CAPA will need to be verified when the firm is in production.

[redacted] Components

- [redacted] as secondary containers for media components have been replaced with [redacted] stated that the [redacted] used as secondary containers for media components are no longer used but was not able to provide verification since the [redacted] were not previously referred to in any procedures. During the walkthrough on 2 June 2021, I did not observe any [redacted] in the warehouse or manufacturing areas.
- [redacted] as secondary containers for [redacted] components have been replaced with [redacted] preparation batch records will be revised to reflect this change: [redacted] provided me with a sample batch record [redacted] version 3.0, effective 6/1/2021) and showed me that in each relevant step [redacted] the batch record references the use of a [redacted] also provided me with a copy of change control 2100006447 under which changes to all of the batch records used for client [redacted] (Janssen) [redacted] will be changed to add use of [redacted] Finally, [redacted] provided me with the specification (SPE027659, version 3.0, effective 3/5/2019) and manufacturer's description of the [redacted] and specification (SPE042445, version 1.0, effective 7/12/2019) and manufacturer's description of the [redacted] referenced in the BOM in batch record [redacted] for Complete [redacted] medium Client [redacted].
- SOP000390, "Cleanroom Behaviors and Contamination Control in the Production Envelope," will be updated to include specific instructions on lifting from the inner bag and not from the bottom of the container: [redacted] provided me with a revised version of this SOP (SOP000390, version 10.0, effective 5/22/2021) and showed me that section 6.2.16 on page 4 was revised to instruct operators not to touch the bottoms of containers.

- SOP000390 "Cleanroom Behaviors and Contamination Control in the Production Envelope" will be updated to require operators to [redacted] their hands with either [redacted] or [redacted] mmediately after removing the outer bag of double-bagged powder materials to minimize the risk of contamination prior to handling the inner bag: [redacted] provided me with a revised version of this SOP (SOP000390, version 10.0, effective 5/22/2021) and showed me that section 6.2.17 on page 4 was revised to instruct operators not to [redacted] hands with [redacted] or [redacted] mmediately after removing outer bag.
- PLN040854 "Viral Cross Contamination Control Strategy" will be updated to ensure the controlled handling of raw material containers: I did not address this CAPA during the investigation. This CAPA will need to be verified when the firm is in production.

Non-Component Material Movement

- Update SOP001518 to prohibit the movement of materials across areas manufacturing different products: [redacted] provided me with a copy of this revised SOP (SOP001518, version 17.0, effective 6/1/2021) and showed me that section 6.5.1 refers to form [redacted] [redacted] provided me with a copy of this new form [redacted] version 1.0, effective 5/22/2021) and showed me that that the flow of materials and equipment prohibits movement across areas manufacturing different products (including separation of flows across Areas [redacted] and [redacted].

[redacted]

- Include instructions for management of alarms in new SOP044372 v1.0, "Operation of the Weigh Dispense": [redacted] provided me with a copy of this new SOP (SOP044372, version 1.0, effective 5/25/2021) and showed me that section 6.1.12 on page 2 instructs operators ensure the [redacted] visual indicators remain green.

On 3 June 2021, during our discussion of deviation 3100012594, I asked [redacted] about the extended comparability assessment mentioned on pages 3 and 17 of EMOB's initial response to the Form FDA 483 Issued on 20 April 2021. He stated that it is the document entitled "Investigation and Impact Assessment for Contamination of [redacted] Drug Substance Batch [redacted] Manufactured by Emergent manufacturing Operations Baltimore, LLC" that was discussed and provided during the April 2021 inspection, and that no new assessment had been performed.

On 4 June 2021, I discussed EMOB's consideration of QC raw material sampling in deviation 3100012594 with [redacted], Sr Director, MS&T. [redacted] noted that QC raw material sampling was not considered as a potential root cause during the initial

investigation under deviation 3100012112 but was considered under deviation 3100012594. When I asked about the role QC raw material sampling may have played in the cross-contamination event, he stated that it was not ruled out as a potential root cause. He further stated that the changes to gowning practices and gowning training performed would apply to operators in raw material sampling. When I asked about EMOB's consideration of the QC raw material sampling procedures, he stated that they were not considered and are not described in the deviation even though sampling is an open operation (see **exhibit #** [redacted] and **Discussion Item #1**). On 10 June 2021, I had a follow-up discussion with [redacted] who stated that EMOB plans to amend the deviation to add an addendum regarding QC raw material sampling and he provided me with the draft text of this addendum.

Observation #1-1.5
Emergent will revise SOP044115, Setup and Operation of the [redacted] Bulk Filler System, and creating a Work Instruction WI042057, Work Instruction for [redacted] System for Client [redacted] to detail the process for aborting and documenting abortion of a batch process in the batch record. Emergent will train appropriate site personnel on the revised procedure and work instruction on abortion of a batch process and documentation.

[redacted] Coverage:
I reviewed the firm's updated SOP #044115 v4.0 (effective 28 May 2021) as well as WI42057 that now includes instructions for aborting and restarting a recipe. I did not observe a deficiency with the firm's written procedures. The firm's documentation of training activities was noted in the General Discussion with management under **Discussion Item #3** in the General Discussion with Management section.

Observation #2-2.1
Emergent completed a comprehensive gap assessment of the site's cleaning and sanitization procedures.

[redacted] Coverage:
I reviewed the firm's document #ExMEMO040703 v1.0 dated 1 June 2021 that describes the gap assessment performed for cleaning procedures. The memo describes multiple updates to the cleaning program such as removing references to [redacted] updating room classifications, updated instructions for cleaning drains and floor balances, and changed frequencies for specific disinfectants. Due to the lack of manufacturing occurring during the investigation, I was not able to verify the execution of these new cleaning procedures in manufacturing areas with respect to batch production.

Observation #2-2.3

Emergent will revise SOP027886, Quality on the Floor Program, to include routine checks throughout the facility. This includes checks of the manufacturing suites by the shift lead at the [redacted], [redacted] checks by the manufacturing manager, and [redacted] checks by site leadership team members. This also includes [redacted] checks of the QC laboratory and the warehouse by the area manager and [redacted] checks by site leadership team members. These checks will be performed using a checklist to ensure appropriate assessments are performed.

[redacted] Coverage:
On 2 June 2021, I discussed the revisions to SOP027886 with [redacted], Quality Assurance Manager. He stated that this SOP describes the function and responsibilities of quality on the floor and provided me with a copy of the SOP (SOP027886, version 6.0, effective 5/4/2021). He also provided me with a training record to show that employees were trained on the revised SOP. [redacted] further explained that the SOP had been revised to change the warehouse walkthrough frequency from [redacted] to [redacted] and to add [redacted] walkthroughs of the utility area. He also stated that new forms to perform these walkthroughs, [redacted] and [redacted] were created and referenced in the SOP. When I asked him about what was done previously, [redacted] stated that previously the [redacted] warehouse walkthrough was done without using a form. [redacted] provided me with copies of these forms [redacted] version 1.0, effective 5/4/2021; and [redacted] version 1.0, effective 5/4/2021) on the same day. I also requested a recently completed form [redacted] and [redacted] provided me with a copy dated 5/8/2021.

In addition, I requested copies of the following additional forms referenced in SOP027886 and received them from [redacted] on the same day:

- Compliance Inspection Checklist – Cleaning of Manufacturing Area [redacted] version 3.0, effective 9/9/2020)
- Compliance Inspection Checklist – Quality Control (QC) Laboratory [redacted] version 3.0, effective 9/9/2020)
- Compliance Inspection Checklist – Supply Chain [redacted] version 4.0, effective 9/9/2020)
- Batch Record Review Checklist [redacted] version 6.0, effective 12/11/2020)

I also requested the 2 most recently completed [redacted] forms and [redacted] provided me with completed forms dated 5/10/2021 and 5/20/2021 on the same day.

[redacted] further noted that a new SOP (SOP044405) was under review. [redacted] provided me with the applicable change control 1100003413 as well as a draft version of the SOP (SOP044405, version 1.0, *electronic only*) on the same day. [redacted] stated that this SOP includes [redacted] checks, [redacted] checks by manufacturing management and [redacted] checks by site leadership, all using checklists, as described

in the change control.

Observation #2-2.4
Emergent will decontaminate and decommission Area [redacted] including access limitation, material removal, and [redacted]

[redacted] Coverage:
On 8 June 2021, I asked Mr. Ed Elmore about physical access to Manufacturing Area [redacted] He stated security-badge access has been revoked for almost all employees (with the exception of [redacted] and a few other Director-level individuals) and has not been in use and will not be re-opened until the complete decontamination procedures are completed. This is documented in change control 2100006417 as provided in **exhibit #[redacted]** I had previously verified badge access controls to area [redacted] on [redacted] June 2021. [redacted] – Senior Director MS&T provided a remote video walkthrough of the Area [redacted] manufacturing facility on 9 June 2021. The equipment and facility did not appear to be in use.

Observation #2-2.5
Emergent will replace the floors in the Areas [redacted] corridor to utilize more durable surfaces that can support equipment movement and cleaning requirements.

[redacted] Coverage:
During the walkthrough on 2 June 2021, I was able to visually verify that a new floor had been installed in the Areas [redacted] corridor. I also discussed the new floors with [redacted] who provided me with change control 2100005672 describing the locations where the floors were replaced. [redacted] stated that as described in the change control, the floors were replaced with Area [redacted] Downstream (room 1235), Area [redacted] (room 1237), [redacted] (rooms 1231 and 1232), and a portion of the [redacted] corridor. I stated to [redacted] that the change control does not provide a clear rationale for why certain parts of the floor were replaced and other parts were not replaced, such as the level of deterioration that led to replacement. I was not able to verify that the floors were replaced in locations other than the corridor during the investigation.

Observation #2-2.6
Emergent will replace the floors in material flow path in the warehouse with material conducive to cleaning and sanitization.

[redacted] Coverage:
During the walkthrough on 2 June 2021, I was able to visually verify that a new floor had been installed in the warehouse. I also discussed the replacement of the floor with [redacted] who provided me with change control 2100006434 describing the replacement of

the floor.

Observation #2-2.7
Emergent will install pre-made panels in the [redacted] corridor supporting Areas [redacted] and [redacted] and [redacted]

[redacted] Coverage:
During the walkthrough on 2 June 2021, I was able to visually verify that pre-made panels had been installed in the [redacted] corridor. I also discussed the installation of the panels with [redacted] who provided me with change control 2100006422 describing the replacement of the floor. During my review of the change control, I noted that it contains a picture of the wall panels installed in the [redacted] (room 1079). I was not able to verify that new wall panels had been installed in the [redacted] and [redacted] during the investigation.

Observation #2-2.8
Emergent will clean and disinfect Areas [redacted] and the facility warehouse.

[redacted] Coverage:
I conducted an inspection of Areas [redacted] and [redacted] as well as the warehouse. I observed an area of the de-gowning rooms for Area [redacted] that do not appear to be clean as evidenced by hair and dust observed on the ceiling. Additional concerns were identified with damaged surfaces in Area [redacted] as described in the item six identified in General Discussion with Management section. [redacted] provided the following dates for [redacted] cycles that were previously performed:

- Upstream Area [redacted] – July 2020 and December 2020
- Downstream Area [redacted] – February 2021
- Downstream Area [redacted] – May 2021

During our investigation, Mr. Elmore stated the firm would be conducting a [redacted] cycle in the manufacturing Area [redacted] and other areas such as Area [redacted] and others would be following in the near future according to the schedule provided in **exhibit #[redacted]**

[redacted] Coverage:
On 3 June 2021, I discussed the cleaning and disinfection/decontamination of Areas [redacted] and [redacted] and the warehouses with [redacted], Director, Industrial Microbiology (Johnson and Johnson). He explained that EMOB did not perform a formal risk assessment. Regarding the cleaning and disinfection of the Area [redacted] and [redacted] manufacturing area, [redacted] stated that this was done under two respective protocols (PRO050259, version 1.0, effective 5/12/2021, and PRO050261, version 1.0, effective 5/12/2021) but that the respective reports were still being drafted. [redacted] provided me with copies of the protocols on the same day. When I asked [redacted] about plans for [redacted] of the manufacturing areas, he stated that that this will be done

under a protocol but that the protocol was still being drafted. He further explained that the plan was to [redacted] all manufacturing areas in Areas [redacted] and [redacted] including the [redacted] and [redacted] areas, but excluding the [redacted] corridor. When I asked about the Weigh and Dispense and Raw Material Sampling areas, he stated that these areas would also be [redacted] under a protocol. He further noted that there is also a plan to [redacted] Area [redacted] but that was low priority. [redacted] stated that the timing of the [redacted] was delayed due to the investigation.

Regarding the Bayview Warehouse, [redacted] explained that the cleaning and disinfection was performed under a protocol (PRO050262, version 1.0, effective 5/7/2021) and is described in a report (RPT055885, version 1.0, effective 5/19/2021). [redacted] provided me with copies of the protocol and report on the same day. [redacted] stated that the work was done by a contractor according to a Statement of Work (SOW), and [redacted] provided me with a copy of the project summary report from the contractor [redacted] containing the SOW as well as photographic documentation of the work (*electronic only*). I asked [redacted] about the available data on the survival of viral vectors on a surface, as it was mentioned during the regulatory meeting on 25 May 2021. He stated that such data does not exist for the Janssen viral vector, and the infectiousness data mentioned during the meeting was for the [redacted] virus related to the Janssen viral vector.

Regarding the Central Warehouse, [redacted] explained that the decontamination was performed under a protocol (PRO050256, version 1.0, effective 5/5/2021) and is described in a report (RPT055880, version 1.0, effective 5/18/2021). [redacted] provided me with copies of the protocol and report on the same day. [redacted] stated that this work was also done by a contractor [redacted] according to a SOW, and [redacted] provided me with a copy of this SOW. He further explained that the decontamination was done using a [redacted] explained that components that had been shipped to the Bayview warehouse were returned to the Central warehouse, and present in their [redacted] inside [redacted] during the decontamination. Components that were not previously shipped to the Bayview warehouse were present in [redacted] during the decontamination. He stated that this was done in case those [redacted] were contaminated. When I asked if there was an assessment of the impact of the decontamination agent on the [redacted] packaging, since there was a potential for it to enter the [redacted] containers, [redacted] stated one had not been performed. However, on 8 June 2021, I had a follow-up discussion with [redacted]. He provided me with the safety data sheet for [redacted] as well as information from [redacted] showing that quaternary [redacted] compounds can be used on the types of [redacted] used to package the components stored in the warehouse.

Regarding the trailer decontamination at the central warehouse, [redacted] explained that the decontamination will be performed under a protocol (PRO050299, version 1.0, effective 5/8/2021) but that a report had not yet been written since the decontamination would not be done for another [redacted]s. [redacted] provided me with a copy of the protocol on the same day. [redacted] noted that there is an effort in the protocol (in section 6.0 on page 3) to reduce the amount of corrugated material in the trailer except when necessary (such as to support glass bottles).

Observation #2-2.9
Emergent will demonstrate the functionality of the [redacted] in accordance with a written protocol.

[redacted] Coverage:
On 3 June 2021, [redacted] explained that EMOB has conducted a decontamination [redacted] feasibility study to determine the functional comparability between the decontamination [redacted] in Areas [redacted] and [redacted] and to evaluate the worst-case [redacted] in these [redacted] [redacted] provided a copy of the report (RPT055786, version 1.0, 5/18/2021) and protocol (PRO050246, version 1.0, effective 4/26/2021) during our discussion. He explained that the study was performed using a reduced sterilization time from [redacted] to [redacted] and a shorter [redacted]). [redacted] stated that the study determined that the [redacted] were equivalent based on [redacted] and that the maximum load for these [redacted] was determined to be [redacted]. In addition, during evaluation of the worst-case load, he explained that the [redacted] obtained for the thermocouple placed with component [redacted] packaging was only [redacted] due to the [redacted] becoming [redacted]. The report notes in section 3.2.1 on page 6 that the [redacted] could have caused air pockets leading to lack of sufficient [redacted]. [redacted] explained that based upon this result, EMOB adjusted the [redacted] cycle from a [redacted] sterilization time to a [redacted] sterilization time, and adjusted the handling of waste to segregate waste such as [redacted] packaging and gowning into the special medical waste stream.

Observation #2-2.10
Emergent will optimize and qualify the [redacted] decontamination cycle using [redacted] to demonstrate appropriate viral log reduction.

[redacted] Coverage:
On 3 June 2021, [redacted] and I discussed a second [redacted] study that evaluated the maximum load for the decontamination [redacted] in Areas [redacted] and [redacted] and the reduction in microbial organisms (including viruses) obtained during the decontamination cycle. [redacted] provided a copy of the report (RPT055930, version 1.0, 5/26/2021) and protocol (PRO050357, version 1.0, effective 5/7/2021) during our

discussion. He noted that the study was performed using biological indicators (BIs; *Geobacillus stearothermophilus*) instead of using [redacted] and the same cycle used for the feasibility study. All of the BIs used in the study showed negative results (except for the positive control BIs which were all positive).

Observation #2-2.11
Emergent will revise the [redacted] decontamination SOP000388, Operation of the Decontamination [redacted] and will train operators on the revised procedure.

[redacted] Coverage:
See my discussion regarding the revisions to SOP000388 under Observation 3 below. See my discussion of training of operators on the revised procedure under Observation 1 above.

Observation #3-3.1
Emergent will strengthen the Bayview facility's biowaste handling process. Specifically, under SOP044335, Removal of Special Medical Waste from Manufacturing Areas, when [redacted] capacity requires waste to be bagged and removed without decontamination, site personnel must disinfect each layer of the bag and follow a defined exit pathway to remove the waste from the facility, with cleaning and disinfection performed along the exit route immediately following waste removal.

[redacted] Coverage:
On 2 June 2021, I discussed EMOB's waste [redacted] decontamination capacity and procedures with [redacted] Validation Engineer, and [redacted]. [redacted] stated that EMOB has evaluated their current capacity to decontaminate waste by [redacted] considering several factors. First, EMOB adjusted the [redacted] cycle from a sterilization time from [redacted] to [redacted] and a [redacted]) than was previously used (see discussion of feasibility study below) reducing the total cycle time from [redacted] to [redacted]. Second, EMOB changed their waste handling procedures to segregate non-wetted waste, such as gowning and [redacted] coverings, and wetted waste that is chemically inactivated to the special medical waste process to reduce the amount of [redacted] waste to about [redacted] of what was previously [redacted] decontaminated. He further noted an issue with [redacted] decontaminating [redacted] waste identified during the feasibility study that is discussed below. Finally, [redacted] noted that EMOB has determined that the maximum load per autoclave run is [redacted] versus the maximum of [redacted] they were [redacted] previously. [redacted] provided me with a document showing the calculated waste accumulation ([redacted]) compared to their [redacted] decontamination capacity before and after these changes, supporting that EMOB will have sufficient capacity to [redacted] decontaminate the amount of waste they project will be generated in the future.

I asked [redacted] about the [redacted] limit per decontamination [redacted] load and he stated that this is specified in SOP000388 in section 6.3.7.3 on page 3. [redacted] provided me with a copy of this SOP (SOP000388, version 9.0, effective 6/1/2021) and I verified this step. [redacted] also provided me with training records to show that operators read and acknowledged the revisions to this SOP. I asked [redacted] about EMOB's consideration of when an [redacted] goes out of service, and he responded that in such cases the waste can be diverted to the special medical waste procedure as described in SOP044335 but that the waste would need to be [redacted]. [redacted] provided me with a copy of this SOP (SOP044335, version 2.0, effective 6/1/2021) and I verified this allowance in steps 6.8.3 and 6.9 on page 5. Finally, I asked about integration of waste removal decision tree that was presented during the regulatory meeting of 25 May 2021 (slide 18), and [redacted] responded that it was added to SOP001518. [redacted] provided me with a copy of this SOP (SOP001518, version 17.0, effective 6/1/2021) and I verified that the decision tree is present as appendix A on page 22 of the SOP.

Observation #3-3.2
Emergent will evaluate alternatives to staging raw materials for QC sampling in the warehouse.

[redacted] Coverage:
On 3 June 2021, I discussed EMOB's plans for building a new [redacted] at the Central Warehouse with [redacted], Senior Manager, QC Analytical Services, Emergent Camden. [redacted] stated that EMOB plans to move sampling of raw materials to the Central Warehouse under an ongoing change control (2100006627) so that raw materials do not need to be shipped to Bayview, staged in the Bayview warehouse for sampling, and then shipped back to the Central warehouse. He explained that a temporary [redacted] is being constructed under ongoing change control 2100006510 with the plan to build a permanent [redacted] in the future. He stated that the change controls will include updates to relevant SOPs at both facilities.

Observation #4-4.2
Emergent is implementing revised flows that ensure that waste does not cross paths with materials or personnel involved in manufacturing operations.

[redacted] Coverage:
See my discussion under Observation 1 above. I also observed the revised wasted flows during the walkthrough on 2 June 2021 and confirmed that that waste does not cross paths with materials or personnel involved in manufacturing operations.

Observation #4-4.4
Emergent will define and enforce gowning and de-gowning requirements that will

mitigate the risk of contamination. Specifically, SOP001516 will be revised to define relevant requirements, which will be enforced through third-party oversight.

[redacted] Coverage:
On 2 June 2021, I discussed the revisions to SOP001516 with [redacted], Sr Manager, Upstream, who provided me with a copy of the SOP (SOP001516, version 25.0, effective 6/1/2021). [redacted] stated that the requirement for [redacted] was add to the SOP for level [redacted] gowning when in viral mode in section 6.5.4.1 on page 9, and forms [redacted] were modified for [redacted]. [redacted] also stated that section 6.5.4.3 was added to the SOP on page 9 to prevent operators who have been in viral areas from entering Weigh and Dispense rooms with the same working day. During our discussion of this change, I noted that the requirement for personnel to shower after being in the manufacturing area was removed from this section (as stated on page 31 of EMOB's initial response to the Form FDA 483 Issued on 20 April 2021). Finally, he noted that the plant uniforms used in Weigh and Dispense rooms were switched to [redacted] (though this change is not described in the SOP). When I asked him about the third-party oversight, he stated that [redacted]s performing this function under a protocol (see discussion under Item #1 in the General Discussion with Management section below).

Observation #5-5.5
Emergent will revise SOP001518 to require visual inspection of material totes before each use and to require documentation of this visual inspection in the equipment logbook.

[redacted] Coverage:
On 2 June 2021, I discussed the revisions to SOP001518 with [redacted], who provided me with a copy of the SOP (SOP001518, version 17.0, effective 6/1/2021). [redacted] noted that section 6.1.4.1 on page 4 was updated to require inspection of equipment, section 6.2.1.1 on page 6 was updated to require inspection of carts and a new form [redacted] was added, and section 6.10.1 on page 15 was updated to require inspection of totes and carts and add use of form [redacted] [redacted] also provided me with a copy of this new form [redacted] version 1.0, effective 5/22/2021) and showed me that it included a column to document visual inspection (fourth column, titled "Cart Clean, Rust Free, Fit for Use").

Observation #5-5.6
Emergent will evaluate materials in the Bayview facility according to an approved protocol to determine if they must be discarded based on risk of exposure to contamination, or if they can be cleaned and decontaminated.

[redacted] Coverage:

On 2 June 2021, I discussed EMOB's evaluation of the materials stored at the Central Warehouse with [redacted] [redacted] explained EMOB initially performed a risk assessment of the impact to material stored at the Bayview and Central warehouse in the context of the contamination mitigation strategy employed in response to the cross-contamination event and April 2021 inspection. This risk assessment was performed under a protocol (PRO050257, version 1.0, effective 4/30/2021) and is described in a report (RPT055855, version 2.0, effective 6/1/2021). [redacted] provided me with copies of these documents. [redacted] explained that the process included first generating a list of the materials stored in both warehouse, the manufacturing areas and the QC microbiology laboratory on 24-26 April 2021, and assessing if the outer packaging of the material can be [redacted] or the material itself can be [redacted] prior to delivery for use (report appendix 1). Then raw materials present in the Central Warehouse were extracted and a physical count of these raw materials was performed, including if containers were opened, the number of containers sampled, and the remaining unopened containers for sampled materials (report appendix 2). Finally, a query was run in SAP on 14 May 2021 to confirm the list of raw materials (report appendix 3) and then every batch of raw materials with even a single container that were opened either for sampling or weigh and dispense was placed on hold in SAP (report appendix 4). [redacted] and I spot checked a few entries in the lists to confirm the raw materials stated as placed on hold were actually placed on hold. When I asked [redacted] about the decontamination of the Central warehouse, he stated that it was performed under a separate protocol.

Observation #6-6.4
Emergent will revise BOP040102, Decontamination [redacted] Efficacy Testing Program, to include a requirement for placement of the biological indicator or chemical indicator in a worst-case location inside the [redacted] to support that all of the waste is decontaminated.

[redacted] Coverage:
On 3 June 2021, I discussed the status of the revision to BOP040102 with [redacted]. He stated to me that the BOP is being replaced with a new SOP (SOP044394) which was still in process. I collected a draft version of this SOP during the investigation.

Observation #9-9.2
Emergent will revise SOP001518 to state that the totes must be visually inspected prior to each use, and that this visual inspection must also be documented in the material transfer logbooks, [redacted] and [redacted] (TCD: May 2021 (prior to resuming new manufacturing))

[redacted] Coverage:

See my discussion regarding SOP001518 and [redacted] under Observation 5 above. On 2 June 2021, [redacted] also provided me with draft copies of forms [redacted] and [redacted] and showed me that they both included a column to document visual inspection (fourth column, titled "Cart Clean, Rust Free, Fit for Use").

OTHER AREAS OF REVIEW

Client Complaints
[redacted] Coverage:
On 2 June 2021, I discussed EMOB's client complaint procedures with [redacted], Specialist II, Compliance/Quality Systems. [redacted] explained to me that EMOB implemented an SOP for client complaints (SOP044246, version 1.0, effective 3/11/2021) as well as a client complaint report form [redacted] version 1.0, effective 3/10/2021) in March 2021. When I asked what their process was prior to March 2021 for client complaints, she stated that they only were manufacturing clinical trial material so did not have a formal client complaint procedure. I then requested a list of all client complaints received to date and on the same day received a list of client [redacted] (Janssen) complaints with one complaint listed and a list of client [redacted] (AstraZeneca) complaints with 2 complaints listed. After I reviewed these complaints, I asked [redacted] why the cross-contamination of Janssen batch [redacted] was not listed as a complaint since the control cell sample test results for Janssen batch GMP [redacted] from Leiden indicating the presence of an adenoviral genome containing the [redacted] (which is not present in the Janssen vaccine virus) was reported to EMOB on 11 March 2021 per deviation 3100012112. [redacted] explained that per section 4.1.3, the SOP only applies to product after it is shipped by Emergent to the client, and since GMP [redacted] was never shipped from EMOB, no complaint was opened.

Effectiveness of [redacted] on [redacted]
[redacted] Coverage:
On 3 June 2021, I discussed EMOB's assessment of the efficacy of [redacted] when used on [redacted] with [redacted] and [redacted]. Since EMOB's procedure for Special Medical Waste includes the use of [redacted] on [redacted] with a decontamination time of [redacted], I asked them what information EMOB has to support its virucidal efficacy under these conditions. [redacted] noted that the MSDS for [redacted] states in the general description section that it can be used on [redacted] and in the direction for use section that it can be used as a broad-spectrum disinfectant on items such as equipment and as a sporicide only on hard, non-porous surfaces. He further referenced and provided me with a copy of EMOB's surface virucidal efficacy study (RPT040638, version 2.0, effective 2/23/2018) supporting the efficacy of [redacted] against a number of different viruses using the materials of construction present in the facility's manufacturing areas. I stated that the study did not include [redacted] surfaces and

that the MSDS does not appear to mention use of [redacted] on [redacted] surfaces.

On 8 June 2021, I had a follow-up conversation regarding the efficacy of [redacted] when used on [redacted] with [redacted]. [redacted] stated that he had reached out to [redacted] the manufacturing of [redacted] to see if they could provide any additional information. He provided me an email from [redacted] supporting the use of [redacted] on [redacted] surfaces.

Evaluation of Contamination of the Water System

[redacted] Coverage:

On 3 June 2021, I discussed EMOB's assessment of the potential of their water system to be contaminated with the AstraZeneca COVID-19 viral vector with [redacted]. [redacted] noted that EMOB's water system is a [redacted] and that Janssen had previously performed a thermal inactivation study with the [redacted] viral vector (used for the Janssen drug substance) which showed that the vector undergoes a [redacted] at temperatures ranging from [redacted]. He further stated that the AstraZeneca viral vector would likely have similar thermal stability. [redacted] provided me with the final report for this study [redacted] dated 4/20/2021) on the same day.

Deviation 3100012656 for Batch [redacted]

[redacted] Coverage:

On 4 June 2021, I discussed deviation 3100012765 with [redacted] Manager, Manufacturing, [redacted] and [redacted]. [redacted] explained that deviation 3100012656 was raised on 7 May 2021, after a QA Raw Materials Manager noticed a comment dated 24 March 2021 on page 43 of batch record [redacted] for batch number [redacted] referencing a leak during filling of bottles [redacted] for which no deviation was raised. When I asked if the investigation into this leak included a retrospective evaluation of leaks via a review of batch records, since leaks such as this one were not captured in a deviation at the time of occurrence, [redacted] stated that this had not been done (see **Discussion Item #1**). [redacted] stated that EMOB had a list of leaks kept by the "Leak Squad ", but when she searched that list for the leak associated with deviation 3100012765 she was unable to find it in the list (see **Discussion Item #1**).

Walkthrough of the Warehouse and Areas [redacted] and [redacted]

[redacted] Coverage:

During the walkthrough, I also observed grey totes inside the [redacted] between the Warehouse and the [redacted] corridor (room 1061) that are used to transfer equipment between these areas (see photo provide by [redacted] and **exhibit**

#JW6). I observed that these two totes were respectively labelled for Area [redacted] and Area [redacted] but were on the Warehouse side of the [redacted] as defined by the yellow line present on the floor (see **Discussion Item #4**). In addition, I observed red totes used for removal of Special Medical Waste in Area [redacted] the [redacted] located between Areas [redacted] and [redacted] and the [redacted] corridor, and outside the [redacted] in the [redacted] corridor (but inside the building). I also observed these totes outside the building when looking out the window in the [redacted] corridor (see photo provide by [redacted], **exhibit #**[redacted] and **Discussion Item #4**). I further observed that these totes looked similar or were identical and none of them were labelled (see photos provide by [redacted], **exhibit #**[redacted] and **Discussion Item #4**).

I observed digital clocks in several rooms within the manufacturing area (such as [redacted] between Area [redacted] and the [redacted] corridor, but not in all areas (see my discussion under Observation 1 and **Discussion Item #3**).

The walkthrough did not include Area [redacted] I was also not able to view the elevator between Area [redacted] and the warehouse.

On 10 June 2021, I discussed the labeling of the red totes with [redacted]. He informed me that EMOB had begun the process of labeling the bins as follows:

- Outside bins have been labelled "Outside Waste Transport Only",
- Inside bins on the production side of the demarcation line to be labeled [redacted] and
- Inside bins on the corridor side of the demarcation line to be labeled [redacted]

Walkthrough of Weigh and Dispense Area

[redacted] Coverage:

During the walk-through of the facility, I discussed the change in material movement within the weigh and dispense area as a corrective action noted in EMOB's response to the FDA-483 issued 20 April 2021. Specifically, changes to the movement of materials into and out of the weigh and dispense area were discussed and were noted in the following SOPs: SOP044372v1.0 21 "Operation of the Weigh and Dispense" (effective May 25, 20) and SOP001518v17.0 "Material and Waste Flow" (effective June 1, 2021). These changes included the use of pallets to transport large bulk materials from the warehouse shelves to the [redacted] entry point of the weigh and dispense area. From this point, these bulk materials undergo [redacted] decontamination steps before transport into the core of the weigh and dispense area. This includes a decontamination with [redacted] with [redacted] contact time while on the pallet just outside the [redacted] entry and a second [redacted] treatment when being moved into the [redacted] using an area dedicated dolly (also decontaminated with [redacted] performed on one side of a demarcation line within the [redacted] After [redacted], the decontaminated bulk

material with dolly is transported over the demarcation line and into the core of the weigh and dispense area.

An additional noted change is the location of the [redacted] that is used for the bulk materials for weigh and dispense. There are [redacted] that allow entry into the weigh and dispense area (including the sampling area). Originally, the smaller [redacted] was used for the bulk materials to be moved into the weighed and dispense area and the larger [redacted] was used for raw materials to be move into this area for sampling. Now, the larger [redacted] is used for entry of bulk materials into the weigh and dispense area to allow for more clearance for transport of bulk materials on dollies into this area.

I had additional discussion regarding the use of the weigh and dispense area that focused on changes in the preparation of the materials used to the make [redacted] and media. [redacted], Supervisor of [redacted] indicated that his group is dedicated to weighing and dispensing of raw materials for use in preparing [redacted] and media. In later discussions during the week, I received more clarification regarding the responsibilities of personnel involved in the weighing and dispensing of [redacted] and media, in addition to the preparation of [redacted] and media. I was told that [redacted]'s group is separated into two parts, in which one part of the group weighs and dispenses the [redacted] and also makes the [redacted] in the production area [redacted] used for downstream processes) and the other part of the group is only responsible for preparing kits of media which is then used by production to prepare the media. [redacted]'s group is not involved in the preparation of media and is only involved in weighing and dispensing the media for production. Media is prepared by upstream production personnel.

Deviations/Investigations/CAPA Procedures

[redacted] Coverage:

I [redacted] discussed the following SOPs regarding the handling of deviations, investigations and CAPAs that were referenced in the EMOB's response (submitted 30 April 2021) to the Form FDA 483 that was issued on 20 April 2021.

- SOP044111v2.0 "Global GMP Deviation Management Procedure" (effective April 12, 2021)
- SOP044112v1.0 "Investigation and Root Cause Analysis Procedure for GMP Deviations" (effective date April 5, 2021)
- SOP044131v1.0 "Global GxP CAPA Management Procedure" (effective April 5, 2021)

Emergent is in the process of transitioning over to implementing global corporate procedures regarding the handling of deviations (SOP044111), in addition to conducting investigations (SOP044112), and implementing CAPAs (SOP044131). These global procedures were effective as of 5 and 12 April 2021. I ([redacted]) discussed these procedures, and the timing of the transition. Currently, EMOB is operating from their

local deviation/CAPAs procedures; the site was not yet ready to make the transition to the global procedures at the time the procedures became effective for the other sites. The transition to these global procedures also includes a change in the electronic management system, changing from SAP to [redacted] for management of deviations, CAPAs and change controls. Currently, personnel are undergoing training on these global SOPs and it is anticipated the new global procedures will be effective at EMOB by end of June.

Waste and Material Flow and Special Medical Waste Handling

[redacted] Coverage:

As a corrective action noted in EMOB's response to the 483 issued 20 April 2021, the waste and material flows were modified to ensure segregation of materials and waste movement within the facility. During the facility tour, EMOB pointed out the changes in the waste flows, specifically in Areas [redacted] The major change to the waste flow for Area [redacted] included that waste is no longer routed through the warehouse. Waste is removed from the Area [redacted] and [redacted] production suites in the same way as before through the [redacted] exits; however, the waste is now transported through a different route within the return corridor using a [redacted] that allows waste to be directly removed to an area outside the facility for storage in the red totes. This new route bypasses waste movement through the warehouse and is no longer taken through the direction in the return corridor to the same [redacted] used for incoming materials for production from the warehouse. Plastic red wheeled totes are used to transport Special Medical waste (waste that is not [redacted] from the production area through the [redacted] exit. There is a decontamination procedure the has been implemented for externally decontaminating the [redacted] containing the waste with [redacted] as the waste is moved from the production area to placing in the red totes located in the [redacted] exit. The decontamination with [redacted] with a contact time of [redacted] is documented and verified by a second operator in logbooks that reside in the [redacted] where the red totes reside. These procedures are outlined in SOP044335v2.0 "Removal of Special Medical Waste" from Manufacturing Areas (effective date Jun 1, 2021) and SOP001518v17.0 "Material and Waste Flow" (effective date June 1, 2021).

During the facility walkthrough on the first day of the investigation, 2 June 2021, I was able to see the areas and visualize the path of how waste is removed from the Area [redacted] and [redacted] production areas. I [redacted] noticed that the same [redacted] exit that is used for the removal of Bulk Drug Substance (BDS) from the production area was the same as that used for removal of Special Medical Waste. To mitigate the risk of potential overlap of BDS and waste movement from this area, several strategies were noted. The removal of waste and BDS is temporally separated. The waste is removed from the area after production, thus after BDS is removed from the production area. There are potential for overlaps of waste and BDS that can occur during the filling operations. During filling operations, waste is generated; this includes the replacement of the

[redacted] that occurs after the filling of every 12 bottles. This waste is [redacted] and placed in an opposite area of the production room, away from the filling machine. Generally, waste is not removed until after filling has been completed; however, there can be times when there is not sufficient room for the accumulated waste, thus the waste will need to be moved out of the filling production area. In these cases, there is a washdown of the [redacted] area and [redacted] exit before moving BDS outside of the production room into the [redacted] area. The batch record is undergoing revision to reflect the need to perform a washdown and documenting the activity if needed, and this activity is also noted in SOP001518v17.0 "Material and Waste Flow", specifically section 6.11.2 stating the following: "Prior to transporting Drug Substance from the downstream suite to the exit corridor for bagging and sealing, a washdown of the [redacted] and exit corridor [redacted] must be performed per SOP000392, EMOB Cleaning Program for Controlled Areas [redacted] and [redacted]

Other mitigations include that the [redacted] and tubings are chemically decontaminated with [redacted] before being replaced and discarded into bags. The BDS bottles are also wiped down before being sealed into bags and removed through the [redacted] exit. Additionally, there is no risk of cross-contamination as EMOB is operating as a single-product facility. All these aspects together are implemented to mitigate any risk of contamination. In other discussions, I received clarification on the chemical decontamination of waste and the type of waste that is usually considered Special Medical Waste versus waste that is typically [redacted] before being removed from the area. All product contact equipment used in the manufacturing process is chemically decontaminated in place with [redacted] as part of the manufacturing process. Most of this equipment is also [redacted] with exception to the [redacted] and the [redacted] as this equipment is too large to fit into the [redacted] thus is removed as Special Medical Waste.

Regarding waste removal from Area [redacted], (Sr. Director, MS&T at EMOB) and [redacted] (Sr. Manager, Downstream at EMOB) indicated as there is no longer manufacturing occurring in Area [redacted] and currently no plans to manufacture in Area [redacted] (EMOB is now a single product facility); there is no longer waste movement from Area [redacted] through the warehouse.

Training
[redacted] Coverage:
The training program was discussed with EMOB as a follow-up to the EMOB's response to the 483 issued 20 April 2021. There are three mechanisms of training conducted at EMOB that include Read and Acknowledge, Instructor Led Training (ILT) and On the Job Training (OJT). Before the FDA inspection conducted 12-20 April 2021, the predominant training conducted at EMOB was Read and Acknowledge. This involved

personnel reading SOPs online and acknowledge understanding of the procedures. There did not seem to be a knowledge assessment with this mechanism of training to verify understanding of the procedure. The procedures for ILT/OJT were in place but were not executed at the time of the inspection. The ILT includes training by an instructor, which can be conducted as in person training or visual training (online video presentations/computer course). After the training, there is a knowledge assessment, where personnel are asked questions based on the training provided. For the ILT, Subject Matter Experts (SMEs) work with the QA training group to create specific curriculums and training materials that are built on the specific activities and operations that are required to be performed by personnel. The SMEs are responsible for developing the curriculums and training materials and the QA training group is responsible for assigning the specific curriculums to personnel depending on their job title and responsibilities.

All training is tracked in the [redacted] System [redacted] and supervisors receive automatic notifications from [redacted] when personnel under their charge require training on new or revised SOPs or need refresher training. OGT training involves personnel observing a trainer performing a specific activity, after which the trainee is then expected to perform the activity in front of a supervisor and then perform the operation [redacted] independently. EMOB indicated that they are currently revising the OGT modules and creating new ones. The re-designed OGT modules will be customized per equipment and will include teaching why it is important to perform operations as trained. The modules will have subsections that include troubleshooting and explanation for the significance of following the procedures. The revised OGT training process and enhanced modules are targeted to be fully implemented early to mid-July 2021.

<u>Follow-up Items Regarding Specific Batches</u>
[redacted] Coverage:
During the investigation, I [redacted] followed up on EMA and CBER concerns regarding a deviation associated with GMP [redacted] and testing results relating to batches GMP [redacted] GMP [redacted] and GMP [redacted] EMA received notification from Janssen about an open investigation regarding an identified issue of leaking observed at a tubing connection during the filling of GMP [redacted] High level information was provided, indicating that the investigation is in-progress with the current status having the expectation for the lot to be rejected once the investigation is completed. Regarding Area [redacted] batches GMP [redacted] [redacted] and [redacted] CBER product office requested a follow-up to further evaluate testing results provided by Janssen for batches GMP [redacted] (Area [redacted] specifically, regarding results for the control cell assay for batches GMP [redacted] [redacted] & [redacted] The discussion and evaluation of these follow up items during the investigation are summarized as follows:

GMP [redacted]- I [redacted] reviewed the deviation 3100012765: [redacted] Pump Leaks",

which included an investigation report. This deviation is in association with tube connection leaking incidents that occurred during manufacturing of Batch [redacted]

I discussed this deviation in detail with Edward Elmore, Senior Director of Quality at EMOB. The deviation was initiated 7 May 2021; however, the incident regarding the leaking during the filling of Batch [redacted] occurred 24 March 2021. This deviation was initiated upon discovery during the final batch release review by EMOB QA. There had been an RFFP memo issued for this lot; therefore, by the time of the final batch release review, custody of this lot had already been transferred to Janssen. Additionally, Janssen had shipped this lot to [redacted] filling site (South Africa), also prior to the discovery and initiation of deviation during the final batch release review. According to my discussions with Mr. Elmore, this lot had been partially filled at the [redacted] filling site. I was provided with a letter that was sent to [redacted] by Janssen, External Quality, dated 12 May 2021, indicating that pending further investigation of an Emergent deviation, Janssen requested that [redacted] place a hold on any of the EMOB DS batch [redacted] bottles [redacted] The letter also copied [redacted] and [redacted]

The deviation and investigation report detailed the background of the deviation, investigation, root cause and corrective actions that were initiated. In the deviation summary, it was noted that the issue of leaking was initiated as a deviation seven weeks after the incident occurred. As previously noted, the deviation was initiated during the final batch release review by QA. The observance of the leaking was documented during the run in the "comments" section of the batch record. During the run leaking was also observed at the filling [redacted] affecting bottles [redacted] The bottles were placed on hold and labels were applied, which was documented in the batch record.

The detailed description of the incident involved observations of leaking at tubing connections to [redacted] and [redacted] These [redacted] are involved in the filling process; [redacted] is used to move DS from the [redacted] to the sterilizing [redacted] and into the [redacted] which collects the filtered DS to then be pumped by [redacted] to the [redacted] for filling DS bottles. Thus, the activity of [redacted] occurs [redacted] and the activity of [redacted] occurs [redacted] The cause of these leaking incidents observed at both [redacted] and [redacted] was attributed to loose [redacted]. It was noted that these [redacted] connections can become loose overtime or can slip down [redacted] if not tight enough and therefore cause leaking. These [redacted] come pre-assembled and sometimes may require tightening adjustments. Several other root causes were noted that included the following:

- Management from both QA and Manufacturing failed to provide the correct containment activities to ensure that impact of leaks on the BDS would be mitigated.
- There was a deficiency in the SOP/BPR directing frequent walk throughs inspecting for leaks; in addition, there is a gap in the SOP and Work Instruction for direction on the installation for [redacted] and [redacted]
- There was lack of initiation of a deviation at point of observation in addition to lack of initiation during BPR review.

Other significant information provided in the report included an assessment of the GMP impact, concluding that the entire lot was impacted since the beginning time of the leak cannot be determined. The report further concluded that the leak is isolated to this batch, and leaks that occurred during this batch do not impact other batches as this is an independent event. The report also included a trending analysis using search queries in SAP (over period of 24 March 2020- 25 May 2021) that included [redacted] or "[redacted] and [redacted] and "[redacted]" in addition to [redacted] and "[redacted] The following occurrences were noted:

- DEV 3100012682: BDS Leaks [redacted]
- DEV 310001274: [redacted]
- DEV 3100012791: Leak below [redacted]
- DEV 3100012714: [redacted]

The following CAPAs were initiated to address this deviation:

- CAPA 1100003401 Equipment use and set up
  - Placement of [redacted] and [redacted]
  - Inspect and document hoses are in correct place
  - Evaluation of [redacted] usage
  - Regular inspection for leaks during run
  - Regulator inspection of hose barbs and [redacted] during run
  - Updates to the work instruction
- CAPA 1100003325 To address deviation not being initiated in real time
- CAPA 1100003326 To correct failure to address issue during Batch Release and Review
- CAPA 1100003402 To address escalating issues and documentation in records

Relating to this deviation investigation for GMP [redacted], an issue was discussed with the firm during the final closing of the investigation (item #2 in the General Discussion with Management). This issue was noted as a deficiency in QA oversight responsibilities and the following of procedures with regards to batch record review and approval and the timely initiation of deviations to ensure that all open deviations are assessed before

the Release For Further Manufacturing and the change of BDS custody to Janssen. In the situation with batch GMP [redacted] as the deviation regarding the [redacted] leaking was discovered during review for final batch release, this deviation could not be assessed for product impact during preparation of the Release For Further Processing as per procedures. The firm did acknowledge this deficiency in discussions during the investigation and during the final close out meeting.

Given that there have been several noted incidents of leaking that occurred during DS filling with multiple batches and to evaluate the impact of leaking noted in GMP [redacted] regarding other batches, I discussed the overall issue of leaking during the filling process observed for Batches [redacted]. I requested copies of the comments section from Stage [redacted] module for batches GMP [redacted] from Area [redacted] to review the occurrence of similar leaking incidents and/or other incidents during the filling process. I was provided with the comments sections for 15 batches as two batches (including GMP [redacted] and GMP [redacted] were terminated at Stage 1 and Stage 3 thus did not proceed through to the filling process. After my review, below is a summary of batches with no incidents of leaking occurring during filling, in addition to batches in which there were noted incidents of leaking that occurred during filling.

Below is a listing of GMP batches with no incidents of leaking noted in the comments section during the filling process:

- GMP [redacted] no leaking noted
- GMP [redacted] no leaking noted
- GMP [redacted] no leaking noted
- GMP [redacted] no leaking noted
- GMP [redacted] no leaking noted

Below is a list of GMP batches with notations of leaking incidents in the comments section during the filling process and that had a reference to a deviation also noted in comments section:

- GMP [redacted] DEV 310011216, leaking at Step [redacted] nvolving slight leaking at the [redacted]
- GMP [redacted] DEV 3100012612, leaking at Step [redacted] nvolving s leak observed coming from a [redacted] connection of the o [redacted]
- GMP [redacted] DEV 310012539, leaking step [redacted] nvolving an observation by an operator that a [redacted] was not closed allowing product to get through the unused aseptic connection to the bottle. Bottle placed on hold. [redacted] non-routine bioburden samples were taken for testing.
- GMP [redacted] The following two deviations were noted:

- DEV 3100012707, leaking at [redacted] involving observation of small drippage coming from bottom of the [redacted] Leak [redacted] coming from [redacted] connector not fully engaged
- DEV 3100012721, leaking at [redacted] involving observation of leaking at the [redacted] not correctly installed.

Below is a listing of GMP batches with notations of leaking incidents in the comments section that occurred during filling process with no reference to a deviation noted in comments.

- GMP [redacted] Leaking noted at step [redacted] leaking at [redacted] sampling component- Deviation 3100011549
- GMP [redacted] Leaking noted at step [redacted] involving the following, Deviation 3100011539:
  - Primary [redacted] observed dripping during filling operation
  - Pinch [redacted] on [redacted] bottle unsecured causing dripping
  - Leaking observed from aseptic connector for bottle [redacted] loose connection
- GMP [redacted] Leaking noted at step [redacted] involving leaking from primary [redacted] ([redacted])-connected to Deviation 310001161 (an overarching deviation relating to leaking at the [redacted]
- GMP [redacted] Leaking noted at step [redacted] involving [redacted] leaking
- GMP [redacted] Leaking noted at step [redacted] and step [redacted] involving the following, Dev 3100011961 initiated 8 March 2021 (time of occurrence):
  - [redacted] Leaking observed at [redacted]
  - [redacted] Leaking observed at [redacted] of [redacted] (occurred during [redacted] bottles [redacted] put on hold.

Batches including GMP [redacted] indicated above did have associated deviations initiated with exception to GMP [redacted] GMP [redacted] was the batch associated with the cross contamination event, thus the firm did not proceed with initiating a deviation due to the intention to reject this lot. The firm acknowledged that a deviation should have been initiated for this lot if only for trending purposes.

The types of leaks noted during the filling process for all batches can be categorized into two major types, those leaks that occur [redacted] and leaks that occur [redacted] leaks are considered to have a more direct impact on the DS filling process since these leaks occurred after the DS has [redacted] There were several incidences of leaking occurring at the [redacted] which is a [redacted] leak, and seemed to be more frequent in occurrence in batches manufactured prior to GMP [redacted] and after which appeared to not occur in the later batches. Additionally, there were multiple instances of leaking from the connections to [redacted] and [redacted] including occurrences noted with

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

lots GMP [redacted] and GMP [redacted]

I [redacted] discussed in detail the leaking issues observed during the DS filling process with [redacted], Associate Engineer at EMOB. To better understand the leaking issues and how EMOB is addressing them, I discussed the set up and operation of the filling system used to fill BDS. I was provided with SOP 044115v4.0 "Set up & operation of [redacted] Bulk Filler System"(latest document date 24 May 2021 (indicated as new document), currently an "authorized" procedure with no effective date) and the associated Work Instruction WI042057v2.0 "Work Instruction for [redacted] System for Client [redacted] latest document date 24 May 2021, associated with a list of revisions, currently an "authorized" procedure with no effective date). We discussed specific sections of SOP044115 and WI042057 including sections that explain how the [redacted] are installed and connected to the filling system. I inquired about common areas within the system where leaks might occur and other areas of weakness in the system regarding leaks. She indicated that the main areas where leaking can occur is with the [redacted] such as the type of leaking that occurred with GMP [redacted] There are several locations within the system where these [redacted] are used. [redacted] are purchased as pre-assembled systems, thus there is limited option in adjusting the connections to the system. [redacted] indicated that leaking occurrences from the [redacted] can either be related to defects in the [redacted] or operator installation, basically, checking that the connections are secure and tightened. She indicated that there is some ability to tighten these [redacted] To address the leaking issues with the [redacted] she noted that a WI was created 24 May 2021 to accompany the SOP044115 "Setup and Operation of the [redacted] Bulk Filler System" that provides a reminder after an installation step, to "Hand tighten all [redacted]". The occurrence of [redacted] has significantly been reduced with lots after GMP [redacted]

[redacted] and I also discussed the issues relating to the [redacted] leaking incidents, which were prominent in occurrence with several lots prior to GMP [redacted] The overarching deviation 310001161 was initiated 10 Feb 2021 during the second FDA site visit 9-11 February 2021, in which the [redacted] leaking issue was discussed in detail and was recently re-opened 6 May 2021 to amend per FDA inspection 483 response commitment to re-open the [redacted] leak deviation investigation to include the vendor's impact assessment. This overarching deviation covers the investigation of three batches that have their associated deviation, all of which had issues relating to leaking at the [redacted]. These include the following:

- Batch [redacted] (GMP [redacted] Deviation 3100011549
- Batch [redacted] (GMP [redacted] Deviation 3100011539
- Batch [redacted] GMP [redacted] Deviation 3100011611

The investigation and root cause analysis determined that it was due to an equipment

issue relating to [redacted] in the system exceeding the manufacturer recommendations. Thus, the investigation led to change controls that included the following:

- Change control 2100006077 "Modify [redacted] Control"
- Change control 2100006079 [redacted] Bulk Filler Recipe Change"

Change controls noted above were implemented to correct the overpressure during filling and CAPA 1100003392 was initiated to ensure changes have been effective and to make changes for other areas as applicable. Additionally, a document change control was implemented DCC-043642 to revise SOP044115v1.0 to include instructions for how to abort a fill recipe and initiate a new recipe, in addition, there was a revision to include an instruction to initiate a deviation if a leak is discovered [redacted] during processing (section 6.27.4). This was included since there was a gap identified relating to a delay in initiating a deviation and the leaking event only being recorded as a comment in the batch record (Deviation 31000011784). Overall, based on these changes to the SOP, Work Instructions and other document changes and a review of the batch records, there appears to be an improvement with a reduction in the occurrence of leaking incidents as evidenced in the later batches.

GMP [redacted] Prior to the investigation of EMOB, Janssen provided testing results of batches [redacted] from Area [redacted] to CBER. I was asked to follow up on the result for the control cell assay for GMP [redacted] indicated as "Pending". This result is unusual since this testing should have been completed given the manufacturing was completed 1 April 2021. I discussed the "Pending" status for the result of the control cell assay for GMP [redacted] with [redacted], QC Manager, Immunology from EMOB. She indicated the reason for the pending status for the control cell [redacted] is due to a mistake in testing and thus the need to perform re-testing. [redacted] indicated the GMP [redacted] samples were mistaken as GMP [redacted] and therefore, were removed from the incubator prematurely. As a result of this mistake, the assay needed to be repeated. She indicated that the delay in the results was because fresh cells are required to perform a re-test. The time lag is due to having the cells being shipped from Leiden to EMOB and then requiring [redacted] to grow the cells for the assay. I discussed the use of fresh cells for the re-test as this re-test did not seem to evaluate the actual cells used in GMP [redacted] [redacted] indicated that the procedure for the re-testing of the control cell assay is different from the original procedure and indicated that for re-testing of the control cell assay, frozen cell retains cannot be used. For the re-test procedure, the fresh cells are [redacted] and then are [redacted] with the [redacted] from the cell retains for GMP [redacted]; the use of the [redacted] to [redacted] the fresh cells simulates the conditions of the GMP [redacted] control cell assay. [redacted] indicated that this is the procedure that is used for re-testing at Leiden and thus was used at EMOB. I was provided with the control cell testing protocol TMD040615v4.0 [redacted] and the re-test plan for GMP

[redacted] PLN041106v1.0[redacted] (TMD040615) Retest" (effective May 11, 2021), which provide details of the procedures regarding control cell assay testing and the re-test plan that was used for GMP [redacted]

I asked [redacted] how this mistake regarding removal of cells for GMP [redacted] instead of GMP [redacted] occurred. She indicated that the incubator used in the control cell assays can have up to [redacted] lots at time; there are [redacted] per lot and the incubator is able to hold up to [redacted] at a given time. To conduct the assay, there is a minimum of a [redacted] incubation time. As samples are pulled every [redacted] from manufacturing, the testing of multiple lots is concurrently running and are at staggered stages during the [redacted] incubation time for the assay. In order to complete a valid testing, the testing needs to be conducted with a minimum of [redacted] passages and/or a maximum of [redacted] passages within the [redacted] period. In the testing of GMP [redacted] bottles for GMP [redacted] were pulled out and tested by mistake, thus human error. The GMP [redacted] bottles were pulled out too early having only been incubated for [redacted] instead of the required [redacted] to complete the testing, thus, the test was invalid, requiring GMP [redacted] to be re-tested. The GMP [redacted] control cell assay was not impacted as the GMP [redacted] bottles had reached the appropriate required number of passages and incubation time for the results to be considered valid. Deviations were initiated for both GMP[redacted] (DEV 3100012280) and GMP [redacted] (DEV 3100012662) to evaluate the impact due to this mistake.

GMP [redacted] & [redacted] Prior to the investigation of EMOB, Janssen provided CBER with testing results for batches GMP[redacted] The results for the control cell assay for GMP [redacted] & [redacted] were noted as "Investigation in Progress". I discussed this result with an onsite Janssen representative and [redacted] Sr. Director MS &T at EMOB. They indicated that for these lots, the [redacted] sample failed to meet the specification, with the cells showing signs of [redacted] I was provided with a slide deck describing the details into the investigation for the OOS result. During the discussion, I was informed that the control cell testing had been transferred back to EMOB, and EMOB has been performing the control cell testing of all lots currently manufactured, including GMP [redacted] in Area [redacted] nd all lots in Area [redacted] However, previously, due to this same issue regarding the control cell assay, for GMP lots [redacted] there was a change control implemented to temporarily move the control cell testing to Leiden, Netherland for lots GMP [redacted].

The locations for the investigation testing regarding the OOS for GMP [redacted] & [redacted] is a combination of EMOB and Leiden. EMOB performed testing for bacterial contamination and [redacted] vector testing of drug substance and control cell samples and results were negative. Leiden performed [redacted] testing for the [redacted] in addition to [redacted] testing, confirming that the OOS for the control cells for both GMP [redacted] and GMP [redacted] was due to contamination with Janssen [redacted] vector and not AZ vector. The investigation is still ongoing to determine the source of the

contamination and if it was the media sample or the control cell sample that was contaminated.

The investigation noted the following probable and most likely root causes for further investigation:

- Sampling handling and transfer
  - Inadequate disinfection of sample container exteriors during transfers into QC Lab
  - Inadequate segregation of viral/non-viral samples in Sample Management and during transfers to QC Immunology
- Personnel movement
  - Inadequate controls for personnel entry to Lab [redacted] Lab [redacted]
- Lack of equipment/process for handling virally contaminated samples/waste in QC Laboratory
  - Due to lack of additional equipment for control cell testing, GMP [redacted] along with other parallel cultures were required to be processed in the same laboratory with same equipment as GMP [redacted] which was contaminated. There are no procedures for handling of suspected contaminated samples in the QC Control Cell Laboratory

Before a root cause is identified, EMOB has already initiated CAPAs to address identified mitigations based on the potential causes. These include but are not limited to updating procedures to implement additional controls for segregation relating to sampling handling and transfer (including implementing an immediate handoff with no intermediate storage in Sample Management), decontamination of samples and equipment (use of dedicated equipment), and implementing more regular decontamination of microscope and incubator.

Laboratories [redacted]
[redacted] Coverage:
As a reference to the control assay issues regarding GMP [redacted] GMP [redacted] and [redacted] I [redacted] covered Laboratories [redacted] which is the laboratory area used to perform control cell assay testing for Janssen vaccine. There is one entrance into Laboratories [redacted] Entry into the lab area is through Laboratory [redacted] Laboratory [redacted] s currently the lab area that is used for control cell testing for Janssen. Laboratory [redacted] are two separate lab areas; however, are not completely physically segregated. The rolling incubator that is used to incubate cells for the control cell assay is located in laboratory [redacted] and is dedicated for [redacted] cells. This rolling incubator [redacted] can hold up to [redacted] bottles. At the time of the walkthrough, two shelves of the incubator were being used. Shelf [redacted] had [redacted] bottles for the GMP [redacted] retest and shelf [redacted] has two roller bottles that were in-progress for training a new analyst. I asked about how control cell samples are obtained and received in the laboratory. [redacted] indicated that manufacturing obtains the samples, pulls cells samples [redacted]

from the [redacted] bioreactor and takes samples of the media used for [redacted] bioreactor. These samples are first taken to Sample Management intermediately handled before arriving to the laboratory for testing. Regarding the contamination of the control cell assay with Janssen vector, for GMP [redacted] and [redacted] I asked [redacted] if there is any shared equipment with vector containing samples as it was indicated that laboratory [redacted] is a vector free lab. [redacted] did indicate that a centrifuge used to spin down the cells is not dedicated and can be used with vector containing samples. She indicated that there is a change control to purchase a new centrifuge to be stored in Room 1405, thus allowing a dedicated centrifuge to be used for the control cell assay.

Laboratory [redacted] currently not in use, was previously used for infectivity assay related to the AZ vector, prior to April 15. There are plans to modify the laboratory (starting 8 June 2021) including the ordering of new equipment to convert Laboratory [redacted] into a duplicate lab to be used for control cell testing.

Bioburden controlled facility
[redacted] Coverage:
On 2 and 3 June 2021, I observed manufacturing areas defined as "Area [redacted] and "Area [redacted] as defined in the facility diagram presented in **exhibit #**[redacted] I verbally discussed the following items with the firm's management and are captured in photographs in **exhibit #**[redacted]

- Un-identified debris in overhead lights of upstream room: Area [redacted] and [redacted]
- Broken Diffusers of overhead lights in upstream Area [redacted] and [redacted] create direct path from interstitial space to manufacturing area
- Hair and dust on ceiling of de-gown area [redacted] and [redacted]
- Blistering and peeling paint on ceiling due to [redacted] cycles of decontamination
- Dislodged fire suppression covers in upstream area [redacted] processing room ceiling create direct path from interstitial space to manufacturing area
- Difficult to clean and damaged metal wall in upstream area [redacted] and dislodged outlet cover
- Uncleanable dislodged utility panel in area [redacted] creates path to interstitial space above ceiling

Line Clearance criteria of weigh/dispense area
[redacted] Coverage:
On 2 June 2021, I observed the firm's weigh/dispense area near the warehouse where certain raw materials are prepared for manufacturing activity in Area [redacted] and [redacted] [redacted] stated that the firm performs line clearance between customer materials, but the firm is now only serving a single customer in manufacturing. This is found in the firm's written procedure for conducting line clearances in SOP 043687 v1 on page 5 of 6 as presented in **exhibit #**[redacted]

I stated to Mr. Ed Elmore and Ms. Mary Oates, that in a single customer facility, the criteria in the written procedure doesn't seem to be applicable.

Data integrity practices
[redacted] Coverage:
On 2 June 2021, I observed the PC and scanner in the de-gown area of Area [redacted] which showed written instructions for scanning batch records into a network storage location (photograph in **exhibit #[redacted] p41**) on the M:\ drive.

On 3 June 2021, [redacted] demonstrated the ability to delete files from the M:\ drive location and provided a screen shot as seen in **exhibit #[redacted]** Additionally, he clarified that the written procedure identifying location for scanned Batch records within the file path of the M:\ drive is inaccurate as can be seen by comparing the photograph of the written instruction to the screen shot showing the actual batch record scanned files.

On 8 June 2021, [redacted] demonstrated the view of the network storage location for [redacted] data generated by the [redacted] chromatography equipment in Stage [redacted] of manufacturing the drug substance. An example of this batch record is provided in **exhibit #[redacted]** The [redacted] data is primarily absorbance data that demonstrated the performance of the chromatography steps such as [redacted] and [redacted] provided an example of the [redacted] data as seen in **exhibit [redacted] 0** and also demonstrated the network file storage location as seen in the screen shot in **exhibit #[redacted]**

Inventory System Does Not Adequately Track Applicable Storage Locations and Material
[redacted] Coverage:

On 2 June 2021, I observed freezer and LN2 storage equipment in the warehouse for viral seed and cell bank material respectively. When I reviewed written log books associated with cell bank material (client [redacted] in equipment #10044111 and 10044004 and compared to inventory in SAP as demonstrated by the warehouse employee [redacted], the inventory numbers did not match. The log books showed (as seen in **exhibit #[redacted] and [redacted]** that all Janssen material #1901305 was moved on 29 May 2021 from equipment 10044111 to 10044004. The SAP electronic inventory still showed the inventory in equipment 10044111 as seen from screenshots in **exhibit [redacted]** stated he had moved the material and confirmed that the SAP inventory was not accurate.

Additionally, I observed freezers in GMP warehouse such as equipment FZ-19946

(pictured in **exhibit #[redacted] p7**) that are not documented in the firm's GMP inventory system that contained commercial sample materials (also photographed in **exhibit #[redacted] p9**). See the list I requested from the firm that states which freezers are documented in SAP from **exhibit #[redacted]**

Combined Tech Transfer/Process Qualification Shows Failed Batches (2), Deviations for In-Process Specifications and No Statistical Analysis of Batch-To-Batch Variation

[redacted] Coverage:

The firm's combined Tech Transfer/PPQ document (dated 2 MARCH 2021) is provided in **exhibit #[redacted]** that shows failed batches occurring ([redacted]) during this protocol-controlled activity as well as out-of-specification in-process controls such as viable cell density, flow rates, and control cell testing. A total of seventeen deviations where raised during this protocol.

On 9 June 2021, [redacted] (Janssen) described the Janssen protocol #TV-TEC-180942 v3.0 (**exhibit #[redacted]** that stipulates criteria for tech transfer to EMOB. [redacted] acknowledged that the PPQ report does not mention anything about tech transfer, but he verbally stated the PPQ and tech transfer was a combined effort and he referred to the internal EMOB document #PLN 040817 (**exhibit #[redacted]** that describes the protocol for tech transfer which calls out the need for a final report to be generated for tech transfer. [redacted] stated this report has not yet been generated.

I stated to firm management that the protocol also does not contain any statistical evaluation of batches to determine the level of variation coming from manufacturing processes. I stated it appears the firm is using routing batch acceptance criteria as the criteria for PPQ acceptance. I stated this combined PPQ and tech transfer document does not appear to meet the firm's own acceptance criteria and also does not appear to be in alignment with 2011 FDA Guidance for Industry Process Validation: General Principles and Practices.

[redacted] (Janssen) stated the PPQ report and strategy for qualification (PPQ) was presented to CBER in the EUA under Amendment 37.

Examples of [redacted] Test Failures and Specification errors

[redacted] Coverage:

Through my review of batch records, I identified either missing or failing [redacted] test data related to GMP13, Area [redacted] and GMP [redacted], Area [redacted] These are shown by [redacted]. On 9 June 2021, I asked [redacted] to describe why [redacted] tests were failing with no investigation and no apparent impact on proceeding with manufacturing. [redacted] stated that [redacted] is intended to prevent introduction of [redacted] and [redacted] is intended to reduce bioburden in the product stream. He stated the general expectation is for the [redacted] to pass [redacted] esting or to hold production until it can be investigated. He stated if this is not happening, it is in error.

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

[redacted] described procedure SOP448 for [redacted] testing calls for all [redacted] to be [redacted] prior to testing and the procedure allows for one re-test and then a deviation must be opened if the [redacted] fails again. [redacted] provided the summary in **exhibit #**[redacted] that describes the use of nine [redacted] n the manufacturing process. He also provided the supplier specifications for [redacted] testing and the testing recipes currently in use at the firm which are included in the same exhibit. After reviewing the supplier specifications against the firm's testing recipes, I stated that two out of the [redacted] recipes use the wrong acceptance criteria for the pass/fail determination:

[redacted]

Bioburden Result TNTC Not Investigated

[redacted] Coverage:

On 4 June 2021, I reviewed an in-process bio-burden result sample from manufacturing stage [redacted] from lot [redacted] (GMP 7B, Area [redacted]. This result was described as follows in a lab investigation #LI 21-020 (**exhibit #STB23**):

[redacted] was the reported result in LIMS with a comment that all [redacted] plates had a lawn of growth covering the agar"

On page 6 of the same report, it contains the following statement:

"A laboratory error was not identified."

The following timeline is applicable to the sample and reporting:

- 6 FEB 2021 - >100 cfu result recorded for bioburden test
- 11 FEB 2021 – Lab Investigation opened and no lab error found
- 1 APR 2021 – Result in LIMS changed to zero cfu with comment "…no growth present"

A screen shot from LIMS showing the history of changes to the result is provided in **exhibit #**[redacted] Additionally, the lab investigation log book shows the initial date of the investigation and the date it was lined out as cancelled with no evidence to note a lab error.

[redacted]– QC Micro supervisor stated she changed the bioburden result in LIMS on 1 APR 2021 because of her expertise in mirobiology. She stated the analyst employee who recorded the result was not a microbiologist and made a mistake. I asked both [redacted] and [redacted] if the analyst was properly trained on the analytical procedure (TMD2185, **exhibit #**[redacted] They both stated she was properly trained as noted in the lab investigation. She stated the visual observation was of cell culture cells, not microbial growth. The plate was not sent out for identification.

I asked Mr. Elmore to present all data that indicates the batch was not contaminated as indicated by the bioburden test results. [redacted]– Lab Lead Janssen presented the data in **exhibit #**[redacted] as part of deviation #3100013036 opened to address my question. [redacted] described in-process data such as dissolved oxygen levels, cell viability and subsequent bio-burden testing to determine the batch was not contaminated.

This was mentioned as an example of an unexpected event that was not investigated with a deviation under Discussion Item #1 in the General Discussion with Management section.

BATCH RECORD REVIEW

[redacted] We reviewed batch records and associated records such as deviations and change controls pertaining to drug substance batches that have already been manufactured. A summary of the batch record review is as follows:

***Batch Reference: GMP*[redacted] *Area*[redacted]**
***Lot #:*[redacted]**
Date of Manufacture: 7 May 2021
Findings*[redacted]*:

On 7 June 2021, I received the following batch records for Janssen drug substance batch [redacted] (GMP[redacted] from Area [redacted] from [redacted]:

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

Batch Record	Batch Number	Title
[redacted]		

On the same day, I received a document listing the batch records and batch numbers for all of the solutions and manufacturing process steps from [redacted]. I confirmed that all of the batch records listed on the document were included in my review. During my review of the batch records, I noted that they had not been reviewed by either manufacturing or quality assurance. After reviewing the batch records, I discussed the following batch records:

- On 7 June 2021, I discussed the Bill of Materials (BOM) with [redacted]. I stated to [redacted] that during my review of the batch records I noted that they contained a supplemental BOM under a temporary change. [redacted] clarified that EMOB has an open change control (#210006054) to revise the BOMs in the applicable batch records. [redacted] provided me with a copy of this change control on the same day, and I noted during my review of the change control that it impacted the [redacted] different batch record used to manufacture the Janssen drug substance (not all [redacted] are used for each drug substance batch). I also asked [redacted] about the blank rows in the BOMs and he stated that this is because the batch records have not been reviewed by manufacturing or quality

assurance, and that such missing entries would normally be addressed during that process.

- On 7 June 2021, I discussed batch record [redacted] record number [redacted] with [redacted]. I stated to [redacted] that during my review of the batch records, this record was missing. He stated that this record number is incorrect and should be [redacted]. I further noted that this batch number is listed in the BOM in batch record [redacted] record number [redacted] [redacted] stated that deviation 3100013048 was open on 6 June 2021 to address this incorrectly recorded batch number in this batch record.
- On 7 June 2021, I discussed batch record [redacted] record number [redacted] with [redacted], Principle Engineer. I stated to [redacted] that during my review of the batch I record I noted on page 21 that there is a comment regarding [redacted]. [redacted] explained that [redacted] is a single-use conductivity sensor and that this is considered a nuisance alarm since conductivity is not measured during the step (sanitization). He further clarified that the sanitization is based on volume and not conductivity.
- On 8 June 2021, I discussed batch record [redacted] record number [redacted] with [redacted]. I stated to [redacted] that during my review of the batch record I noted on pages 15, 17, and 19 it states that the [redacted] recipe was aborted and rerun and the cassette was repressurize due to improperly seated gaskets, and that no deviation had been initiated for this event. [redacted] agreed that this event sounded like a deviation and [redacted] confirmed on the same day that no deviation had been initiated (see **Discussion Item #2**).
- On 8 June 2021, I discussed batch record [redacted] record number [redacted] with [redacted], Manufacturing Compliance Manager. I stated to [redacted] that during my review of this batch record I noted that on page 93 there is a comment regarding the slowing of the [redacted] rate with no deviation mentioned. [redacted] stated that this issue occurs with the [redacted] and does not require a deviation to be initiated. Instead, EMOB has a work instruction for restarting the [redacted] in such instances (WI041991, version 1.0, effective 12/13/2020). The work instruction requires sign-off by quality assurance and manufacturing management before restarting the [redacted] [redacted] provided me with a copy of the work instruction as well as the signed approval log dated the same day the event occurred (4/29/2021) on the same day.

On 7 June 2021, I requested and received the following deviations associated with Janssen batch [redacted] (GMP[redacted] from Area [redacted] from [redacted]:

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

Deviation Number	Short Summary (verbatim from Deviation)	Status
3100011873	NFC: Conditional Release of Raw Material	Open
3100012535	[redacted]Weight out of Rg	Open
3100012553	[redacted]Sample Time Missed	Closed
3100012598	QC Test Solution not Stored Properly	Closed
3100012633	[redacted]insufficient [redacted]	Open
3100012701	Exceeding hold time of [redacted]cycles	Open
3100012741	[redacted]cleaning deviated from sop	Open
3100012745	Pinhole leak from [redacted]	Open
3100012757	[redacted]not tested	Open
3100012776	BDS Bottle Overfill	Open
3100012777	NFC: Expired [redacted]	Open
3100012788	[redacted]Bioburden plates read time	Open
3100012848	Incubator Temp out of range	Open
3100012849	[redacted]Filter Broken	Open
3100012867	[redacted]Missing [redacted]batch number info	Open
3100012951	[redacted]Assm Form	Open
3100012981	[redacted] time discrepancy [redacted]	Open
3100012998	OOS Tagged Freezer Used for BDS Lot	Open

During my review of the batch records, I noted that they had not been reviewed by either manufacturing or quality assurance. After reviewing the deviations, I discussed the following deviations:

- On 7 June 2021, I discussed deviation 310012867 with [redacted]. [redacted] noted that of the 5 [redacted] for which there was missing batch numbers, the batch numbers are provide during the [redacted] so are available. He further noted that EMOB is still investigating the batch numbers for the other 2 [redacted]

- On 8 June 2021, I discussed deviation 3100012701 with [redacted]. I stated to [redacted] that during my review of this deviation I noted that the [redacted] [redacted] cycles exceeded the final hold time of [redacted] so were not run during [redacted] (as noted in batch record [redacted] record number [redacted] and asked about the impact on downstream manufacturing steps. [redacted] noted that as shown in the comment on page 72 of this batch record, due to exceeding the hold time and being unable to run the last [redacted] [redacted] the [redacted] was [redacted] to bring it up to the minimum weight of [redacted] required to move into Stage [redacted] He then stated that because of this dilution, the bulk clarified harvest volume used to calculate the volume of [redacted] to add in step [redacted] of Stage [redacted] (as shown on page 36 of batch record [redacted] record number [redacted] was required to be adjusted (to [redacted] of the amount listed) for the actual weight of [redacted] from Stage [redacted] but that this adjustment was not done leading to an over-dilution during

this step, and that the second [redacted] steps were adjusted to compensate. He further stated that the same issue occurred during Stage [redacted] performed on [redacted] (batch record [redacted] record numbers [redacted] and Stage [redacted] performed on [redacted] (batch record [redacted] record number [redacted]) but that for step [redacted] the correct amount of [redacted] buffer was added. I stated to [redacted] that the deviation was initiated for the final 2 [redacted] cycles not being run since they exceeded the final hold time of [redacted] and the adjustments to the calculations in Stage [redacted] were part of this event. However, the incorrect addition of [redacted] in Step [redacted] (as described above) was a separate event (unrelated to the hold time being exceeded). When I asked him if a deviation had been initiated for this event, he stated that one had not been initiated (see **Discussion Item #2**).

On the same day, I further discussed this deviation with [redacted] who confirmed the [redacted] event during step [redacted] on Skid [redacted] He explained that because of this [redacted], further adjustments were made during steps [redacted] on page 49 and [redacted] on page 64 of batch record [redacted] record number [redacted] However, in step [redacted] the [redacted] addition was reduced to [redacted] due to the minimum working volume for the [redacted] (as described in the comments on page 69 of the batch record). [redacted] explained that even though the amounts of [redacted] added in steps [redacted] and [redacted] were [redacted], they still led to an [redacted] of the [redacted] product (compared to the required [redacted] required concentration). When I asked about the impact to the drug substance, he explained that because the [redacted] from the [redacted] in Stage [redacted] are combined, the [redacted] in step [redacted] led to an [redacted] of the drug substance.

On the same day, I discussed the [redacted] of drug substance batch [redacted] and if the bulk drug substance is tested for viral concentration with [redacted]. He stated that a sample of the drug substance is taken (as shown in the [redacted] record number [redacted] but he was unsure of what testing is performed. On 9 June 2021, [redacted] stated that this sample is sent to Janssen's Leiden facility for testing. On the same day, [redacted] provided me with a copy of the drug substance specification showing testing for viral particles (vector concentration) with a specification of [redacted] on page 6. [redacted] also provided me with a copy of an email from [redacted] at J&J dated 8 June 2021 and stating that the result for the Area [redacted] GMP5 batch was [redacted] (pending review).

- On 8 June 2021, I discussed deviation 310011745 with [redacted]. I stated to [redacted] that during my review of this deviation I noted that it relates to a leak. [redacted] explained that there is a transfer step from the [redacted]

into a [redacted] mixer bag, which includes filling a [redacted] mixer bag with [redacted] He further noted that due to the need to [redacted] manipulate this [redacted], leaks are sometimes observed. He noted that this same bag is used for sanitization but in this case the bag was replaced. I noted that there is no mention in the batch record of the details of the event which are only captured in the deviation (see **Discussion Item #5**).

- On 8 June 2021, I discussed deviation 310012757 with [redacted]. I stated to [redacted] that during my review of this deviation I noted that it stated that three of four [redacted] testers were out of service and moved off-site for repairs, and the fourth was not operational leading the [redacted] to be unable to be tested (and discarded). [redacted] confirmed that this was the case but was not aware of the timeframe during which all four [redacted] testers were not usable. He further noted that the [redacted] was discarded due to human error and it led to the [redacted] being unable to be tested when an [redacted] tester was available.

  On 9 June 2021, I had a follow-up discussion regarding the timeframe during which all four [redacted] testers were not usable with [redacted]. She provided me with 4 work orders as follows:

  [redacted]

  On 9 June 2021, I discussed [redacted] testing with [redacted]. I stated to [redacted] my understanding that there was a timeframe during which all four [redacted] testers were not usable. I further stated that without an understanding of the reason why all of the [redacted] testers were malfunctioning, it is not clear if there would be concern about the correct readings be accurate. [redacted] responded by acknowledging my concern, but stated that for issues such as printing problems, it is unlikely that there would be concern about the validity of the readings.
- On 8 June 2021, I discussed deviation 3100012981 with [redacted], Manufactruing Analyst, and [redacted]. I stated to [redacted] and [redacted] that during my review of this deviation I noted that it was initiated due to an error in the batch record [redacted] template in which the [redacted] step (step [redacted] should be 60-120 minutes, but the template states a minimum of [redacted]. I

asked if EMOB had assessed the impact to other batches manufactured using the same template. [redacted] stated that this error in the batch record was caught during trending and the following 9 additional deviations for other batches were opened for this error:

Deviation Number	Impacted Batch	Status
3100012798	[redacted]	Closed
3100012952		Open
3100012953		Open
3100012977		Open
3100012978		Open
3100012979		Open
3100012980		Open
3100012982		Open

[redacted] also states that change control 210006247 had been opened on 21 March 2021 to address this error and another error in batch record [redacted] regarding the target [redacted]. [redacted] provide me copies of these 9 deviations and the change control on the same day. My review of the closed deviation 3100012798 confirmed that it references this change control and that it assessed the deviation as having no product impact due to the batch exceeding the transfer time limit of [redacted] by [redacted].

Batch Reference: GMP [redacted] Area [redacted]
Lot #: [redacted]
Date of Manufacture: 15 MAY 2021
Findings [redacted]:

On 9 June 2021, I received the following batch records for Janssen drug substance batch [redacted] (GMP [redacted] from Area [redacted]) from [redacted]:

Batch Record	Batch Number	Title
[redacted]		

[redacted]

On the same day, I also received a document listed the batch records and batch numbers for all of the solutions and manufacturing process steps from [redacted]. I confirmed that all of the batch records listed on the document were included in my review. After reviewing the batch records, I discussed the following batch records:

- On 9 June 2021, I discussed batch record [redacted] record number [redacted] with [redacted]. I stated to [redacted] that during my review of this batch record I noted that it states on page 64 that step [redacted] was aborted to maintain quality levels on the biowaste [redacted]. He explained the biowaste system to me and that sometimes it needs to be paused to allow it process waste, as was the case during the manufacture of the batch. He stated that there was no risk to the batch due to aborting this step.
- On 9 June 2021, I discussed batch record [redacted] record number [redacted] with [redacted]. I stated to [redacted] that during my review of this batch record I noted that there is a comment on page 42 stating that the fill was paused due to the flow sensor not reading. [redacted] noted that this issue required installation of a new part, so engineering was called as described in the comment. She further noted that the work was performed under a work order (also noted in the comment) and that no deviation was opened since there would be no potential product impact from this event.

On 9 June 2021, I requested and received the following deviations associated with Janssen batch [redacted] (GMP [redacted] from Area [redacted]) from [redacted]:

Deviation Number	Short Summary (verbatim from Deviation)	Status
3100011873	NFC: Conditional Release of Raw Material	Open
3100012573	[redacted] Samples	Closed

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

3100012617	[redacted] Exceeded kg Range	Open
3100012660	[redacted] DO Excursion	Open
3100012781	[redacted] time exceeded out of range	Open
3100012782	Quarantined Material used in Production	Open
3100012843	Small leak on top tote bag	Open
3100012848	Incubator Temp out of range	Open
3100012855	Leak from [redacted]	Open
3100012871	NFC: PDT30704 ALARM 135/1140 12 May2021	Closed
3100012899	[redacted] Incorrect setup of spine	Open
3100012900	[redacted] Recipe ended prematurely	Open
3100012904	Bottles Improperly Crimped [redacted]	Open
3100012946	Samples tested late	Open
3100012949	Mis-Labeling [redacted] Side Samples to [redacted]	Open
3100012982	[redacted] time discrepancy 21004662	Open

After reviewing the deviations, I discussed the following deviation:

- On 9 June 2021, I discussed deviations 3100012899 and 3100012904 with [redacted]. I stated to [redacted] that during my review of these deviation I noted that they each state that drug substance bottles were placed on hold. [redacted] and I discussed the process for how bottles placed on hold during our discussion of deviations 3100012790, 3100012791, and 3100012835 so I did not ask for confirmation that bottles associated with deviations 3100012899 and 3100012904 were actually placed on hold.

Batch Reference: GMP [redacted], Area [redacted]
Lot #: [redacted]
Date of Manufacture: 10 MAY 2021
Findings [redacted]:

On 8 June 2021, I received the following batch records for Janssen drug substance batch [redacted] (GMP[redacted] from Area [redacted] from [redacted]:

Batch Record	Batch Number	Title
[redacted]		

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

[redacted]

On the same day, I received a document that listed the batch records and batch numbers for all of the solutions and manufacturing process steps from [redacted]. I confirmed that all of the batch records listed on the document were included in my review. After reviewing the batch records, I discussed the following batch records:

- On 9 June 2021, I discussed batch record [redacted] record number [redacted] with [redacted] and [redacted]. I stated to them that during my review of the batch record I noted that there is a comment on page 17 that states that the [redacted] does not get [redacted] clarified that there is a change control that includes removing the requirement to [redacted] provided me with a copy of this change control (2100006409) on the same day, and [redacted] identified on page of the change control where the requirement to [redacted] was removed.

- On 9 June 2021, I discussed batch record [redacted] record number [redacted] with [redacted]. I stated to [redacted] that during my review of the batch record I noted on pages 70 and 76 there is a comment regarding a temporary disconnect from the [redacted] He explained that this was a computer issue and required restarting the computer and running a second recipe. When I asked about potential for product impact and the need for a deviation to be initiated, he stated that there would be no product impact since the program runs a required number of column volumes so initiation of a deviation would not be required.

- On 9 June 2021, I discussed batch record [redacted] record number [redacted] with [redacted]. I stated to [redacted] that during my review of this batch record I noted that on page 20 it states that during step [redacted] the recipe was aborted, system was reset, and mixer attached to [redacted] clarified that this was a software change and not a physical reconnection. He further explained that the location of the mixer during setup was incorrect leading to the error and that after the reset the proper location of the mixer was identified with no further error.

On 8 June 2021, I requested and received the following deviations associated with Janssen batch [redacted] (GMP[redacted] from Area [redacted] from [redacted]:

Deviation Number	Short Summary (verbatim from Deviation)	Status
3100011873	NFC: Conditional Release of Raw Material	Open
3100012444	Material Rec'd and rels'd incorrect[redacted]	Open
3100012591	[redacted]weight and [redacted]	Open
3100012651	client [redacted]controller	Open
3100012708	MFCs on [redacted]As-Found Values OOT	Closed
3100012738	[redacted]Missed Entries	Open
3100012763	7 out of [redacted]Cycles Processed during [redacted]	Open
3100012785	[redacted]not stabilizing during [redacted]	Open
3100012789	Discoloration observed in [redacted]	Open
3100012790	[redacted]	Open
3100012791	[redacted]eak below [redacted]	Open
3100012835	[redacted]ncorrect volume of fill	Open
3100012848	Incubator Temp out of range	Open
3100012866	[redacted]Missing [redacted]batch number info	Open
3100012912	NFC: [redacted]rebatch 200L Bioreactor	Open
3100012979	[redacted] time discrepancy [redacted]	Open

During my review of the batch records, I noted that they had not been reviewed by either manufacturing or quality assurance. After reviewing the deviations, I discussed the following deviations:

- On 9 June 2021, I discussed deviation 3100012591 with [redacted]. I stated to [redacted] that during my review of this deviation I noted that based on the error made during step [redacted] as described in the deviation, the batch record states that - [redacted] of media was added in step [redacted] on page 43. He noted that there is a change control to modify this step when this situation occurs and that the manufacturing was performed correctly (i.e., no [redacted] was removed). I stated to him that there was no comment in the batch record about this step (either on page 43 or in the comment log) or reference to the deviation, and that the only information is provided in the deviation itself, and suggested that such items should be clearly documented in the batch record (see **Discussion Item #5**).

- On 9 June 2021, I discussed deviation 3100012763 with [redacted]. I stated to [redacted] that during my review of this deviation I noted that adjustments to the [redacted] volume used to calculate the volume of [redacted] added steps [redacted] were required to be made since the full number of cycles were not run during Stage [redacted] as described in this deviation (see discussion above regarding the adjustments under deviation 3100012701). We reviewed the calculations that were performed, and he verified them for me using a calculator. I suggested to him that the calculations should be documented in the batch record so anyone would have a clear understanding of what was done during a future review of the batch record (see **Discussion Item #5**).

- On 9 June 2021, I discussed deviation 3100012789 with [redacted] and [redacted] I stated to [redacted] and [redacted] that during my review of this deviation I noted that it involved discoloration of [redacted] batch [redacted] explained that EMOB had formed a multi-disciplinary team to investigate the discoloration, but no information was currently available as they are still investigating.

- On 9 June 2021, I discussed deviations 3100012790, 3100012791, and 3100012835 with [redacted]. I stated to [redacted] that during my review of these deviations I noted that they each state that drug substance bottles were placed on hold, and I asked for confirmation that these bottles were actually placed on hold. [redacted] provided me with a copy of the QA Hold Logbook (LOG040360, version 1.0, effective 3/25/2021) and showed me that it identified that bottles from this drug substance batch were placed on hold (though the actual bottle numbers are not identified on the log). He then stated that in the [redacted] completed during Stage [redacted] (and included at the end of batch record [redacted] record number [redacted], the bottles placed on hold are identified. We reviewed this document together and confirmed that all of the bottles listed in the 3 deviations were flagged at being placed on hold. [redacted] further noted that those bottles would be placed in quarantine with a hold sticker and would be identified in the documentation sent to [redacted] with the drug substance batch. He further noted that even if bottles on hold were sent to [redacted] under Released for Further Processing, they could be returned to EMOB.

Batch Reference: GMP[redacted], Area [redacted]
Lot #: [redacted]
Date of Manufacture: 13 JAN 2021

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

Findings [redacted]:

On 4 June 2021, I received the following batch records for Janssen drug substance batch [redacted] (GMP[redacted] from Area [redacted] from [redacted]:

Batch Record	Batch Number	Title
[redacted]		

On the same day, I received document ExMEMO040571 version 1.0, [redacted] Batch Genealogy from [redacted]. Based on my review of the batch genealogy against the records listed above, the following batch records were not included in my review:

Batch Record	Batch Number	Title
[redacted]		

After reviewing the batch records, I discussed the following batch records:

- On 4 June 2021, I discussed batch record [redacted] batch number [redacted] with [redacted]. I stated to [redacted] that during my review of this batch record, I noted on page 1 of the attached form [redacted] there is a comment stating

that [redacted] were not used due to a shortage. [redacted] explained that lack of [redacted] would have no impact on the assembly and that during normal operations the [redacted] referenced in this form is [redacted] to [redacted] but that this [redacted] procedure is not explicitly described in the batch record (step [redacted] on page 28). When I asked how he could be sure that operators are not using the [redacted] to make connections (versus [redacted] since it is not explicitly stated in the batch record, he stated that he was not sure if the bags included connectors that could connect to a [redacted] On the same, day [redacted] provided me with the material requirements (document SPE044281, version 2.0, effective 4/26/2021) and the diagram (drawing 6404-1352V) for the bags that connect to the [redacted]. [redacted] identified the lines used to connect the [redacted] to the bags and showed me that they would not be able to connect to a [redacted]

- On 7 June 2021, I discussed batch record [redacted] batch number [redacted] with [redacted]. I stated to [redacted] that during my review of this batch record, I noted on page 39 that there is a comment describing a leak that occurred during step [redacted] with no mention of a deviation. [redacted] stated that deviation 3100011549 should have been reference in the batch record as it was initiated due to this leak.

- On 7 June 2021, I discussed batch record [redacted] batch number [redacted] with [redacted]. I stated to [redacted] that during my review of this batch record, I noted on page 94 that there is a comment describing a issue with the [redacted] system with no mention of a deviation. [redacted] stated that deviation 3100010989 should have been reference in the batch record as it was initiated due to this issue. I therefore requested and received a copy of this deviation from [redacted] on 7 June 2021.

- On 7 June 2021, I discussed batch record [redacted] batch number [redacted] with [redacted]. I stated to [redacted] that during my review of this batch record, I noted on page 65 that there is a comment stating that a deviation was initiated for the [redacted] that twice failed [redacted] testing. [redacted] stated that no deviation had been initiated for this event until 6/7/2021 (see **Discussion Item #2**) and he provided me with a copy of deviation 3100013056. I noted that this batch record had been reviewed by quality assurance on 3/4/2021, and he confirmed that quality assurance failed to identify that a deviation was never initiated (see **Discussion Item #2**).

- On 7 June 2021, I discussed batch record [redacted] batch number [redacted] with [redacted]. I stated to [redacted] that during my review of this batch record, I noted on page 35 that there is comment referring to a leaking bag during batch during the manufacturing process recorded in Table 5, but that I did not observe that a deviation was initiated for this leak. [redacted] explained that the leak occurred during the batching of [redacted] and the batch of [redacted] was discarded so no deviation would be necessary.

On 4 June 2021, I requested and received the following deviations associated with Janssen batch [redacted] (GMP[redacted] from Area [redacted] from [redacted] based upon my review of the batch records:

Deviation Number	Short Summary (verbatim from Deviation)	Status
3100010433	[redacted] w/o required [redacted] testing	Closed
3100010743	Material fully release in SAP in error	Closed
3100010757	Incorrect [redacted] expiry date on BRs	Closed
3100010874	NFC: Conditional Release w/o ID Testing	Closed
3100010877	[redacted] lines	Closed
3100011022	[redacted] leak	Closed
3100011054	[redacted]	Closed
3100011056	[redacted]	Closed
3100011091	[redacted] no pre-use [redacted]	Closed
3100011423	[redacted] Missing Assembly Forms	Closed
3100011537	RM sampling procedure not followed	Closed
3100011548	[redacted] used for GMP[redacted]	Closed
3100011549	[redacted] leak	Closed
3100011575	[redacted] not connected	Closed
3100011912	[redacted] Incorrect [redacted] material	Closed

After reviewing the deviations, I discussed the following deviations:

- On 7 June 2021, I discussed deviations 3100010743 and 3100010874 with [redacted]. I stated that during my review of these deviations, I noted that they reference client [redacted] versus client [redacted] (Janssen) which is the correct client for batch [redacted] On the same day, I had a further discussion of these deviations with [redacted] and [redacted]. [redacted] explained that two deviations were opened for the conditional release of [redacted] pellets, deviation 3100010873 for client [redacted] (Janssen) and 3100010874 for client [redacted] He clarified that the incorrect deviation was referenced in the batch record when quality assurance performed their review, and that deviation 3100010743 was linked to deviation 3100010874 so would not be applicable to batch [redacted] (see **Discussion Item #2**). [redacted] further noted that EMOB will annotate the batch record to address the incorrectly referenced deviations.

- On 7 June 2021, I discussed deviation 3100010877 with [redacted]. He stated that during this event the air lines between [redacted] and [redacted] were switched leading to the incorrect pressure being applied. He noted that as a solution the lines were switched and the issue was resolved. When I asked about the potential for contamination due to the lines being connected incorrectly, [redacted] stated that the [redacted] are closed system, there would be no risk, and the measured values [redacted] samples taken for bioburden and endotoxin) all support that there was no contamination.

- On 7 June 2021, I discussed deviation 3100011022 with [redacted]. He explained that as part of the process EMOB collects the [redacted] from both [redacted] into a [redacted] mixer bag which is then mixed for a minimum of [redacted]. He stated that during this step a small drip was noted by the operators so after contacting management, the [redacted] was transferred using a pump to a new [redacted] mixer bag and that a sample was taken for bioburden/endotoxin testing. When I asked him about contamination risk, he noted that the only risk would be from the leak (and not from the transfer procedure) and that the sample would support a lack of contamination.

- On 7 June 2021, I discussed deviation 3100011056 with [redacted], Principle Engineer. She stated that during this process step, [redacted] product was discarded due to the [redacted] not being turned on. When I asked about the potential impact to the rest of the batch in terms of mixing, she stated that this issue only impacted this sub-batch as the drug substance is segregated into [redacted] sub-batches in their [redacted] mixer during the step, so the lack of mixing for this sub-batch would have no impact on the other sub-batches. She noted that the [redacted] was turned on for the other sub-batches.

- On 7 June 2021, I discussed deviation 3100011423 with [redacted], Validation Engineer, and [redacted]. I stated that during my review of this deviation, I noted that it refers to batch [redacted] at the top of the form as well as many other batches in the detailed description, but that it does not refer to batch [redacted] I further noted that this deviation is referred to of page 34 of media batch record [redacted] batch number [redacted] used to manufacture batch [redacted] explained that batch number [redacted] was also used to manufacture batch [redacted] and that is why this batch is mentioned in the deviation. When I asked about EMOB's ability to trace this deviation to batch [redacted] she stated that the batch genealogy would allow for this tracing.

- On 7 June 2021, I discussed deviation 3100011549 with [redacted]. I stated to [redacted] that during review of this deviation, I noted on page 3 that no bottles were rejected for batch [redacted] but that bottles [redacted] and [redacted] from batch [redacted] and bottles [redacted] and [redacted] from batch [redacted] were rejected. [redacted] explained that for batches [redacted] and [redacted] there were separate leaks from the [redacted] leaks that are the subject of this deviation, and that these bottles were rejected due to these separate leaks. He further stated that EMOB does not reject bottles due to [redacted] leaks. When I asked [redacted] to discuss the investigation included in the deviation that supports this decision-making, he stated that it was outside his responsibilities.

  On 7 June 2021, I had a further discussion of deviation 3100011549 with [redacted] and [redacted] with a focus on the investigation. [redacted] stated that the investigation, which was conducted by the supplier, consisted of two parts. First, [redacted] was run through the [redacted] as increasing flowrate to determine the pressure at which leaking is observed. She noted that the leaks were first observed around [redacted] which is above the normal operator pressure for the [redacted] [redacted] then described the second part of the investigation in which a negative pressure of [redacted] was applied to the [redacted] by reversing the pump with the [redacted] placed in a [redacted]. The inside of the [redacted] was then visually inspected to determine if any [redacted] into the [redacted]. [redacted] stated that no [redacted] into the [redacted] was observed. I then stated that I had several concerns about this investigation and applicability to the conditions under which leaks were observed during manufacturing. I first noted that the design of the investigation assessed different conditions then those occurring during manufacturing – liquid flowing through the [redacted] at positive pressure versus air in the [redacted] at negative pressure. I also noted concerns about the sensitivity of visual inspection of [redacted] to determining if a leak occurred that could have led to contamination of the drug substance inside the [redacted] [redacted] noted that the investigation was conducted under worst-case conditions and therefore should support EMOB's decision to not reject bottles when they observe [redacted] leaks.

  On 8 June 2021, I had a third discussion of deviation 3100011549 with [redacted], [redacted], [redacted] and [redacted], [redacted] Janssen. During the discussion, I reiterated by concern about the investigation being applicable to the conditions during production where leaks were observed. [redacted] stated that the conditions during the investigation were worst-case as stated by [redacted], but I noted that under the conditions of the investigation no leaking was

observed while leaks were observed during manufacturing. I stated that this feature of the investigation would suggest that it did not represent worst-case conditions. I again stated that the forces applied to the [redacted] during the investigation (negative pressure) were different than the forces applied to the [redacted] during manufacturing (positive pressure). [redacted] stated that EMOB and Janssen believes that the investigation can be used to support that there is no defect in the manifold, and that using the fact that the [redacted] is under high positive pressure, that there is testing of the drug substance for bioburden and endotoxin, that there is further testing and [redacted] of the drug substance during drug product manufacturing, and that the drug substance manufacturing is considered a bioburden-controlled process, any leaks that occur in the [redacted] are considered low risk and would not require discarding bottles of drug substance. This position would differ for other leaks where the total assessment of the conditions during the leak would support rejecting bottles (such as when there is back pressure during the leak that might draw air into the tubing or bottle.) I stated understanding of this approach.

Batch Reference: GMP [redacted], Area [redacted]
Lot #: [redacted]
Date of Manufacture: 26 DEC 2020
Findings [redacted]:

I reviewed the following operational Batch Record modules for batches GMP [redacted] with assessment summaries included below:

[redacted]

During the review of these records, I also reviewed and discussed select deviations requiring further clarification and understanding. Overall, I requested copies of deviation reports and had discussions with the firm regarding deviations noted in the batch records. The deviations of most concern included those occurring during Stage [redacted] and were mostly associated with issues with the operation of the [redacted] system. These deviations included the following:

- **Deviation 3100010890 (closed)**: Aseptic connection error regarding connection to the [redacted] mixers [redacted] and [redacted] to transfer product. The aseptic connector did not connect all the way before the white paper was removed.
- **Deviation 3100010879 (closed)**: [redacted] Conductivity Alarm- Alarm caused issue in transferring product to the [redacted] Mixer. Sensor was replaced.
- **Deviation 3100011312 (closed)**: [redacted] Recipe Incorrect- Recipe [redacted] restart and aborted and restarted not following the batch record
- **Deviation 3100011475 (closed)**: [redacted] volume too low due to calculation error on step [redacted]

A discussion with firm regarding the deviations occurring during the manufacturing of GMP [redacted] provided an understanding of the events that occurred, in addition to the investigation and corrective actions taken; no objectionable findings were noted.

Batch Reference: GMP [redacted], Area [redacted]
Lot #: [redacted]
Date of Manufacture: 31 MAR 2021
Findings [redacted]:

I reviewed the following operational Batch Record modules for batches GMP [redacted] with assessment summaries included below:

[redacted]

During the review of the batch records for GMP [redacted], I also reviewed and discussed select deviations requiring further clarification and understanding. Overall, I requested copies of select deviation reports, two change controls and one CAPA report and had discussions with the firm regarding deviations noted in the batch record.
The following deviations were of most interest in investigating in detail:

- **Deviation 3100012251** (closed): 9 out of [redacted] cycles completed for [redacted] Only 9 cycles out of [redacted] were completed before the process duration would have been exceeded. This was due to delay in getting [redacted] into manufacturing.

- **Deviation 3100012282** (closed): [redacted] Leak [redacted] During manipulation of the bag at the end of Cycle [redacted] a small leak of less than [redacted] of product became apparent. The bag was damaged near mixer's [redacted]. Management was contacted and bag replaced.
- **Deviation 3100011697** (closed): During execution of Stage [redacted] for GMP [redacted], alarm notifications were not enabled, and operators were not able to see a [redacted] trending below the acceptable range for [redacted]. CAPA 1100003171 was initiated to enable local alarms for equipment being used during the process to allow operators to be notified in a timely manner of any excursions for any critical process parameter. Stages [redacted] and their equipment will be evaluated to determine alarm levels and their correct implementation.
- **Deviation 3100012778** (open): Stage [redacted] DO excursion- At inoculation, the bioreactor dissolved oxygen (DO) was under the acceptable range for total of [redacted] - change control was implemented to correct identified issue.
- Issue identified with no associated deviation open (firm is opening deviation)- Deficiency in the batch record for the Stage [redacted] Fill and Freeze included no result for the [redacted] testing for the sterilizing grade [redacted] preliminary discussion regarding with the firm regarding this issue indicate that not having this data is due to retrieving the data from the [redacted] tester that was sent out for repairs; however, this is very preliminary.

Deviations of lesser concern (but noteworthy) that were discussed included the following:

- **Deviation 3100012836** (open): Late Bioburden Testing- In-process bioburden results for the several lots were testing outside the [redacted] window as per SOP testing is to be conducted within [redacted] of sample collection. Impact of late testing is being evaluated.
- **Deviation 3100012662** (open): Incorrect sample GMP [redacted] [redacted] Invalid- Deviation is to capture the invalid test and retest plan of Lot [redacted] GMP [redacted] Control Cell Assay

In my discussions of **Deviation 3100011697** and **Deviation 3100012778** for the excursions with dissolved oxygen (DO) and alarms regarding trending, I was told that a CAPA was initiated as a preventive action following deviation 3100011697. This CAPA, initiated 22 February 2021, was to install local alarms including alarms for DO monitoring.

Currently, EMOB reviews monitoring data for the [redacted] and this data is

discussed in the Daily Pulse meetings with EMOB and Janssen management. However, there are no local alarms to alert operators immediately if the DO should drop below the range and these drops would only become noticed after a review of the [redacted] trending data. This CAPA to install local alarms is still in progress with a due date of 12 July 2021.
Overall, the discussion with firm regarding the deviations occurring during the manufacturing of GMP [redacted] provided an understanding of the events that occurred, in addition to the investigation and corrective actions taken; no objectionable findings were noted.

Batch Reference: GMP [redacted] Area [redacted]
Lot #: [redacted]
Date of Manufacture: 21 APR 2021
Findings [redacted]:
I reviewed the following operational Batch Record modules for batches GMP [redacted] with assessment summaries included below:

[redacted]

During the review of these records, I also reviewed and discussed select deviations requiring further clarification and understanding Overall, I requested copies of deviation reports (and a change control) and had discussions with the firm of the deviations noted in the batch record.
The following deviations were of most interest in investigating in detail:

- **Deviation 3100012661** (open): [redacted]Control Cell failure- The control cells for [redacted] were sampled on Day [redacted] of the assay (25Apr2021). The viability of cells on Day [redacted] was [redacted] with a specification of [redacted]. Investigation ongoing.
- **Deviation 3100012612** (open): Post-Filtration [redacted]Drip- during fill of first [redacted] bottles for batch [redacted] in Area [redacted] downstream, a small drip was observed

from a [redacted] on the bottle of the [redacted] bag. Action- bottles [redacted] placed on hold.

- Comment noted in batch record for Stage [redacted] that small amount of liquid was observed in top inlet of [redacted] his observation was discussed in Daily Pulse meeting with EMOB and Janssen and determined to not require further action with decision made to proceed with normal processing.

Deviations of lesser concern (but noteworthy) that were discussed included the following:

- **Deviation 3100012523** (open): DO dropped, [redacted] increased- the DO dropped below [redacted] setpoint to approximately 25%-occurred due to [redacted] addition of [redacted] where [redacted] breaks the [redacted] on the surface of culture.

A discussion with firm regarding the deviations occurring during the manufacturing of GMP [redacted] provided an understanding of the events that occurred, in addition to the investigation and corrective actions taken; no objectionable findings were noted.

Batch Reference: GMP [redacted] Area [redacted]
Lot #[redacted]
Date of Manufacture: 4 MAY 2021
Findings [redacted]:
I reviewed the following operational Batch Record modules for batches GMP [redacted] with assessment summaries included below:

[redacted]

During the review of these records, I also reviewed and discussed select deviations requiring further clarification and understanding Overall, I requested copies of select deviation reports (and a change controls) and had discussions with the firm. Investigations for the deviations are currently ongoing thus, deviations have an open status.

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

The following deviations were of most interest in investigating in detail:

- **Deviation 3100012787** (open): Control Cell Viability out of range- The Control Cells for [redacted] were sampled on Day [redacted] (25Apr2021). The viability of the cells on Day [redacted] was [redacted] with specification [redacted] Source material for control cells comes from Manufacturing.
- **Deviation 3100012714** (open): [redacted] of inlet [redacted] During fill operations for Lot [redacted] a leak was identified when filling product into the [redacted] mixer bag. Approximately [redacted] of product was transferred into the [redacted] mixer at time leak was identified.
- **Deviation 3100012707** (open): - STAGE [redacted] Small drip observed—a small slow drip was observed from the [redacted] shortly after completion of the product [redacted] phase (operation [redacted]). [redacted] connector was not completely engaged.
- **Deviation 31000012694** (open): [redacted] an operator noticed dripping from the bottom of [redacted] while daisy chaining the [redacted] and alerted the team lead

The following deviations of lesser concern (but noteworthy) that were discussed:

- **Deviation 3100012721** (open): [redacted] leak due to improper set up. Leaking was discovered [redacted]. It was observed that the [redacted] was incorrectly installed.
- **Deviation 3100012641** (open): [redacted] connection- Stage [redacted] and Clarification there was a faulty [redacted] on the [redacted] tubing. The operators welded the [redacted] connection from an unused [redacted] to the [redacted] tubing.
- **Deviation 3100012631** (open): [redacted] Leak- a small leak in the [redacted] connection for [redacted] was noticed (on the [redacted] side).After discussion with the firm, providing an understanding of the events that occurred and investigation and corrective actions taken, no objectionable findings were noted.

A discussion with firm regarding the deviations occurring during the manufacturing of GMP [redacted] provided an understanding of the events that occurred, in addition to the investigation and corrective actions taken; no objectionable findings were noted.

Batch Reference: GMP [redacted] Area [redacted]
Lot #: [redacted]
Date of Manufacture: 15 MAR 2021
Findings [redacted]:

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

On 7 June 2021, I received the following batch production records (BPR) for Janssen drug substance batch [redacted] (also known as GMP [redacted] from Area [redacted], from [redacted] (Director of Quality Operations). I reviewed these BPR on 7-8 June 2021, with a focus on Stages [redacted] and comments and deviations.

Step Description	BPR Number	BPR Title	Batch Number
[redacted]			

All these BPR had been reviewed and approved by the manufacturing and quality assurance (QA) department. Batch [redacted] was "released for further processing" (RFFP) and the current disposition is quarantine (refer to **exhibit** [redacted]). I had the following comments regarding the following BPRs.

- [redacted] Stage [redacted] [redacted] Client [redacted]

It appeared that the [redacted] temperature during passage was sometime out of the range without comments in the batch record or a deviation. For example, per step [redacted] (page 47) of [redacted] for batch number [redacted] (drug substance batch [redacted] (**exhibit** [redacted] the actual temperature was 32.9°C and the range should be [redacted] Of note, there were similar issues in [redacted] for step [redacted] where the vessel temperature was 28.8°C (page 29) for batch [redacted] (drug substance batch [redacted] (**exhibit** [redacted] Also, for step [redacted] the vessel temperature was 28.8°C (page 29) for batch [redacted] (drug substance batch [redacted] No comments were made in the batch record for batch [redacted] or [redacted] to the process note or it being outside the process range of [redacted]

Furthermore, [redacted] for batch number [redacted] states on step [redacted] (page 59) "only use [redacted] and [redacted]" However, [redacted] was used with a note that [redacted] was used instead of [redacted] after management was contacted." There was no justification in the BPR why [redacted] was used and no deviation was initiated for not following the BPR (see **Discussion Item #1**). [redacted] and [redacted] stated that [redacted] was used because the [redacted] was more in the middle of the range requirements.

- [redacted] Stage [redacted] (Client [redacted]

During the review of [redacted] for batch number [redacted] (drug substance batch [redacted] (**exhibit** [redacted] I noted that the firm did not follow their document control procedures related to requesting supplemental pages as outlined in SOP001659 (Batch Production Record Issuance and Control, v 11.0, effective 29 Mar 2021) (**exhibit** [redacted] had duplicate pages; two set of pages 2, 9, 10, 14, and 21-28, three set of pages 8, 11-13, and 16-20, and one set of pages 8-28 had the letter [redacted] after the batch number [redacted] Per [redacted] (Supervisor of Document Control) and [redacted] (Director of Quality Operations), manufacturing requested supplemental pages two times. The nomenclature of adding [redacted] after the batch number should not have been added to pages 8-28 as that indicates that the whole batch record was reprinted per step [redacted] of SOP000269 (Assignment of Batch Numbers, v 11.0, effective 29 Mar 2021) (**exhibit** [redacted] As of 10 June 2021, no deviation was initiated for not following SOP000269 (see **Discussion Item #1**).

- [redacted] Stage [redacted] (Client [redacted] and Stage [redacted] Client [redacted]

Since only 12 of the 14 [redacted] cycles were performed, as described in Deviation QN3100012041 (**exhibit** [redacted] the calculated amount of [redacted] diafiltration buffer to add for [redacted] recovery needed to be adjusted. The amount of [redacted] diafiltration buffer, based on the BPR, is based on the [redacted] volume (per steps [redacted] (page 34), [redacted] (page 47), and [redacted] (page 60) of [redacted] (**exhibit** [redacted]

and [redacted] (**exhibit** [redacted] for batch [redacted] However, since some of the [redacted] was not processed on the [redacted] the an adjusted [redacted] volume of [redacted] was used. There was no rationale in the BPR or Deviation QN3100012041 how the adjusted volume was determined. [redacted] (Manufacturing Manager) and [redacted] (Associate Engineer II) explained that calculation is [redacted] I explained my concern that this calculation/formula is not documented in any records and that others may not know how to calculate [redacted] (see **Discussion Item #5**). On 8 June 2021, [redacted] stated that they are in the process of updating the RPT052769 (Client [redacted] Process Description Stages [redacted] with the calculation.

- [redacted] Stage [redacted] (Client [redacted]

Per step [redacted] (page 20) of [redacted] for batch [redacted] (**exhibit** [redacted] the acceptable fill range per bottle is [redacted] and the target fill weight is [redacted]. [redacted] (Janssen) explained the bulk drug substance fill volume requirement is related to the thaw time requirements as part of the drug product filling process. According to comments made in [redacted] under step [redacted] (page 27) and step [redacted] page 30) and [redacted] (Client [redacted] DS Label Tracker) (**exhibit** [redacted] bottles [redacted] were either under or overfilled and placed on hold. These bottles, and bottle [redacted] were left blank on [redacted] which lead to deviation QN3100012853 (**exhibit** [redacted] There was no comment in [redacted] or [redacted] for bottle [redacted] Refer to QN3100012853 below for my concerns about this event.

[redacted] (QA Manager) stated manufacturing contacted him on the day of the fill about the under/overfilled bottles and he instructed them to weigh an empty bottle and the filled bottles and to annotate on [redacted] the actual fill weight (fill bottle weight minus empty bottle weight). [redacted] stated that the weights were provided to him through a chat via MS Teams and that bottles [redacted] had the proper fill weight requirement. However, manufacturing did not annotate on [redacted] the missing fill weights. [redacted] was not able retrieve the MS Teams chat with the fill weight as older chats are deleted automatically.

[redacted] said based on the MS Teams chat, he decided bottles [redacted] should be rejected since they were outside the specification. [redacted] provided me with SAP printouts for batches [redacted] and [redacted] (**exhibit EH12**), which is the nomenclature for bottles [redacted] respectively. The SAP print out showed that bottles [redacted] had a code of [redacted] and "code date" of "23.03.2021", indicating that those bottles were rejected on 3/23/2021 in SAP. Bottles [redacted] and

[redacted] had no code in SAP.

[redacted] stated that he decided bottles [redacted] could be shipped to [redacted] and released for further processing. Therefore, [redacted] signed on [redacted] (Authorization to Transfer BDS to Off-Site Storage Checklist, v 1.0, effective 12 Mar 2021) for batch number [redacted] (**exhibit EH13**) that [redacted] bottles were where authorized to transfer on 3/23/2021, bottles [redacted] He also signed off on [redacted] that "all filling process steps had been completed/verified/ dated", "all filling attachments complete and accurate", and "all errors clearly corrected, and justified provided" although [redacted] had missing entries for bottles [redacted] said that he reviewed the scanned version of the filling records and although the filling records were missing entries, he decided to sign off on the form since manufacturing told him that they would fill out the records with the fill weights.

[redacted] provided to me [redacted] BDS Hold Time Registration from Storage to Shipping Vessel, v 1.0, Effective 26 Dec 2020) for process order number [redacted] (**exhibit** [redacted] the form the documents which bottles that are shipped to [redacted] indicates that bottles [redacted] were shipped on 3/24/2021. [redacted] also provided me the "Shipment for Forward Processing of [redacted] Batch [redacted] Conditionally Released under Quarantine Status" memo (**exhibit** [redacted] dated 4/26/2021; per the memo [redacted] bottles of batch [redacted] were released for further processing.

In conclusion, bottles [redacted] were released for further processing to Janssen and shipped to [redacted] without any documentation if it met the fill volume requirement. As of 10 June 2021, no deviation was initiated for this discrepancy (see **Discussion Item #1**).

On 9 June 2021, [redacted] stated to me that bottles [redacted] were not filled into drug product and were still at [redacted] He provided me photographs of bottles [redacted] (**exhibit** [redacted] which are bottles [redacted] Also, of note, I did not notice that bottle [redacted] was missing an entry during the investigation and I was not able to ask [redacted] if bottle [redacted] was filled into drug product.

- [redacted] Client [redacted]

According to Deviation QN3100012041 (**exhibit EH7**), a leak that occurred at the [redacted] did not allow enough time to complete 14 [redacted] cycles. Although the leak occurred at the [redacted], [redacted] for batch [redacted] (**exhibit EH17**) and [redacted] (Batch Record Review Checklist) for

[redacted]/batch number [redacted] had no reference to the deviation or leak (see **Discussion Item #5**).

During the review of the batch records associated with Batch [redacted] (GMP[redacted]), I also reviewed and/or discussed select deviations, including the following in the table below:

Deviation Number	Short Summary (verbatim from Deviation)	Status
QN3100011913	[redacted] shutdown	Closed
QN3100012041	[redacted] 12 out of [redacted] [redacted] Cycles Completed	Closed
QN3100012174	BPR043374, Lot# [redacted]	Closed
QN3100012581	[redacted] Missed verification	Closed
QN3100012598	QC test Solution not stored properly	Closed
QN3100012643	[redacted] Stage [redacted] excursions	Closed
QN3100012703	Missing training of SOP04415 V1.0	Open
QN3100012755	[redacted] multiple [redacted] Tests	Open
QN3100012836	late bioburden testing	Open
QN3100012853	[redacted] blanks in label tracker	Closed

I only performed a limited review on open deviations as these deviations only included a short description of the event and did not include details about the investigation. Below are comments I have on the deviations I reviewed.

- QN3100012041 (**exhibit** [redacted]

  On 11 March 2021, during Stage [redacted] process step only 12 of the required [redacted] cycles were completed because of a delay with [redacted] preparation. Each [redacted] was required to load [redacted]. The delay was due to a leak occurred at the [redacted] on the [redacted] and there was not enough time to complete cycle [redacted] within the process time limit of [redacted]. Therefore, the firm decided to only complete [redacted] cycles on each [redacted] and [redacted] of [redacted] was not able to be processed and was put to the waste drain.

  As noted in my comment above for [redacted] ([redacted]), I expressed my concern that the leak occurred at the [redacted] and there is no reference to a leak in [redacted] and QN3100012041 also did not indicate how the [redacted] was calculated. Furthermore, QN3100012041 only references the BPRs for Stages [redacted] and [redacted] and does not reference the BPRs for Stage [redacted] and the [redacted] even though the deviation impacted the amount of [redacted] needed for Stage [redacted] and the deviation occurred at the [redacted] stage.

  Additionally, according to the event investigation for QN3100012041, personnel were aware of leaks on the [redacted] during previous runs, but they were able to resolve before they resulted in a deviation. I expressed my concern that since the firm is not opening deviations unless there is the potential for product impact, the firm was not aware that leaks were occurring at the [redacted] on the [redacted] until there was product impact (see **Discussion Item #1**).

- QN3100012853 (**exhibit** [redacted]

  During the manufacturing of drug substance batch [redacted] which was filled between 15-16 March 2021, no fill volumes were documented for bottles [redacted] in [redacted] (Client [redacted] DS Label Tracker) (**exhibit** [redacted] QN3100012853 was initiated on 12 May 2021 for these missing entries. The deviation indicates that [redacted] bottles were missing entries, however I noted after the investigation [redacted] bottles were missing entries on [redacted] (pages 2-3 and 5). The QN also incorrectly stated that "all [redacted] bottles were immediately placed on hold and rejected." Per [redacted], there was no documentation that these bottles were placed on QA hold since the procedures at that time did not require documentation. Also, per SAP printouts (**exhibit** [redacted] provided to me by [redacted], only bottles [redacted] were rejected and per the shipping records and [redacted] bottles [redacted] were shipped to [redacted] and release for further processing. This QN, which was closed, had no evidence "all [redacted] bottles were…rejected." See **Discussion Item #1**.

Batch Reference: GMP [redacted], Area [redacted]
Lot #: [redacted]
Date of Manufacture: 12 MAY 2021
Findings [redacted]:
On 8 June 2021, I received the following batch production records (BPR) for Janssen drug substance batch [redacted] (also known as GMP [redacted] from Area [redacted]) from [redacted]. I reviewed these BPR on 8-9 June 2021, with a focus on Stages [redacted] and comments and deviations.

Step Description	BPR Number	BPR Title	Batch Number
[redacted]			

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

[redacted]

These BPRs have not been reviewed and approved by the manufacturing and QA department. Batch [redacted] current disposition is quarantine (refer to **exhibit** [redacted]).
I had the following comments regarding the following BPRs.

- [redacted] Stage [redacted] Client [redacted]

  [redacted] for batch [redacted] drug substance batch [redacted] (**exhibit** [redacted] states on step [redacted] (page 59) "only use [redacted] if [redacted] are out of range." Both bags were in range, however, [redacted] was used and there was no comment or note indicating why [redacted] was used and if management/QA was contacted and agreed with this change. No deviation was initiated as of 8 June 2021 for deviating from the BPR (see **Discussion Item #1**). [redacted] explained that if they had used [redacted] they would not have enough volume of culture to [redacted] the [redacted] and referred step [redacted] in [redacted] (page 38). I stated if the volume of culture is a factor in the decision to determine which [redacted] to use, that should be included in [redacted]

- [redacted] Stage [redacted] in Area [redacted]

  Per a discussion with [redacted] (Principle Engineer) on 9 June 2021 through MS Teams, for step [redacted] (page 19) of [redacted] for batch [redacted] (**exhibit** [redacted] a pressure hold test is performed of the [redacted] skid to ensure there are no leaks. I expressed concerns that the BPR had no specification for the test. [redacted] stated is [redacted] and it was added to later BPRs, which I was not able to confirm prior to the end of the investigation. The pressure hold test was performed [redacted] times before it passed and the final pressure from the first run was not documented in the BPR. Furthermore, [redacted] was not able to explain what happened in the various runs

by reviewing the BPR. I expressed concern that the test was repeated multiple times until it passed and that the BPR is not clear (no specification, first run final pressure results not documented, and unclear what the results were for subsequent runs). Lastly, it is not clear if management or QA was contacted during the event. See **Discussion Item #5**.

- [redacted] Stage [redacted] Fill and Freeze (Client [redacted]

  While reviewing [redacted] for batch [redacted] (**exhibit** [redacted] I noted a deviation event on 13 April 2021 associated when filling the second set of bottles (QN3100012532) (refer to step [redacted] (page 23) and process observations section (pages 42-43) in [redacted] On 9 June 2021 [redacted] explained that due to this deviation, bottles [redacted] and [redacted] were placed on hold for low fill volume.

  I requested the hold documentation on 9 June 2021 and on 10 June 2021, [redacted] presented to me various hold records. I expressed concerns about the hold process to [redacted] (see **Discussion Item #2**). For example, according to [redacted] (QA Hold Form, v 1.0, Effective 25 Mar 2021) for QA Hold Numbers HOLD-21-0004 and HOLD-21-0005 and batch/lot numbers [redacted] and [redacted] (**exhibit** [redacted] the "quantity on hold" was "[redacted]" and the "Hold Driver/Source" as "underweight". However, according to page 1 of [redacted] (Client [redacted] DS Label Tracker) (**exhibit** [redacted] the fill amount of bottles [redacted] and [redacted] were [redacted] and [redacted] respectively; not [redacted] as noted in [redacted] Note that after the investigation I noted what I believe is a discrepancy in the units in [redacted] it appears that units should actually be [redacted] as the quantity in SAP printout (**exhibit** [redacted] indicate that batch [redacted] and [redacted] had [redacted] and [redacted] respectively.

  According to the printout of SAP, status of batches [redacted] and [redacted] was [redacted] and had a code date of "16.04.2021", indicating that bottles [redacted] and [redacted] were rejected in the inventory system on 16 April 2021. The Special Medical Waste Tracking Form for Tracking Form Number 158215 (**exhibit** [redacted] indicate that batch [redacted] and [redacted] were physically removed by their contractor [redacted] for incineration on 12 May 2021. However, [redacted] did not indicate that the bottles were removed from hold and the new disposition (reject). LOG040360 (QA Hold Logbook, v 1.0, Effective 25 Mar 2021) that included QA Hold Numbers HOLD-21-0004 and HOLD-21-0005 (**exhibit** [redacted] also did not indicate the date removed from holds and removed by/date. Step [redacted] of SOP044256 (QA Hold, v 1.0, effective 25 Mar 2021) (**exhibit** [redacted] was not followed in that QA did not complete Part 2 (Hold Removal) of the [redacted] including QA Management Approval, and QA did not update the corresponding logbook entry in LOG040360 indicating the date the hold was removed. Contrary to

SOP044256, the SAP usage decision and the physical movement of bottles [redacted] and [redacted] were performed without these steps being performed.

During the review of the batch records associated with Batch [redacted] (GMP [redacted] from Area [redacted], I also reviewed and/or discussed select deviations, including the following in the table below:

Deviation Number	Short Summary (verbatim from Deviation)	Status
QN3100012240	[redacted] Matl issues w/o QA Release	Close
QN3100012354	Client [redacted] Stage [redacted]	Open
QN3100012355	Client [redacted] Temperature set point table	Open
QN3100012397	Client [redacted] Lot [redacted] Leak	Close
QN3100012409	[redacted]	Open
QN3100012421	[redacted] sub batch [redacted]	Open
QN3100012433	[redacted] excursion during [redacted]	Close
QN3100012532	[redacted] Alarm	Open
QN3100012798	Stage [redacted] time discrepancy	Close
QN3100012944	[redacted] excursions in stage [redacted]	Close
QN3100012945	[redacted] Stage [redacted] DO excursion	Open
QN3100012957	[redacted] eng batch used with GMP lot	Open
QN3100013009	[redacted] ncorrect expiry [redacted]	Open

I only performed a limited review on open deviations as these deviations only included a short description of the event and did not include details about the investigation. Below are comments I have on the deviations I reviewed.

- QN3100012397 (**exhibit** [redacted]

  [redacted] for batch number [redacted] (**exhibits** [redacted] and [redacted] reference Deviation QN3100012397 (**exhibit** [redacted] during the preparation of Stage [redacted]. A leak was observed at the bottom of the [redacted] containing the [redacted]. To contain the leak, the [redacted] was transferred to a [redacted] tote. The [redacted] tote does not have mixing capabilities, and therefore the [redacted] could not be mixed for [redacted] minutes at [redacted], as required at step [redacted] (page 29) of [redacted] and [redacted]. Per QN 3100012397, "mixing is required to ensure the product is homogenous prior to loading." To justify that the [redacted] was homogenous without the required mixing, QN3100012397 referenced "Technical Document Memo, TV-TEC-179025 # [redacted] in Various Containers" (**exhibit EH28**). QN3100012397 stated the Technical Document Memo "[redacted] Since the [redacted] is not a concern in the [redacted] Tote, the product can be deemed homogeneous." In reviewing the technical memo, I noted TV-TEC-179025 evaluates the [redacted] of [redacted] virus particles in [redacted] from Stage [redacted]. There is no justification in the technical memo or QN3100012397 how TV-TEC-179025 is applicable to [redacted]

  Per a conversation with [redacted] (Scientist from Janssen) on 8 June 2021, [redacted] is

significantly different than [redacted] as [redacted] is a [redacted] and [redacted] is a growth promoting medium. I expressed concern that the justification for that the [redacted] was homogenous was based on a study that is not relevant to the product at this stage (see **Discussion Item #1**).

Batch Reference: GMP[redacted], Area [redacted]
Lot #:[redacted]
Date of Manufacture: 28 APR 2021
Findings [redacted]:

On 9 June 2021, I received the following batch production records (BPR) for Janssen drug substance batch [redacted] (also known as GMP[redacted] from Area [redacted] from [redacted]. I reviewed these BPR on 9-10 June 2021, with a focus on Stages [redacted] and comments and deviations.

Step Description	BPR Number	BPR Title	Batch Number
[redacted]			

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

[redacted]

These BPRs have not been reviewed and approved by the manufacturing and QA department. Batch [redacted] current disposition is quarantine (refer to **exhibit** [redacted]).
I had the following comments regarding the following BPRs.

- [redacted] Stage [redacted]

  Per step [redacted] of [redacted] for batch [redacted] (drug substance batch [redacted] (**exhibit** [redacted] (page 89), the [redacted] of [redacted] to [redacted] a sterile assembly. A note in the BPR stated that [redacted] was used in place of [redacted] No justification was provided in the BPR why [redacted] is an appropriate substitute for [redacted] and no deviation was initiated for not following the BPR. Refer to **Discussion Item #1**.

- [redacted] Stage [redacted] [redacted] (Client [redacted]

  Per step [redacted] (page 20) of [redacted] for batch [redacted] **exhibit** [redacted] should be the load volume of [redacted] to load per cycle. Step [redacted] (page 31) indicates that [redacted] was the load volume for [redacted] (performed date of 24APR2021) with a reference to deviation 3100012613 (date 26APR2021). According to the Deviation Log Section of the BPR (page 78), "deviation occurred…where air bubble was trapped over the [redacted] to improperly record the volume that flowed through it during the load. Therefore, more volume passed across the volume than the cycle called for…Steps forward were determined to continue processing volume already loaded onto the column for [redacted] and all cycles after to continue using the cycle load volume of [redacted]. An adjusted volume of [redacted] was used for all cycles on [redacted] Per QN3100012613 (**exhibit** [redacted] and [redacted] (per conversation on 9 June 2021), the volume of [redacted] had decreased by approximately [redacted] during the first [redacted] in [redacted] (instead of [redacted]). [redacted] explained that they knew the volume based on the differences of the [redacted] However, the BPR does not indicate that load volume was [redacted] and there is no supporting evidence that was the actual load volume (**Discussion Item #5**). The only place [redacted] is recorded is in QN3100012613, which is an editable record and was still open during the investigation. I expressed my concern that the BPR did not reflect what happened.

  Also, the BPR did not explain how they determined that the adjusted load volume should be [redacted] for all cycles of [redacted] On 9 June 2021, [redacted] explained he thought the calculation should be [redacted] and was not able to determine how the [redacted] was determined. On 10 June 2021, [redacted] provided a

draft version of the deviation report form for QN3100012613 (**exhibit** [redacted]), which explained how [redacted] was calculated. I expressed my concern that the BPR did not document how the adjusted load volume was determined. Refer to my discussion below on QN3100012613 and **Discussion Item #5**.

- [redacted] Stage [redacted] in Area [redacted] (Client [redacted] and [redacted] Stage [redacted] in Area [redacted] (Client [redacted]

  For steps [redacted] (page 36), [redacted] (page 49), and [redacted] (page 62) of [redacted] and [redacted] for batch [redacted] (**exhibits** [redacted] and [redacted] respectively), it is not clear how the [redacted] volume was determined to be used since the incorrect amount of [redacted] was loaded at for Cycle [redacted] (Stage [redacted] The volume [redacted] was used in the BPR. I expressed concern that the BPR and deviation did not indicate how [redacted] volume was determined for these steps (see **Discussion Item #5**).

- [redacted] Stage [redacted] (Client [redacted]

  While reviewing [redacted] for batch [redacted] (**exhibit** [redacted] I noted that steps [redacted] (pages 31-37) and steps [redacted] (page 38) were missing entries. These steps covered to filling of carts [redacted], the time the first and last cart were loaded into the freezer, and the calculated duration from last [redacted] cycle loading end time to the last rack of bottles placed in the freezer. The firm was able to provide other documentation that support those steps were completed and within range.

  Step [redacted] (page 24) referred to the comment section (page 42) and deviation QN3100012682 (**exhibit** [redacted]). The comment stated "operators noticed a small leak coming from a [redacted] .Bottles [redacted] were placed on hold." I requested the QA Hold Form [redacted] and QA Hold Logbook (LOG040360) for Bottles [redacted] on 9 June 2021. On 10 June 2021, [redacted] informed me that bottles [redacted] were not placed on hold and thus do not have a QA Hold Form on QA Hold Logbook to provide me. SOP044256 (QA Hold, v 1.0, effective 25 Mar 2021) (**exhibit** [redacted] was not followed (see **Discussion Item #2**). Mr. Kirk stated they opened a deviation on 10 June 2021 for not following their hold procedures (QN3100013082) (**exhibit** [redacted] Refer to QN3100013082 below for further discussion on this deviation.

During the review of the batch records associated with Batch [redacted] (GMP [redacted] from Area [redacted], I also reviewed and/or discussed select deviations, including the following in the table below:

Deviation Number	Short Summary (verbatim from Deviation)	Status
QN3100012560	[redacted]	Open
QN3100012588	[redacted] from stage [redacted]	Open

QN3100012610	[redacted] Bag Leak	Open
QN3100012613	[redacted]oad volume recalculation	Open
QN3100012682	BDS Leaks [redacted]	Open
QN3100012948	Missing bio-endo samples	Open
QN3100012980	[redacted] time discrepancy [redacted]	Open
QN3100013082	[redacted] No QA Contacted During Leak	Open

I only performed a limited review on open deviations as these deviations only included a short description of the event and did not include details about the investigation. Below are comments I have on the deviations I reviewed.

- QN3100013082 (**exhibit** [redacted]

  Per Step [redacted] (page 24) and the comment section (page 42) of [redacted] for batch [redacted] (**exhibit** [redacted] a leak occurred during filling and bottles [redacted] were placed on hold (associated with QN3100012682). On 9 June 2021, I requested the QA Hold Form ([redacted] and QA Hold Logbook (LOG040360) for Bottles [redacted] from drug substance batch number [redacted] On 10 June 2021, [redacted] informed me that bottles [redacted] were not placed on hold and SOP044256 (QA Hold, v 1.0, effective 25 Mar 2021) (**exhibit** [redacted] was not followed (see **Discussion Item #2**). On 10 June 2021, EMOB opened a new deviation (QN3100013082) for this event. QN3100013082 states "During review of [redacted] v3.0 (Stage [redacted] Fill and Freeze) batch [redacted] it was discovered that a leak occurred during the filling process of bottles [redacted] According to the comment section (section 7.0) on page 42 or 46, QA was never contacted during this event. This violates 6.1.2 of SOP044256 v1.0 – the QA Hold procedure."

  After the investigation, I noted that it was not accurate to state "During review of [redacted]..it was discovered that a leak occurred" because the firm had created a deviation for the leak (QN3100012682, **exhibit** [redacted] on 29 April 2021. Also, per a printout of SAP (**exhibit** [redacted] it shows that batches [redacted] have the status of [redacted] with a code date of "03.05.2021" and a "UDec.made by" TIPPETTB. That indicated that the bottles [redacted] were rejected in SAP on 5/3/2021 by [redacted], who is a QA Manager. It is unclear how [redacted] was aware to reject these bottles.

  In addition, I did note that the Special Medical Waste Tracking Form for Tracking Form Number 158215 (**exhibit** [redacted] included batch numbers [redacted] The Special Medical Waste Tracking Form indicates that bottles [redacted] were physically removed by their contractor [redacted] for incineration on 5/12/2021.

  Steps [redacted] of SOP044256 (QA Hold, v 1.0, effective 25 Mar 2021) (**exhibit** [redacted] was not followed in that QA did not place bottles [redacted] on hold and the SAP

usage decision and the physical movement of bottles were performed without these steps being performed.

Batch Reference: GMP [redacted] Area [redacted]
Lot #:[redacted]
Date of Filling: 24 MAR 2021
Findings [redacted]:
I reviewed the following documents for this batch:
[redacted]

I discussed the following comments/deviations found in the batch records as concerns:

- Pumping spent media in reverse direction for [redacted], stage [redacted] step [redacted] (**exhibit #[redacted]**
- Repeated failed conductivity measurements in stage [redacted] which indicates problems with installing the [redacted] like air in the line (**exhibit #[redacted] p22**)
- Leaks identified in filling stage [redacted] as noted in deviation #3100012656 (**exhibit #[redacted]**

Batch Reference: GMP [redacted] Area [redacted]
Lot #:[redacted]
Date of Manufacture: 8 APR 2021
Findings [redacted]:
I reviewed the following documents records for this batch:
[redacted]

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

[redacted]

I discussed the following comments/deviations found in the batch records as concerns:
[redacted] test shows zero diffusion on printed ticket (**exhibit**

- [redacted] data on flow and pressure of chromatography saved to unsecure network location; see screen shot of storage location in **exhibit #**[redacted]
- Missing [redacted] data for stage [redacted] and [redacted] test failures, see copies of applicable batch records in **exhibit #**[redacted]

Batch Reference: GMP [redacted] ***Area*** [redacted]
Lot #:[redacted]
Date of Manufacture: 17 APR 2021
Findings [redacted]***:***
I reviewed the following documents records for this batch:

[redacted]

I discussed the following comments/deviations found in the batch records as concerns:

- Missing [redacted] test tickets in batch record (**exhibit #**[redacted] **p45**)
- Unexplained second [redacted] consumed for [redacted]
  - I asked [redacted] about why a second [redacted] would be needed for the [redacted] of the drug substance. He stated it is not documented in the batch record and he doesn't know why. He stated that a [redacted]

[redacted] contains [redacted] in case [redacted], but a [redacted] being installed is not normal.

- Dissolved oxygen above limits for Stage [redacted] no limits listed in batch record (see **exhibit #** [redacted] p 36 for batch record pages)
- [redacted] failure for [redacted] (see test result in **exhibit #** [redacted]

GENERAL DISCUSSION WITH MANAGEMENT

[redacted] On 10 June 2021 a close-out meeting was held with the firm. Attendees included representatives from EMOB, Janssen, and BARDA as seen in **exhibit #** [redacted] During the close-out meeting, I opened with the following items:

- I stated to Ms. Mary Oates that this is an investigation that does not resolve the previous inspection results and we are not issuing a 483
- I asked Ms. Mary Oates if the schedule provided earlier was still accurate and she confirmed the timetable of June 26th to re-start manufacturing and she stated they will update our compliance branch if it changes
- I commented that the firm had verbally noted that certain batches would likely be rejected (GMP [redacted]), but this had not actually occurred as of the closing meeting
- I asked Ms. Oates if there was any plan for the firm to perform manufacturing of [redacted] products due to the presence of [redacted] labeled items in warehouse freezers. She stated there is no plan to conduct manufacturing for [redacted]
- I stated to [redacted] that the investigation relevant to Janssen was closed without noting concerns. He verbally acknowledged this statement.

The following concerns were verbally described to the firm's management and directly to Ms. Mary Oates – Senior Vice President Global Quality. No written form FDA483 was issued.

1. Lack of adequate investigation/root cause analysis for unexpected events in manufacturing of client [redacted] drug substance, for example:
   - Multiple instances of leaks
   - Dilution errors
   - [redacted] test failures
   - Out of specification bioburden results
   - Consideration of QC raw material sampling procedures in cross-contamination of batch GMP [redacted]
2. Responsibilities applicable to the quality unit not fully followed
   - Initiation of deviations not done in timely manner to assess before RFFP (release for further processing)

- Not following procedure on hold for finished drug substance, inventory units transition to reject not verified
- Improve QA (quality assurance) review of batch record to include specific coverage of batch record deviations not documented

3. Employee Training not adequately documented
   - not adequately recorded/documented, reconstituted from memory of trainers after the fact, duplicate/inaccurate records found
   - [redacted] decontamination time required in rooms without clocks; SOP allows use of network connected laptop clocks but how to monitor time is not part of training.
4. Procedures for transporting materials and waste are not followed (segregation of waste totes)
5. Batch Records do not always contain the primary data/documentation relevant to investigations of batch manufacturing
6. Bioburden controlled facility cleanliness and disrepair
   - Un-identified debris in overhead lights of upstream room: Area [redacted]
   - Broken Diffusers of overhead lights in upstream Area [redacted] create direct path from interstitial space to manufacturing area
   - Hair and dust on ceiling of de-gown !rea [redacted]
   - Blistering and peeling paint on ceiling due to [redacted] cycles of decontamination
   - Dislodged fire suppression covers in upstream Area [redacted] processing room ceiling create direct path from interstitial space to manufacturing area
   - Difficult to clean and damaged metal wall in upstream Area [redacted] and dislodged outlet cover
   - Uncleanable dislodged utility panel in area [redacted] creates path to interstitial space above ceiling
7. Line Clearance criteria of weigh/dispense area is not clear in single customer facility due to wording of the SOP
8. Data integrity practices
   - Batch record scans can be deleted from network file location
   - Written procedure identifying location for scanned batch records is inaccurate
   - Data [redacted] software that controls chromatography and filtration equipment) can be deleted from network drive
9. Inventory system does not adequately track applicable storage locations and material
   - LN2 log book movements of cell banks do not match SAP inventory software
   - Freezers in GMP warehouse with contents not in SAP inventory software
10. Combined Tech Transfer/Process Qualification shows failed batches (2),

deviations for in-process specifications and no statistical analysis of batch-to-batch variation

At the conclusion of the close-out meeting, I asked if there were any further questions from the firm. Ms. Mary Oates and Mr. Ed Elmore stated they understood the concerns described by our investigation team.

I asked Ms. Mary Oates if the firm would respond in writing. She stated they would and I directed her to the OBPO communication sheet that I had provided during the meeting to provide electronic communications with our compliance department. She acknowledged the communication information that I provided.

EXHIBITS

[redacted]1 – Corporate Registration documents
[redacted]2 – Opening Presentation
[redacted]3 - change control 2100006417
[redacted]4 – Future Production Schedule
[redacted]5 – Facility Diagram
[redacted]6 - Photographs taken by Investigator Ballard
[redacted]7 – Line Clearance SOP 043687 v1
[redacted]8 – Screen shot of scanned batch record storage location
[redacted]9 – Stage [redacted] batch record for [redacted] data that references [redacted]
[redacted]10 – Example of [redacted] export data saved on network drive
[redacted]11 – Screen shot of Network storage location for [redacted] data
[redacted]12 – Freezer Logbook for eq# 10019954
[redacted]13 – Freezer Logbook for eq# 10019936
[redacted]14 – LN2 logbook for eq# 10044004
[redacted]15 – LN2 Logbook for eq#10044111
[redacted]16 – SAP inventory for LN2 storage locations
[redacted]17 – Summary of freezers in SAP and those not in SAP
[redacted]18 – Summary of [redacted] used in manufacturing and supplier specs for [redacted] testing
[redacted]19 – PPQ report
[redacted]20 - protocol #TV-TEC-180942 v3.0
[redacted]21 – Internal EMOB tech transfer plan #PLN 040817
[redacted]22 – Diagram of Bioburden sample bag
[redacted]23 – Lab investigation LI 21-020
[redacted]24 – Bioburden LIMS results #2161426
[redacted]25 – Bioburden Test procedure TMD – 2185
[redacted]26 – Bioburden deviation #3100013036

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

[redacted]27 - [redacted] record [redacted] Stage [redacted] pumping spent media
[redacted]28 - record [redacted] Stage [redacted] repeat failures of [redacted]
[redacted]29 - Leaks identified in [redacted] [redacted] deviation #3100012656
[redacted]30 – [redacted] filter test shows zero flow
[redacted]31 - record [redacted] Stage [redacted] missing [redacted] data
[redacted]32 - record [redacted] Stage [redacted] missing [redacted]
[redacted]33 – GMP [redacted] [redacted] record don't have number, Stage [redacted] dissolved 02 above limits
[redacted]34 – [redacted] failures for [redacted]
[redacted]35 – Close-out Meeting Attendance list
[redacted]36 – Summary of Contract Testing performed on site
[redacted]37 – Media Feeding Diagram

[redacted]1 – TRN040737 Training Evidence, 24 pages
[redacted]2 – TRN040754 Training Evidence, 26 pages
[redacted]3 – TRN040727 Training Evidence, 35 pages
[redacted]4 – CC 2100006389 Training Evidence, 11 pages
[redacted]5 – Deviation 3100012594, 180 pages
[redacted]6 – Grey Transfer Tote Picture, 1 page
[redacted]7 – Red SMW Tote Outside Picture, 1 page
[redacted]8 – Red Tote Similarity Pictures, 2 pages

Exhibit [redacted]1 – Emergent Current Batch Location and Status, 1 page
Exhibit [redacted]2 – [redacted], Stage [redacted] batch [redacted] drug substance batch [redacted] 65 pages
Exhibit [redacted]3 – [redacted], Stage [redacted] batch [redacted] (drug substance batch 21004323), 64 pages
Exhibit [redacted]4 – [redacted] Stage [redacted] (Client [redacted] batch [redacted] (drug substance batch [redacted], 166 pages
Exhibit [redacted]5 – SOP001659 (Batch Production Record Issuance and Control, v 11.0, effective 29 Mar 2021), 25 pages
Exhibit [redacted]6 – SOP000269 (Assignment of Batch Numbers, v 11.0, effective 29 Mar 2021), 11 pages
Exhibit [redacted]7 – QN3100012041, [redacted] 12 out of [redacted] [redacted] Completed, 15 pages
Exhibit [redacted]8 – [redacted], Stage [redacted] (Client [redacted] batch [redacted] 78 pages
Exhibit [redacted]9 – BPR043490, Stage [redacted] Client [redacted] batch [redacted] 85 pages
Exhibit [redacted]10 – [redacted], Stage [redacted] Fill and Freezing (Client [redacted] and [redacted] (Client [redacted] DS Label Tracker), batch [redacted] 61 pages

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

Exhibit [redacted]11 – QN3100012853, [redacted] blanks in label tracker, 7 pages
Exhibit [redacted]12 – SAP printouts for batches [redacted] and [redacted] 3 pages
Exhibit [redacted]13 – [redacted] (Authorization to Transfer BDS to Off-Site Storage Checklist, v 1.0, effective 12 Mar 2021), batch number [redacted] 1 page
Exhibit [redacted]14 – [redacted] BDS Hold Time Registration from Storage to Shipping Vessel, v 1.0, Effective 26 Dec 2020) for process order number [redacted] 16 pages
Exhibit [redacted]15 – Memo on Shipment for Forward Processing of [redacted] Batch [redacted] Conditionally Released under Quarantine Status, 3 pages
Exhibit [redacted]16 – Photos of bottles [redacted] at [redacted], 3 pages
Exhibit [redacted]17 – [redacted] Client [redacted], batch [redacted] 56 pages
Exhibit [redacted]18 – [redacted] Stage [redacted] in Area [redacted] (Client [redacted], batch [redacted] 75 pages
Exhibit [redacted]19 – [redacted] Stage [redacted] Fill and Freeze (Client [redacted] and [redacted] (Client [redacted] DS Label Tracker), batch [redacted] 61 pages
Exhibit [redacted]20 – [redacted] QA Hold Form, v 1.0, Effective 25 Mar 2021) for QA Hold Numbers HOLD-21-0004 and HOLD-21-0005 and batch/lot numbers [redacted] and [redacted], 1 pages
Exhibit [redacted]21 – SAP printout for batches [redacted] and [redacted], 1 page
Exhibit [redacted]22 – Special Medical Waste Tracking Form for Tracking Form Number 158215, 5 pages
Exhibit [redacted]23 – LOG040360 (QA Hold Logbook, v 1.0, Effective 25 Mar 2021) that included QA Hold Numbers HOLD-21-0004 and HOLD-21-0005, 1 page
Exhibit [redacted]24 – SOP044256 (QA Hold, v 1.0, effective 25 Mar 2021), 7 pages
Exhibit [redacted]25 – QN3100012397, Client [redacted] Lot [redacted] Leak, 17 pages
Exhibit [redacted]26 – [redacted], Stage [redacted] batch number [redacted], 115 pages
Exhibit [redacted]27 – [redacted] Stage [redacted] batch number [redacted] 117 pages
Exhibit [redacted]28 – Technical Document Memo, TV-TEC-179025 # [redacted] of [redacted] Virus Particles in [redacted] in Various Containers, 22 pages
Exhibit [redacted]29 – [redacted], Stage [redacted] batch [redacted] (drug substance batch [redacted] 102 pages
Exhibit [redacted]30 – [redacted] Stage [redacted] (Client [redacted] batch [redacted] 88 pages
Exhibit [redacted]31 – QN3100012613, [redacted] oad volume recalculation and draft version of the deviation report form for QN3100012613, 20 pages
Exhibit [redacted]32 – [redacted] Stage [redacted] in Area [redacted] (Client [redacted] batch [redacted] 76 pages

FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
1201 Main Street, Ste 7200, Dallas, TX 75202
[redacted]

Exhibit [redacted]33 – [redacted] Stage [redacted] in Area [redacted]
(Client [redacted] batch [redacted] 75 pages
Exhibit [redacted]34 – [redacted] Stage [redacted] (Client [redacted] and [redacted]
(Client [redacted]DS Label Tracker), batch [redacted] 60 pages
Exhibit [redacted]35 – QN3100012682, BDS Leaks Post [redacted] 1 page
Exhibit [redacted]36 – QN3100013082, [redacted]No QA Contacted During Leak, 1 page
Exhibit [redacted]37 – SAP printouts for batches [redacted] 1 page

ATTACHMENTS

1. FDA482 issued on 2 June 2021 to Ms Oates – EMOB
2. FDA482 issued on 4 June 2021 to [redacted] – Janssen
3. FDA482 issued on 7 June 2021 to Ms Oates – EMOB
4. FDA482 issued on 7 June 2021 to [redacted] – Janssen

[redacted]

[redacted], **NE Investigator**

[redacted]

[redacted], **Senior Advisor**

[redacted]

[redacted], **Senior Advisor**

[redacted]

[redacted], **Chemist**