FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
Food and Drug Administration
6000 Metro Drive, Suite 101, Baltimore, MD 21215
[redacted]

Date: August 5, 2021

From: [redacted], Investigations Branch, Division 1, Office of Biological Products Operations (OBPO)/Office of Regulatory Affairs (ORA)
[redacted], Senior Advisor, Office of Biological Products Operations (OBPO)

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

Subject: Investigation of Emergent Manufacturing Operations Baltimore LLC; Investigation Dates: 26-27 July 2021

FEI: 3015448605

eNSpect Op ID: 204578

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

This document was authored by both members of the investigation team. Each section is indicated with the initials of the author that wrote the text as follows:

[redacted]

Endorsement:

This investigation was initiated to assess pre-production corrective actions undertaken by the firm in response to the FDA 483 issued at the close of the inspection that occurred 12-20 April 2021 that were not completed prior to or not covered during the June 2-10, 2021 pre-production investigation, and the items discussed with the firm's management at the close of the June 2-10, 2021 pre-production investigation as described in the June 28, 2021 response.
Review of corrective actions during this investigation were limited by the fact that the firm has not resumed manufacturing operations. A post-production inspection will be necessary to fully assess the proposed corrective actions to the deficiencies identified during the previous inspection and investigation.

Of note, regarding EMOB's plan for restarting manufacturing the firm indicated that an evaluation of the Area [redacted] performance effectiveness will be performed before restarting manufacturing in Area [redacted] The comprehensive assessment will be performed after [redacted] to allow for execution of one full manufacturing run in Area [redacted] In addition, EMOB will change the

cadence of manufacturing in Area [redacted] to a [redacted] cadence (thawing to start manufacturing a new lot of drug substance every [redacted] days).

At the conclusion of the investigation, the team shared five discussion items with firm management. The firm indicated they would respond directly to OBPO/Division 1 Compliance Branch regarding investigational findings.

Routing: OBPO/Division 1 Compliance Branch
Cc: CBER/OCBQ

[redacted]

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

BACKGROUND AND INTRODUCTION

[redacted]
This investigation of Emergent Manufacturing Operations Baltimore LLC (referred to as "EMOB") was initiated to assess pre-production corrective actions undertaken by the firm in response to the FDA 483 issued at the close of the inspection that occurred 12-20 April 2021 but were not completed prior to or not covered during the June 2-10, 2021 pre-production investigation, and the items discussed with the firm's management at the close of the June 2-10, 2021 pre-production investigation as described in the June 28, 2021 response.

ADMINISTRATIVE INFORMATION

[redacted]
On 7/22/2021, I pre-announced the investigation by calling Edward Elmore, Senior Director of Quality, who stated that COVID-19 preventative measures in place at the firm had not changed since the previous investigation. During this call I requested that all documents relevant to the corrective actions completed since the June 2-10, 2021 pre-production investigation be prepared for review on the morning of 7/26/2021. Mr. Elmore stated he would arrange for preparation of these materials.

On 7/26/2021, the investigation team [redacted] arrived at the firm and presented our credentials and issued a Form FDA482 Notice of Inspection to Mary D. Oates, Senior Vice President Quality **(Attachment 1)** who identified herself as the most responsible person on site for the firm. We also presented our credentials and issued a Form FDA482 Notice of Inspection to [redacted], Senior Director of Quality, Janssen Pharmaceuticals Inc. **(Attachment 2)**. Ms. Oates stated the firm's legal identification and organization has not changed since the previous investigation.

During the opening meeting on 7/26/2021, Mr. Edward "Ed" Elmore provided an opening presentation to summarize the current state of the facility and operations with slides **(Exhibit [redacted]1)**.

During the close-out meeting on 7/27/2021, the investigation team verbally discussed five items with the firm management as described in the General Discussion with management section below.

Walkthrough of Warehouse, QC Laboratories and Manufacturing Areas [redacted] and [redacted]

[redacted]
On 7/26/2021, Mr. Elmore led a walkthrough of the EMOB warehouse, QC laboratories and manufacturing Areas [redacted] During the walkthrough of the QC laboratories, [redacted], Director of QC, identified the new sample refrigerator in the Microbiology Laboratory. He noted that EMOB was in the process of qualifying this refrigerator.

During the walkthrough of manufacturing Area [redacted] Mr. Elmore, noted that EMOB has changed their procedure for handling waste and is now using single-use black barrels instead of the re-usable red totes (for Special Medical Waste) observed during the June 2021 pre-production investigation. He explained that these barrels follow a unidirectional flow from manufacturing Area [redacted] out through the [redacted] corridor surrounding manufacturing Areas [redacted] and [redacted] to the outside of the building and are then destroyed. I was also able to observe the new flooring installed in Area [redacted] downstream only (but not in upstream, or in the media prep or [redacted] areas) but not in Area [redacted] as it was not in service at the time of the pre-production investigation (see below for more information). During the walkthrough, I discussed the cleaning of the floor in Area [redacted] downstream with [redacted], Central Services Manager. [redacted] explained that the floor was cleaned [redacted]. When I asked how the cleaning is performed accounting for the equipment present in the room, he stated that the cleaning was performed with a flexible mop that allows access to the floor. [redacted] further noted that equipment that can be moved (such as chairs) is moved when the floor is cleaned and that EMOB cleans the floor around other larger equipment (using these mops). The manufacturing area appeared to be clean and in good order.

During the walkthrough of the [redacted] surrounding manufacturing Areas [redacted] and [redacted] [redacted], Senior Director, MS&T, identified new [redacted] wall panels installed floor to ceiling in some sections of the corridor. When I asked him why they were not installed in the entire corridor, [redacted] explained that they were installed in the sections where [redacted] were used to transport components that could damage the upper portion of the walls. During the walkthrough, I observed grey totes used to transport components in the corridor that were labeled with their location of use (Area [redacted]). [redacted] also noted that manufacturing Area [redacted] was currently out of service but that [redacted] decontamination of Area [redacted] had been completed (see below for more information). Mr. Elmore stated that EMOB has not set a date when manufacturing Area [redacted] will come back into service (see below under EMOB's Manufacturing Restart Plan for more information). We did not enter Area [redacted] during the walkthrough, and I was not able to observe the new floors. During the walkthrough of the corridor, [redacted] explained that EMOB is using dedicated rolling carts to move the black waste barrels with these carts segregated to the manufacturing areas, [redacted] and outside. When I asked him about labeling of these carts, he explained that EMOB was in the process of labeling them based upon their location.

During the walkthrough of the QC laboratory that supports manufacturing Areas [redacted] and [redacted], Manager, QC Micro, identified the other new sample refrigerator (also still in the process of being qualified).

[redacted]
During the walkthrough of the EMOB warehouse, QC laboratories and manufacturing Areas [redacted] and [redacted] I did not observe debris in overhead lights and on ceilings, broken lights, or blistering and peeling paint noted during the previous investigation. I observed that fire suppression covers in upstream Area [redacted] processing room ceiling had been secured.

I observed [redacted] had been installed on the ceiling in Area [redacted] downstream, which [redacted] referred to as [redacted] **(Exhibit [redacted] 2).** When I asked if the cleaning SOP had been updated to include the [redacted] stated that he did not know **(see Discussion Item #2)**.

REVIEW OF CORRECTIVE ACTIONS

[redacted]
During this investigation, we reviewed the firm's corrective actions from the previous investigation as follows. The coverage related to each corrective action is indicated with the investigators initials in each case.

Corrective Actions Implemented in Response to the April 2021 Inspection

[redacted]
CAPA 1100003410
During the June 2021 pre-production investigation, while discussing deviation 3100012594, [redacted], Director, Quality Assurance, stated that this CAPA was still in process and due June 2020. On 7/26/2021, I discussed this CAPA with [redacted] who provided me with a copy of the CAPA. [redacted] explained that as stated in the CAPA, the signage will not be changed from "low bioburden" to "viral operation" until EMOB resumes manufacturing.

Revised SOP001516 (dedicated plant shoes)
During the June 2021 pre-production investigation, while discussing deviation 3100012594, [redacted] stated that SOP001516, "Personnel Flow and Gowning Procedure for the Production Envelope", would be updated to have dedicated plant shoes for the Weigh and Dispense Area. On 7/26/2021, I discussed this SOP with [redacted] who provided me with a copy of the revised SOP (version 26.0, effective 7/23/2021). [redacted] identified the changes to sections 6.4.4.2 and 6.4.4.3 as being where this change was made.

During the June 2021 pre-production investigation, [redacted] also noted that this SOP would be updated so that employees now enter the Weigh and Dispense Area via the [redacted] in street clothes and don level [redacted] gowning. During my review of the revised SOP provided to me by [redacted] on 7/26/2021, I was able to verify the new gowning practices in section 6.4.4.5.

PLN040854, Viral Contamination Control Strategy
During the June 2021 pre-production investigation, while discussing deviation 3100012594 with [redacted], I noted that it stated that PLN040854, "Viral Contamination Control Strategy", will be revised to (1) include the defined training necessary to ensure employees understand the

necessary controls and their role in viral containment, (2) reflect the use of both the [redacted] and [redacted] procedures as acceptable waste removal processes, (3) restrict material flows across areas designed for different products, and (4) ensure the controlled handling of raw material containers. On 7/26/2021, I discussed the status of the revision of this plan with [redacted], who provide me with the current version of the plan (version 1.0, effective 1/31/2021) and stated that the revision is still ongoing due to EMOB now being a single product facility. He explained that the scope of the revision is being still being discussed by EMOB with the plan to have it implemented by August 2021 (**see Discussion Item #3**).

CAPA 1100003412

During the June 2021 pre-production investigation, while discussing deviation 3100012594, [redacted] stated that inclusion of viral containment education in the annual training for EMOB facility personnel was being addressed under CAPA 1100003412 and was due in July 2021. On 7/26/2021, I discussed the status of this CAPA with [redacted], who provide me with a copy of the CAPA **(Exhibit [redacted]1)** and stated that the corrective action of providing this training would not be completed in July 2021 due to the ongoing discussions regarding PLN040854, as described above. On 7/27/2021, I had a follow-up discuss with [redacted], who explained that EMOB intends to require all EMOB employees to take a revised version of the contamination control training (TRN040703, "Contamination Control Best Principles and Practices") using a computer-based method that same week. He further noted that EMOB was still in the process of revising the contamination control training. He provided me with a copy of the current version of the training (approved on 4/16/2021; **Exhibit [redacted]2**) that was previously given to EMOB employees. [redacted] stated that this training would be completed prior to EMOB resuming manufacturing (**see Discussion Item #3**).

QC Waste Flow Diagrams

During the June 2021 pre-production investigation, while discussing deviation 3100012594, [redacted] stated that QC waste flows were changed to ensure that waste does not cross paths with materials or personnel involved in manufacturing operations. On 7/26/2021, I discussed the flows with [redacted] who provided me with a copy of the two revised waste flow diagrams, one entitled "Waste Flow for Areas [redacted]" ([redacted], version 2.0, effective 7/8/2021) and one entitled "Weigh Dispense and Quality Control Sample Booth Waste Flow" ([redacted] version 1.0, effective 5/22/2021). During my review of the waste flow diagrams, I was able to verify that waste should not cross paths with materials or personnel involved in manufacturing operations.

SOP001510, System Level Impact Assessment Process

During the June 2021 pre-production investigation, while discussing deviation 3100012594 with [redacted], I noted that it stated that 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. On 7/26/2021, I discussed this change with [redacted] who provided me with a copy of the revised SOP (version 7.0, authorized 7/19/2021 but not yet effective). [redacted] identified the change to section IV.e on page 12 stating that decontamination [redacted] will be treated as indirect impact systems.

TRN040751 v1.0, Bayview Operation of the Decontamination [redacted]

During the June 2021 pre-production investigation, while discussing deviation 3100012594, [redacted] stated that training TRN040751 v1.0, "Bayview Operation of the Decontamination [redacted] was still in process and due in June 2021. On 7/26/201, I discussed the status of

this training with [redacted], who stated that it was included in CAPA 1100003412 (see discussion above) and that the training was completed by the June 2021 due date specified in the CAPA. [redacted] provided me with training records to support that this instructor-led training was provided in June 2021.

[redacted] Decontamination of Manufacturing Areas [redacted] and [redacted] and Associated Areas

During the June 2021 pre-production investigation, while discussing EMOB's corrective actions performed in response to observation 2 from the FDA Form 483 issued during the April 2021 inspection, [redacted], Director, Industrial Microbiology (Johnson and Johnson) stated that EMOB planned to [redacted] decontaminate all areas in manufacturing Areas [redacted], including the [redacted] and [redacted] and [redacted] preparation areas, but excluding the [redacted], as well as the Weigh and Dispense and QC Raw Material Sampling areas. He further stated that this decontamination would be performed under a protocol. On 7/26/2021, I discussed the status of the [redacted] decontamination of these areas with [redacted], who provided me with protocol PRO0505034, "[redacted] Disinfection of Area [redacted] Area [redacted] and [redacted] (version 1.0, effective 6/2/2021; **Exhibit [redacted]3**), and report RPT056455, "Final Report for Evaluation of Microbial Inactivation in Area [redacted] Area [redacted] and [redacted] by [redacted] (version 1.0, effective 7/24/2021; **Exhibit [redacted]4**). He identified in these documents that the [redacted] decontamination included the Area [redacted] and [redacted] manufacturing suites and associated [redacted], gowning rooms, and QC laboratories, as well as the Weigh and Dispense and the QC Raw Material Sampling areas. [redacted] also noted the single deviation described in the report in which a [redacted] run was performed in the Weigh and Dispense area due to personnel entering the area after the first run (root cause was determined to be ineffective communication). [redacted] also provided me with the final reports both entitled "Room Bio-Decontamination Final Report" covering the two runs (dated 7/19/2021 and 7/8/2021, respectively; **Exhibits** [redacted]) from the vendor that performed the [redacted] decontamination ([redacted] During my review of the documents, I noted that the protocol did not include pre-specified acceptance criteria **(see Discussion Item #5)**. Having acceptance criteria for such studies was previous recommended to EMOB during the February 2021 site visit.

On 7/27/2021, I discussed the environmental monitoring (EM) performed by EMOB in these areas after completion of the [redacted] decontamination with [redacted]. He explained that EM was performed after bringing Area [redacted] back in service (after the [redacted] decontamination) but that since Area [redacted] has not yet been brought back into service, the EM (to qualify it for manufacturing) had not yet been performed. He provided me with EM data for Area [redacted] covering 7/5-7/2021 and including monitoring of particulates, viables in the air, surface sampling for viables, and surface sampling for mold. During my review of these data, I noted that there were two Out-of Specifications, one for surface viables on 7/5/2021 in room 1205 on a table and one for mold also on 7/5/2021 in room 1201 on the floor. On the same day, I discussed these results with [redacted], Sr Director, Quality. [redacted] noted that these results occurred on the first day of sampling and that there was no trend on subsequent days. When I asked [redacted] if the surface viable result was also for mold, she stated that it was not mold but rather bacterial colonies.

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Discussion Items from the June 2021 Pre-Production Investigation

Discussion Item 1
During a review of records relating to previously manufactured batches of Janssen Covid-19 drug substance, the investigators identified instances where deviations had not been initiated for apparent nonconformances or root cause analyses could be strengthened in existing deviations.

[redacted]
Deviation 3100012594
As discussed with [redacted] during the June 2021 pre-production investigation, EMOB stated in their response that deviation 3100012594 was amended to include an explicit assessment of QC raw material sampling as a potential root cause of the cross-contamination event. On 7/26/2021, I discussed the amended deviation with [redacted] who provided me with a copy of the deviation and identified the addendum section (dated July 2021) which contains an explicit assessment of QC raw material sampling as a potential root cause of the cross-contamination event on pages 15-16 of the deviation.

[redacted]
During the June 2021 pre-production investigation, the investigation team expressed concerns regarding lack of adequate investigation/root cause analysis for unexpected events in manufacturing, and deviations not being initiated in a timely manner. On 7/26/2021, [redacted], Specialist II, Compliance/Quality Systems, provided me with the following deviations that were opened or re-opened as a result of the previous investigation. These deviations were requested during the pre-announcement call on 7/22/2021.

Deviation 3100012397
Subject Description: "Client [redacted] Lot [redacted] Leak" (dated July 2021). This amended deviation includes an updated assessment referencing run chromatogram data instead of Technical Document Memo, TV-TEC-179025 to support that the [redacted] was homogenous.

Deviation 3100013079
Subject Description: "Bottles Shipped and RFFP'd w/o GMP data" (dated June 2021). This deviation was initiated in response to bottles of drug substance being released for forward processing to [redacted] without proper GMP documentation of the weights of the bottles.

Deviation 3100013154
Subject Description: "[redacted] Product" (dated June 2021). This deviation was initiated in response to an event where operators miscalculated and [redacted] client [redacted] lot [redacted] with [redacted].

Deviation 3100013056
Subject Description: "[redacted] failed" (dated July 2021). This deviation was initiated in response to an event discovered during a review of [redacted] v.2.0.

Deviation 3100013153
Subject Description: "Client [redacted] Lot [redacted] Lot [redacted] Recipe aborted" (dated June 2021). This deviation was initiated in response to an event where operators aborted the recipe of [redacted] during [redacted]) during the execution of [redacted]

Deviation 3100013036
Subject Description: "[redacted] OOS" (dated June 2021). This investigation was reopened on 06/04/2021.

Additional Controls Implemented Regarding Lab Investigations
On 7/26/2021, [redacted], Director of Quality Control; [redacted], Manager of QC Immunology; and [redacted], Janssen Laboratory Lead at Emergent gave a brief presentation entitled "Enhancements to Laboratory Investigations." This presentation provided an overview of enhancements to lab investigation management for out of specification, out of trend, and atypical results at the firm. Changes are documented in SOP002034 "Laboratory Investigation Procedure for Unexpected Results" (v 9.0, Effective 23 July 2021), which has been updated to include new and corrected forms and a requirement for the performing analyst to sign an approved test plan prior to executing work.

Improvements to [redacted] Test Program
On 7/26/2021, [redacted], Director of Manufacturing, gave a brief presentation entitled "Enhancements to [redacted] Testing." This presentation provided an overview of enhancements related to [redacted] testing at the firm. Changes are documented in SOP000448 "Operation and Maintenance of [redacted]" (v 8.0, Effective 23 July 2021), which has been updated to include timeframes for testing, [redacted] storage conditions, labeling and testing receipts, and verification that the correct recipe was selected and used.

Leak Prevention
On 7/26/2021, [redacted], Senior Director of MS&T, gave a brief presentation entitled "Emergent Process Integrity Remediation." This presentation provided an overview of handling and management of leaks at the firm. Changes are documented in SOP04441 "Handling of In-Process Leaks" (v 1.0, Effective 23 July 2021), a new SOP created to require materials and equipment to be inspected for defects, real-time documentation of observed leaks, and deviations for all leaks.

Corporate Quality Procedure on Deviation Investigations and Related Training
On 7/26/2021, [redacted], Director of Operational Excellence/Interim Head of Manufacturing, gave a brief presentation entitled "Enhancements to Quality Investigations." This presentation provided an overview of deviation management at the firm. Changes are documented in SOP0044111 "Global GMP Deviation Management Procedure" (v 2.0, Effective 12 April 2021), a new SOP for deviation investigations that includes procedures for employees to escalate unexpected events and to initiate investigations, and SOP000285 "Quality Assurance and Manufacturing Review of Manufacturing Records" (v 9.0, Effective 23 July 2021) to define on-the-floor review of batch records.

Discussion Item 2
The investigators identified several areas to strengthen quality oversight.

([redacted]
On 7/26/2021, I discussed the corrective actions implemented by EMOB to address this discussion item with [redacted], Quality Assurance Manager. [redacted] explained that SOP27886, "Quality on the Floor", was revised to add a larger role of quality on the floor during manufacturing. He provided me with a copy of the current version of the SOP (version 7.0, effective 7/23/2021), and identified several changes including (1) in section 6.2.9 adding real-time review of production batch records by quality, (2) in section 6.2.11 adding quality assuring that deviation are initiated, (3) in section 6.4.1.3 adding quality assuring that the warehouse and warehouse rooms are clean and in a good state of housekeeping, and (4) addition of Appendix A, entitled "QA Shopfloor Standard Work Walkthrough Inspection Checklist". [redacted] noted that this new appendix requires quality to ensure that all batch record entries are within range or else that deviations are identified, annotated and referenced. [redacted] also provided me with a copy of a new form [redacted] "QA Shopfloor Walkthrough Observations Logbook" (version 1.0, effective 7/23/2021) for use during the QA Shopfloor Walkthrough.

[redacted] also stated that SOP000285, "Quality Assurance and Manufacturing Review of Manufacturing Records", was revised to be more bulleted list of procedures to be performed. He provided me with a copy of the current version of the SOP (version 9.0, effective 7/23/2021), and identified several changes including (1) in section 6.1.1.1 adding the expectation that every page of each batch record will be reviewed by quality and (2) in section 6.2.11 adding that quality must ensure that all deviations are referenced in the batch record at the applicable step and in the deviation log of the batch record.

[redacted] also stated that SOP044405, "Bayview on the Floor Program", was revised. He provided me with a copy of the current version of the SOP (version 2.0, effective 7/23/2021) and identified that statements were added for during each type of walkthrough (manufacturing areas, warehouse, and QC laboratories) the area manage and quality are to be notified of any findings that might potentially be product impact.

Discussion Item 3
The investigators identified several areas to strengthen documentation relating to training attendance.

[redacted]
On 7/26/2021, I discussed the corrective actions implemented by EMOB to address this discussion item with [redacted], Sr Manager, Quality Assurance, and [redacted], Manager Quality System Training. [redacted] explained the issue of incomplete attendance taking identified during the June 2021 pre-production investigation and described in deviation 3100013030 was due to the trainings being given by EMOB Subject Matter Experts (SMEs) who had not completed the Qualified Trainer program which includes procedures for recording attendance in the [redacted] system. He stated that EMOB has therefore qualified [redacted] EMOB SMEs as trainers under the Qualified Trainer program. He stated that this process was being performed under CAPA Plan-000194 and provided me with a copy of this CAPA **(Exhibit [redacted]7)** as well as the associated deviation 3100013030 **(Exhibit [redacted]8)**. [redacted] further noted that [redacted] would be supporting training of EMOB employees in the future and that the

SOP governing EMOB's training (SOP001653 as noted in the CAPA) was currently under revision to include clear criteria to document training attendance.

When I asked [redacted] about what EMOB had done to address the trainings for which attendance could not be verified, he stated that these trainings were re-executed by [redacted]

On 7/27/2021, I had a follow-up discussion regarding training with [redacted] and [redacted] from [redacted] explained that [redacted] had performed four on-the-job trainings of EMOB employees based upon the checklists that [redacted] uses for oversight of EMOB manufacturing operations during their walkthroughs. When I asked about confirmation of learning from these trainings, he stated that they were interactive so assessed the understanding of the employees. [redacted] further explained that the employees who participated in these trainings were the operators and support staff including managers.

When I asked how these trainings related to the trainings for which attendance could not be verified, [redacted] stated that the trainings performed by [redacted] covered the same material. [redacted] provided me with the [redacted] oversight checklist used to guide the trainings and the training record for the following four trainings:

- TRN040817, "Movement of Material and Waste for Areas [redacted] and [redacted] version 2.0, approved 7/13/2021
- TRN040889, "Raw Material Sampling", version 1.0, approved 7/8/2021
- TRN040909, "Operation of the Weigh Dispense", version 1.0, approved 7/14/2021
- TRN040888, "Movement of Waste from the QC Laboratory", version 1.0, approved 7/8/2021

When I asked [redacted] about the current process for trainings given by EMOB SMEs considering that the applicable SOP is being updated, he stated that it would be the same as the process used by [redacted] He further stated that EMOB plans to have a combination of on the job and instructor-led trainings in the future.

[redacted]
On 7/26/2021, [redacted], Director of Manufacturing; [redacted], Sr. Manager of Quality Assurance; [redacted], Manager, QS Trainer; and [redacted], Sr. Manager of Manufacturing Operations gave a brief presentation entitled "Training Improvements." This presentation provided an overview of changes made to the training program at the firm. [redacted] stated that employees are now linked to curricula assignment profiles based on their job title or role instead of department. Reports of overdue or upcoming required training are still automatically generated and sent to management by [redacted] Training completion is recorded in [redacted] or on [redacted]

[redacted] stated that training is assigned when an SOP is created or revised, unless the update is only for an administrative change. I asked [redacted], [redacted], and Mr. Elmore for a list of all new training that had been initiated since the previous investigation. They all stated that they were unaware of a way to provide this information from the system.

I reviewed records of the following training, which included instructor led training and Read and Acknowledge training:

- SOP 044111, v 2.0 "Global GMP Deviation Management Procedure" - Read and Acknowledge
- SOP 044112, v 1.0 "Investigation and Root Cause Analysis Procedure for GMP Deviations" - Read and Acknowledge
- TRN040897 v 1.0 "Bayview OOS/OOT Training for SOP002034 Updates"
- TRN040898 v 1.0 "Bayview Invalid Events (SOP042317)"
- TRN040881 v 1.0 "QC [redacted] Audit Trail Reviews"
- TRN040817, v 2.0 "Bayview [redacted] – Training Reinforcement for Manufacturing Personnel Working in Areas [redacted] and [redacted]
- SOP000048, v 8.0 "Operation and Maintenance of the [redacted] Tester" Read and Acknowledge
- SOP 043924, v 2.0 "Management of Recipes and Methods" Read and Acknowledge
- SOP002034, v 9.0 "Laboratory Investigation Procedure for Unexpected Results"
- SOP044245, v 4.0 "Warehouse Cleaning Procedure" – Read and Acknowledge
- WI041959, v 1.0 "Administration Work Instructions for the [redacted] Testers" – Read and Acknowledge
- SOP027868, v 1.0 "[redacted] – The Operation of [redacted] and [redacted] Mixer Drive Units" – Read and Acknowledge
- SOP027886, v 7.0 "Quality on the Floor Program" – Read and Acknowledge
- SOP001518, v 19.0 "Material and Waste Flow" – Read and Acknowledge
- SOP044335, v 4.0 "Removal of Special Medical Waste from Manufacturing Areas" – Read and Acknowledge
- SOP000392, v 15.0 "Cleaning Program for Controlled Areas [redacted] and [redacted] – Read and Acknowledge
- SOP044131, v 1.0 "Global CAPA Management Procedure" – Read and Acknowledge

During my review of the training documentation, I noticed multiple instances of double documentation of employee training for instructor led courses. During my discussion with [redacted], it was determined that most of these occurrences correctly documented employees attending training in person and again via Microsoft Teams. One employee was entered into [redacted] twice in error and one employee was entered as receiving training on a date when she was the instructor **(see Discussion Item #1)**.

Discussion Item 4
While noting significant improvement since the April 2021 inspection, the investigators identified areas for further enhancement with respect to the Bayview facility's waste decontamination and removal processes

On 7/26/2021, [redacted], Associate BioProcess Specialist and [redacted], Senior Manager of Upstream gave a brief presentation entitled "Enhancements to Waste Management Processes." This presentation provided an overview of enhancements related to waste management at the firm. Changes are documented in SOP001518 "Material Waste and Flow" (v 19.0, Effective 23 July 2021), which was updated to include a waste removal decision tree and defined [redacted], and SOP044335 "Removal of Special Medical Waste from

Manufacturing Areas" (v 4.0, Effective 23 July 2021), a new SOP which contains requirements for use of [redacted] and provides paths for waste removal.

Discussion Item 5
The investigators identified areas to strengthen batch record review to ensure that relevant details appear in both the batch records and deviation reports.

[redacted]
On 7/26/2021, I discussed the corrective actions implemented by EMOB to address this discussion item with [redacted]. He stated that updates to the master batch records were being performed under consolidated change control 2100006692. He provided me with a copy of this change control **(Exhibit [redacted]9)** that addressing the 19 open change controls, seven CAPAs at the implementation stage and 14 additional CAPAs that have been initiated for master batch record revisions. During review of the change control, I noted that it has a due date of 8/30/2021, and therefore asked [redacted] about the status of the updates to the master batch records as it relates to EMOB's ability to resume manufacturing.

On the same day, I had a follow-up discussion with [redacted], Interim Sr Manager, Manufacturing, who explained the current status of the updates to the master batch records, stating that not all of the master batch records have been updated and training completed **(see Discussion Item #4)**. He stated the status of the updates to the master batch records as follows:

- The update of the master batch record used for media in Stage [redacted]) was completed, and training on the revised version was completed. He provided me with the current version of the batch record (version 5, effective 7/23/2021) as well as a read and acknowledge complete training record.
- The update of the master batch record used for media in Stages [redacted]) was completed, and training on the revised version was completed. He provided me with the current version of the batch record (version 4, effective 7/23/2021).
- The updates to the master batch records used for some of the [redacted] were also completed with the rest being in process.
- The update of the master batch record used for Stage [redacted]) was completed, and training on the revised version was completed. He provided me with the current version of the batch record (version 5, effective 7/23/2021) as well as a read and acknowledge complete training record.
- The update of the master batch record for Stage [redacted]) was completed but needed a minor update. He provided a memo dated 7/24/2021 that describes the required updates and explained that training on the current version would be complete that day (7/26/2021). [redacted] also provide me with a copy of page 1 of the current version of the batch record (version 5, effective 7/26/2021) as well as a read and acknowledge complete training record on versions 4 and 5 of the master batch record.
- The update of the master batch record used for Stage [redacted]) was completed, and training on the revised version was underway and anticipated to be completed by 7/29/2021.
- The update of the master batch record for Stage [redacted]) was complete and being reviewed by the client.

- The update of the master batch records for the other manufacturing Stages was not yet complete but was in process.

[redacted] and I then discussed the current version of the master batch record used for media in Stage [redacted]) and he identified where the three changes listed in change control 2100006692 **(Exhibit [redacted]9)** were present in the revised batch record.

Additional information regarding the corrective actions implemented by EMOB to strengthen the batch record review process are provided under Discussion Item 2 above.

Discussion Item 6
The investigators identified additional areas to strengthen the Bayview facility's cleaning and maintenance program.

[redacted]
On 7/27/2021, I discussed the corrective actions implemented by EMOB to address this discussion item with [redacted], VP of Engineering, Facilities and Validation. [redacted] stated that every light in the manufacturing area had been inspected, cleaned and repaired. He stated that all fixtures were inspected for loose or missing screws and checked to ensure that no gaps to the interstitial space remained. [redacted] stated that new flooring had been installed in area [redacted] downstream areas, bubbling and peeling paint had been removed and repainted, and [redacted] wall panels had been installed to cover painted surfaces to prevent damage and facilitate cleaning. He stated that more [redacted] wall panels will be installed to cover the remaining painted wall areas. [redacted]
showed me the work orders related to these corrections, and corrections were observed during the walkthrough of the EMOB warehouse, QC laboratories and manufacturing Areas [redacted] on 7/26/2021.

On 7/27/2021, I had a discussion with [redacted] and [redacted] regarding the tubing hooks in Area [redacted] downstream **(see Discussion Item #2)**. [redacted] stated that a [redacted] tool will be procured and used for cleaning the [redacted] in this area. [redacted] provided me a copy of SOP000392 "EMOB Cleaning Program for Controlled Areas [redacted] and [redacted] (v 15.5, Draft), which has been updated to include the [redacted] in 4.3.4, and procedures for cleaning the [redacted] in section 6.6.36 **(Exhibit [redacted]3)**.

Discussion Item 7
The investigators identified an area to strengthen the clearance procedure for the weigh and dispense area.

[redacted]
On 7/27/2021, I discussed the corrective actions implemented by EMOB to address this discussion item with [redacted]. [redacted] stated that SOP043687 "EMOB Line Clearance and Manufacturing Readiness for Controlled Areas" had been revised and he provided me with the current version (version 3.0, effective 7/23/2021). [redacted] identified that section 6.1 was revised to clarify that it applies to return to shutdown activities and client or product changes, and that section 6.2 was revised to clarify that it applies to not only client or product changes, but also between [redacted] for the same client and same product.

Discussion Item 8
The investigators identified areas to strengthen the Bayview facility's document and data management program.

[redacted]
On 7/27/2021, I had a discussion with [redacted], [redacted] Consultant; [redacted], Site Data Integrity Representative; [redacted], Janssen Compliance Officer; [redacted], Director of Quality Control; and [redacted], Janssen Laboratory Lead at Emergent regarding this discussion item.

[redacted] provided an overview of SOP044463, "Scanning Batch Records in Viral Areas for Business Continuity at Bayview" (v 1.0, Authorized), which documents secure network storage locations and access for defined user groups. He stated that batch records are scanned for use in the event that batch records are damaged or destroyed during the [redacted] process. [redacted] stated that batch records are maintained for [redacted].

[redacted] and [redacted] provided an overview of SOP000299, "Review of Quality Control (QC) Data (v 13.0, Effective 22 July 2021), which updated the responsibilities in section 3.0 and added 6.8 for [redacted] audit trail review.

Discussion Item 9
The investigators identified areas to strengthen the Bayview facility's inventory management program (SAP).

[redacted]
On 7/27/2021, I discussed the corrective actions implemented by EMOB to address this discussion item with [redacted], Warehouse Manager. [redacted] explained that EMOB performed a complete inventory of the warehouse (including all locations) to identify all of the non-SAP managed material present in the warehouse. EMOB then performed an assessment to determine if any of the identified material should be SAP managed, and based on this assessment, decided that none of the material fit into this category. EMOB therefore moved the material either to the QC laboratory, Emergent's Winnipeg, Canada location, or to [redacted] (a contract warehouse via a new agreement for storage of this material).

[redacted] also stated that the relevant SOPs both at EMOB (SOP043593, "Receiving and Distributing Purchased Materials") and at the Central Warehouse (SOP044252, "Material Receiving from External Vendors") had been updated to state that non-SAP managed materials must not be stored in an SAP managed location. He provided me with copies of these respective SOPs and identified the sections that were revised, sections 6.2.1 and 6.4.3 in document SOP043593 (version 6.0, effective 7/9/2021) and section 7.4.2 in document SOP044252 (version 2.0, effective 7/16/2021). [redacted] also provided me with three sets of training records (one form [redacted] "Global Training Attendance Roster", dated 7/9/2021 for SOP043593, and two forms [redacted] dated 7/18/2021 and 7/19/2021 for SOP044252) supporting that employees had been trained on these revised SOPs.

Discussion Item 10
The investigators identified areas to strengthen the technology transfer package and process qualification for the Janssen Covid-19 vaccine drug substance manufacturing process.

[redacted]
On 7/27/2021, [redacted], Senior Director, MS&T provided a copy of Bayview Protocol PRO050776 v 1.1 (effective 16 July 2021) entitled "Client [redacted] Process Verification Protocol" **(Exhibit [redacted]4)**. This protocol covers process verification that will be used for [redacted] drug substance manufacturing operations.

Other Items Discussed during the Investigation

[redacted]
EMOB's Manufacturing Restart Plan
On 7/26/2021, I discussed EMOB's plan for restarting manufacturing with [redacted]. He provided me with two memos **(Exhibit [redacted]10)**. In the first memo, dated 7/15/2021, it states that an evaluation of the Area [redacted] performance effectiveness will be performed before restarting manufacturing in Area [redacted] It further notes that this comprehensive assessment will be performed after [redacted] to allow for execution of one full manufacturing run in Area [redacted] In the second memo, dated 7/1/2021, it states that EMOB will change the cadence of manufacturing in Area [redacted] to a [redacted] cadence (thawing to start manufacturing a new lot of drug substance every [redacted] days).

On 7/27/2021, I had a follow-up discussion regarding EMOB's plan for restarting manufacturing with [redacted]. He stated that once given approval, EMOB would require [redacted] days to obtain the necessary materials and then would start on the first weekday (since they would not want to start production on a weekend). When I asked him if there were any other corrective actions that needed to be completed before EMOB would be able to resume production, excluding the contamination control training discussed above **(see Discussion Item #3)** and any other items identified during this pre-production investigation, he stated that there were no other corrective actions that needed to be completed.

GENERAL DISCUSSION WITH MANAGEMENT

[redacted]
On 7/27/2021 a close-out meeting was held with the firm. Attendees from EMOB, Janssen, and BARDA are documented in **Exhibit [redacted]5**. The following items were discussed with EMOB during the closing meeting:

1. Some training documentation contained inaccuracies in the reporting of training attendance. [redacted] stated in discussions during the investigation that EMOB plans to ensure that training is completed and documented accurately going forward.
2. New equipment ([redacted]) was installed on the [redacted] of Area [redacted] downstream, but SOP000392 "EMOB Cleaning Program for Controlled Areas [redacted] and [redacted] was not updated to include cleaning of the [redacted]. During this investigation, EMOB updated the SOP000392 to include the frame suspension hanger tool, as well as procedures for cleaning the [redacted].
3. EMOB had not required employees to take a revised version of the contamination control training as described in CAPA 1100003412. [redacted] stated in discussions during

the investigation that this is due to the ongoing discussions regarding revising plan PLN040854, and that EMOB will give a revised version of this training to all employees using a computer-based method prior to resuming manufacturing.

4. Not all of the master batch records used to manufacture the Janssen COVID-19 vaccine drug substance have been updated as described in change control 2100006692 (and training has not been completed on the master batch records that have not been updated). [redacted] stated in discussions during the investigation that this is due to some of the master batch record revisions still being in process, and that EMOB will ensure that the master batch records required for each manufacturing Stage with be updated and trained on prior to use of those master batch records during manufacturing.
5. The protocol for [redacted] decontamination of manufacturing and associated areas did not contain pre-specified acceptance criteria. I therefore recommended that EMOB include pre-specified acceptance criteria in such protocols in the future as was previously recommended to EMOB during the February 2021 site visit.

At the conclusion of the close-out meeting, we asked if there were any further questions from the firm. Ms. Mary Oates asked what steps should be taken next by the firm. We informed Ms. Oates that she should communicate directly with OBPO/Division 1 Compliance Branch regarding investigational findings, as well as any outstanding items from previous discussions with the compliance branch. I stated to [redacted] that the investigation relevant to Janssen was closed without noting concerns. He verbally acknowledged this statement.

EXHIBITS

[redacted]1 – Opening Presentation – 9 pages
[redacted]2 – Photo of tubing suspension hangers – 1 page
[redacted]3 - SOP000392 "EMOB Cleaning Program for Controlled Areas [redacted] and [redacted] v 15.5 – 30 pages
[redacted]4 - PRO050776 "Client [redacted] Process Verification Protocol" v 1.1 – 17 pages
[redacted]5 – Investigation Participant List – 6 pages

[redacted]1 – CAPA 1100003412 - 1 page
[redacted]2 – TRN040703 "Contamination Control Best Principles and Practices" – 14 pages
[redacted]3 – PRO0505034 "[redacted]) Disinfection of Area [redacted] Area [redacted] and [redacted]" – 9 pages
[redacted]4 – RPT056455 "Final Report for Evaluation of Microbial Inactivation in Area [redacted] Area [redacted] and [redacted])" – 21 pages
[redacted]5 – [redacted] "Room Bio-Decontamination Final Report" dated 7/19/2021 – 36 pages
[redacted]6 – [redacted] "Room Bio-Decontamination Final Report" dated 7/8/2021 – 16 pages
[redacted]7 – CAPA Plan-000194 – 7 pages
[redacted]8 – Deviation 3100013030 – 18 pages
[redacted]9 – Change Control 2100006692 – 30 pages
[redacted]10 – Memos Regarding EMOB's Plan for Restarting Manufacturing – 3 pages

ATTACHMENTS

1. FDA482 issued on 7/26/2021 to Mary D. Oates, Senior Vice President Quality, EMOB
2. FDA482 issued on 7/26/2021 [redacted], Senior Director of Quality, Janssen Pharmaceuticals Inc.

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[redacted]

[redacted], Senior Advisor, OBPO