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SUMMARY

(This section written by KRJ)

A pre-license inspection of this drug substance manufacturing facility at Wyeth BioPharma Division of Wyeth Pharmaceuticals, LLC., in Andover, MA (FEI:1222181), was conducted July 19 – 23, 2021 under eNSpect assignment #204656. The inspection was led by the Center for Biologics Evaluation and Research (CBER) Division of Manufacturing and Product Quality (DMPQ) with assistance from the Office of Vaccines Research and Review (OVRR) and the Office of Regulatory Affairs (ORA). The inspection covered BNT162b2 drug substance manufacturing operations for BioNTech Manufacturing GmbH's Biologics License Application (BLA 125742/0) for the COVID-19 Vaccine, mRNA [COMIRNATY]. The pre-license inspection was based on Inspection of Biological Drug Products (CBER) 7345.848 Compliance Program. This inspection was limited to the operations of the BNT162b2 drug substance, no other products were covered during this inspection. The profile class covered is Vaccine Bulk Product (VBP).

The previous FDA inspection of the facility, a pre-approval inspection in support of BLA 761118/0 for the drug substance of Adalimumab (biosimilar to Humira®) was conducted by CDER from 4/29/2019-05/03/2019, resulted in the issuance of a three-item Form FDA 483, List of Inspectional Observations. Deficiencies identified included: (1) Written procedures are not followed or are inadequate to ensure control over drug substance manufacture and laboratory operation; (2) Facilities, equipment, and utilities are not adequately maintained; and (3) Corrective action to mitigate an insect incursion into Building (b) (4) and Building (b) (4) has not been effective. Due to time constraints, the corrective and preventive actions taken by the firm in response to the Form FDA 483 were not discussed with the firm and should be followed-up on the next surveillance inspection.

The current inspection covered the firm's Quality, Production, Facilities and Equipment, and Laboratory Controls systems, to manufacture the BNT162b2 drug substance (DS). A thirteen (13)-item Form FDA 483 (Attachment) was issued to the firm at the end of the inspection on July 23, 2021 for the following observations: (1) There is insufficient data to support product quality prior to the release of BNT162b2 DS batch (b) (4) manufactured at (b) (4) (b) (4) Pfizer Andover on (b) (4); (2) There is inadequate quality oversight; (3) Deviation investigations were deficient; (4) Cleaning validation has not been performed on (b) (4) (Building (b) (4) (b) (4)); (5) Cleaning of (b) (4) product-contact parts using (b) (4) is not validated; (6) Cleaning efficacy studies are inadequate (Building (b) (4) (b) (4) (7) The ISO-(b) (4) are not monitored to ISO (b) (4) standards; (8) Routine monitoring of the compressed air of Building (b) (4) (b) (4) does not adequately represent all points of use; (9) The environmental program (EM) program in (b) (4) (b) (4) is deficient in ensuring that the cleanrooms are operating in a state of environmental control; (10) Clean status of the room is not verified or documented in the batch record after a preventive maintenance that resulted in a lack of pressure differential; (11) Standard operating procedures are not followed; (12) Facility deficiencies observed; and (13) Documentation of raw material storage is inadequate.

Verbal observations were also made at the conclusion of the inspection and are found in "General Discussions with Management" Section. The firm's management stated that they would provide a response to the inspectional observations within 15 business days. No refusals were encountered, and no samples were collected.

ADMINISTRATIVE DATA

(This section written by KRJ)

Inspected firm:	Wyeth BioPharma Division of Wyeth Pharmaceuticals, LLC FEI:1222181
Location:	1 Burtt Road Andover, MA 01810
Dates of inspection:	19 - 23 July 2021
Days in the facility:	5

Participants: Kathleen R. Jones, Lead Inspector, CBER/DMPQ (KRJ)
Ekaterina Allen, Inspector CBER/DMPQ (EA)
Anissa Cheung, Product Specialist Inspector, CBER/OVRR (AC)
Debra M. Emerson, Investigator ORA/Team Biologics (DME)

The inspection team presented its credentials to Mr. Jonathan Tucker at the beginning of the inspection on July 19, 2021. The FDA Form 482, Notice of Inspection (Attachment) was issued to Mr. Tucker, the most responsible person at the site. Following the presentation of the credentials, the firm presented an overview of the process, facility, and organization.

Each inspector wrote her assigned sections of this report, as identified by her initials.

The lists of attendees present at the opening meeting and at the closeout meeting are provided in **Exhibits KRJ-01** and **KRJ-02**, respectively. During the inspection closeout meeting on July 23, 2021, a 13-item FDA Form 483 was issued to Mr. Tucker (Attachment).

All FDA personnel were present daily and onsite during the inspection.

Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC., which is solely owned by Pfizer, and will be referred to as the firm, Pfizer, and Wyeth throughout the report.

PERSONS INTERVIEWED

(This section written by KRJ)
A list of attendees for the opening/quality systems meeting (**Exhibit KRJ-01**), closeout meeting (**Exhibit KRJ-02**), and subject matter experts and personnel observed during tours (**Exhibit KRJ-03**) were provided.

BACKGROUND AND HISTORY

(This section written by KRJ)
The Wyeth Andover, MA site consists of (b) (4) buildings (b) (4) on approximately 70 acres. The buildings include the following:

- Building (b) (4) (b) (4) (b) (4), Clinical Liquid Dose Manufacturing (LDM), Quality Control (QC) laboratories, and a cell bank (b) (4)
- Building (b) (4) (b) (4) (b) (4)
- Building (b) (4) Central energy plant and cogeneration plant
- Building (b) (4) (b) (4) and warehouse
- Building (b) (4) Analytical research and development (ARD) QC and Pfizer Global Supply (PGS) laboratories
- Building (b) (4) Research and development
- Building (b) (4) Warehouse
- Building (b) (4) Drug Product (DP) Development

Business hours are from 8:30 - 17:00, Monday through Friday. Manufacturing operations in Building (b) (4) are currently performed in (b) (4) from (b) (4) but can (b) (4) as is needed to meet the manufacturing schedules. Manufacturing operations in Building (b) (4) are currently performed (b) (4) There is a (b) (4) that solely performs facility sanitization for (b) (4) and (b) (4) There are a total of (b) (4) Pfizer employees (both part time and full-time employees) and (b) (4) contractors on site.

The Andover site is shared between Pfizer Global Supply (PGS) and Pharmaceutical Sciences BioTherapeutics (BT xPS; Pharm Sci), each with distinct quality units. PGS is responsible for commercial and clinical DS intermediate, DS, and (b) (4) production. PGS consists of (b) (4) (b) (4) QC analytical and microbiology laboratories in Buildings (b) (4) and working cell bank storage in Building (b) (4) Pharm Sci is responsible for product development, process development, and clinical manufacturing functions. Pharm Sci consists of Building (b) (4) LDM, ARD laboratories in Building (b) (4) and cell banking (b) (4) in Building (b) (4)

COVID-19 Vaccine-Andover Responsibilities are delineated as follows:

Description	Pharm Sci	PGS
(b) (4) Working Cell Bank Storage		X
(b) (4) Manufacturing*		X
(b) (4) Testing (In-process and Release)	X	X
(b) (4) DS Manufacturing	X	X
(b) (4) DS Manufacturing *		X
DS In-Process Testing	X	X
DS Release Testing	X	X
DP Release Testing	X	X
DS Stability Testing	X	X
DP Stability Testing	X	X
Raw Material Testing	X	X

*Has not been submitted under Emergency Use Authorization (EUA) or commercial BLA

Detailed organization charts were provided for both PGS (**Exhibit KRJ-05**) and Pharm Sci (**Exhibit KRJ-06**). See **Exhibit KRJ-04** for the opening and quality systems presentations.

WALKTHROUGH

(This section written by EA and DME)

Due to COVID-19 related social distancing restrictions and limits on personnel, no traditional walkthrough for orientation purposes was performed. Instead, inspector(s)

performed walkthroughs of various areas of the facility as they observed different manufacturing and QC operations. Specifically, the following facility areas and testing laboratories were inspected:

Building (b) (4)(b) (4)

- (b) (4) areas (refer to Observation #12 for noted concerns) - walkthrough performed by Inspector Emerson on 7/19/2021 and by Inspectors Allen and Emerson on 7/21/2021
- (b) (4) (b) (4) process for lot (b) (4) and sample (b) (4) - walkthrough performed by Inspectors Allen, Cheung, and Emerson on 7/21/2021
- (b) (4) (b) (4): DS (b) (4), and DS (b) (4) - walkthrough performed by Inspector Jones on 7/21/2021
- ARD Micro Laboratory (refer to Laboratory Section below for additional information) – walkthrough performed by Inspector Emerson on 7/19/2021
- ARD Quality Control (QC) Laboratories (refer to Laboratory Section below for additional information) – walkthrough performed by Inspector Cheung on 7/19/2021
- Packaging of DS lots (b) (4) for shipment to drug product manufacturing – walkthrough performed by Inspector Emerson on 7/21/2021
- (b) (4) Warehouse including temperature-controlled units (refer to Warehouse Section below for additional information and Observation #12 for noted concerns) – walkthrough performed by Inspector Emerson on 7/19/2021
- Dispensing of material used in formulation of (b) (4) (refer to Observation #13 for noted concerns) – walkthrough performed by Inspector Emerson on 7/22/2021

Building (b) (4)(b) (4) (b) (4)

- (b) (4) area (b) (4) - walkthrough performed by Inspector Allen on 7/19/2021
- (b) (4) (b) (4) refer to Observation #12 for noted concerns) walkthrough performed by Inspector Allen on 7/22/2021
- PGS Micro Laboratory (refer to Laboratory Section below for additional information) – walkthrough performed by Inspector Emerson on 7/19/2021 and 7/202/21

MANUFACTURING OVERVIEW

(This section written by AC)

(b) (4) distinct manufacturing buildings are employed for DS manufacture at the Andover site: (b) (4) and (b) (4) (b) (4) The process at both sites is highly similar and involves the same (b) (4) process steps as described below (**Exhibit AC-1**). All unit operations are performed at (b) (4)

(b) (4)

OBSERVATION OF OPERATIONS

(b) (4)
(b) (4) *in* (b) (4) (b) (4)

(This section written by EA)

During a walkthrough of (b) (4) (b) (4) (b) (4) on 7/21/21 performed by EA, AC, and DME, I (EA) observed (b) (4) reagent lot (b) (4) performed by an operator in (b) (4) . See **Discussion Item EA-3** and **Observations 6 and 7** regarding use and environmental monitoring of (b) (4) were passed out of the facility via a passthrough (see **Observation 12c** regarding state and cleaning of pass throughs).

(b) (4) *(DS* (b) (4)
(Written by KRJ)
On 7/21/2021 I observed DS (b) (4) in (b) (4) (b) (4)

(b) (4), (b) (6), (b) (7)(C)

Prior to Inspector KRJ exiting (b) (4) (b) (4) (b) (6), (b) (7)(C) explained the rest of the process operations. Drug substance (b) (4)

See Discussion Item KRJ-1.

(b) (4) (b) (4)
(b) (4) *area* (b) (4)
(This section written by EA)
On 7/19/21, I performed a walkthrough of (b) (4) area (b) (4) which is one of the (b) (4) areas (another is (b) (4) that support the manufacturing operations in (b) (4) (b) (4) The area is

(b) (4)

At the time of the walkthrough, a number of (b) (4) area. Pfizer explained the staged raw materials are those allocated and pre-ordered based on the manufacturing schedule, approximately a (b) (4) in advance. Software program, (b) (4), is used for inventory management and release of reagents. Reagents are (b) (4)

(b) (4)

I requested that (b) (6), (b) (7)(C) , use the (b) (4) system to locate a recently cleaned (b) (4). I inspected (b) (4) which had been cleaned on 7/16/2021 and confirmed the (b) (4) was visually (b) (4).

The supporting area associated with (b) (4) is used for cleaning of non-product contact equipment to support (b) (4) (b) (4). None of such equipment is (b) (4). The (b) (4) is additionally used for cleaning of product-contact parts in support of other products manufactured in (b) (4) other than (b) (4) (b) (4) Any such parts are cleaned in (b) (4) (b) (4) (b) (4) are cleaned inside (b) (4) (b) (4) which was confirmed during (b) (4) (b) walkthrough. No objectionable observations were noted during walkthrough of (b) (4) area.

(b) (4) *(DS* (b) (4)

(This section written by EA)

On 7/22/2021, I (EA) gowned in to observe the following operations in (b) (4) (b) (4) DS (b) (4)

(b) (4)

QUALITY SYSTEMS

Quality Unit

(This section written by KRJ)

I reviewed the (b) (4) , effective 02/24/2021 (PGS). The quality systems elements are as follows:

1.) *Process Performance and Product Quality Monitoring System*
2.) *Investigations and Corrective and Preventive Action (CAPA) System*
3.) *Change Management System*
4.) *Management Review of Process Performance and Product Quality*
5.) *Management of Outsourced Activities and Purchased Materials*
6.) *Management of Change in Product Ownership*
7.) *Additional Quality System Elements and Processes*

I also reviewed the Pharmaceutical Science Quality Plan: Pharmaceutical Science Small Molecule (PSSM), BioTherapeutics (BTx), Global Clinical Supplies (GCS), and Quality Assurance Pharmaceutical Sciences, approved on 04/02/2020. The quality systems elements are as follows:

1.) *Quality:*
Management Controls: QA roles and responsibilities, governance, and notification to management
Regulatory: Regulatory inspections, internal audit program, regulatory submissions, and recall/stock recovery
Change Management: Change management/control
Vendor/Supplier Management: Third party management
Disposition: Batch Record Review/Release
Knowledge Management: Quality system manual, document control, records management, and data integrity
Deviations: Deviations/investigations and complaint/adverse event management
Personnel: Training/learning system
Risk Management: Quality risk management and medical device quality risk management

2.) *Facilities and Equipment:* Design and construction, maintenance, calibration, environment controls, pest control, security, and cleaning/sanitation/ contamination control.

3.) *Laboratory:* Stability testing and monitoring, expiry/use by testing, laboratory test methods/testing, sample management, reference standards, and specifications.

4.) *Validation:* Validation life cycle management, qualification/requalification, validation/revalidation, and computer systems.

5.) *Materials:* Materials control, receipt and sampling, supply chain security, returned goods, retention samples, and warehousing/distribution/logistics.

6.) *Production:* Master/production batch records, manufacturing, aseptic processing controls, environmental monitoring, and rework/reprocessing.

7.) *Packaging/Labeling*: Master/executable batch records, packaging, labeling, and repackaging/relabeling.

8.) *Development:* Formulation development, process development/design control, specification development, analytical method development, packaging development, labeling development, technology transfer, and medical device design controls.

No objectionable observations were identified.

Deviation/CAPA Management
(This section written by KRJ)
On 07/20/2021, I discussed deviation management with the following people:

- (b) (6), (b) (7)(C)
- (b) (6), (b) (7)(C)
- (b) (6), (b) (7)(C)
- (b) (6), (b) (7)(C)
- (b) (6), (b) (7)(C)
- (b) (6), (b) (7)(C)

We discussed (b) (4), (b) (4), effective 02/24/2021 (PGS); (b) (4), (b) (4) Effective 08/05/2020 (PGS); and (b) (4) (b) (4), effective 01/28/2021 (Pharm Sci). The process is the same, but timings are slightly longer in Pharm Sci. Non-conformance events that occur in manufacturing, testing, packaging, labelling, handling, or disposition of drug substance are classified as MIRs. MIRs are documented in (b) (4) system. Incidents need to be documented in QTS within one business day. If the root cause and scope are known and no product impact is confirmed, then an Event Report (ER) is created. ERs have the primary document completed, and further analysis may not be required. CAPAs may not be required as well. If the root cause or scope are unknown, or if there is any product impact, the incident needs to be classified as a Quality Action Report (QAR). QARs require process mapping and thorough evaluation, historical review, in-depth root cause analysis, and CAPAs. CAPA effectiveness is governed by (b) (4), (b) (4), effective 02/26/2021 (PGS) and (b) (4)

(b) (4) (b) (4), effective 05/08/2020 (Pharm Sci). QARs also include final impact assessments and Quality Assurance (QA) product disposition decisions. Events must be classified within (b) (4) business days, and QTS records must be closed within (b) (4) calendar days. Extensions are allowed with QA approval based on an interim report. Additionally, a Notification to Management (NTM) is generated for significant product quality or regulatory compliance issues. I was told that in practice that any BNT162b2 related QAR generates an NTM.

On 07/20/2021, I spoke with (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C) about NTM. We discussed (b) (4), (b) (4), effective 11/04/2020 (PGS) and (b) (4), (b) (4), effective 12/21/2020. NTM is a mechanism to escalate an event to management and broader as events are then evaluated by quality review teams. Quality review teams can be site specific or can be global for any Pfizer facility performing similar operations. Pharm Sci will coordinate with PGS leadership if the need for a quality review team is warranted. Quality review teams are governed by (b) (4), (b) (4), effective 09/16/2020. No objectionable observations were identified.

Deviation Review

(This section written by AC)

Ten deviations related to the (b) (4) during the (b) (4) reaction in (b) (4) and (b) (4) (b) (4) were reviewed by Inspector Debra Emerson and I. I focused only on deviation (b) (4), and Inspector Emerson covered all of the deviations. Deviation (b) (4) was initiated on (b) (4) due to the multiple control limit excursions during the (b) (4) of DS batch (b) (4). The (b) (4) Not compiling the control limits for (b) (4) could have an impact on (b) (4) quality for the affected DS lot. Therefore, the firm decided to enroll this affected DS batch on stability because of the potential impact on product quality. CAPA (b) (4) was opened to facilitate the enrollment of this batch into

the stability program per Protocol (b) (4); however, this batch has not been placed on stability as of (b) (4). The CAPA (b) (4) was only executed on (b) (4) after we discussed this deviation with the firm. See **FDA Observation #1** for additional details. See the "Computerized Systems" section below for details surrounding the (b) (4) deviations.

(This section written by KRJ)
I reviewed QAR (b) (4) */ PF-07305885 / batch* (b) (4) */ DS* (b) (4), opened on 04/12/2021. On 04/09/2021 during execution of batch (b) (4) ((b) (4) the (b) (4) failed the (b) (4) test. Per (b) (4), (b) (4), effective 01/27/2021, the (b) (4) can be tested a maximum of (b) (4) times. The (b) (4) failed to have an acceptable (b) (4) result (b) (4) times. The batch was (b) (4) per (b) (4) and became batch (b) (4). The root cause was determined to be material, as this lot of (b) (4) used had a (b) (4) rate than previous lots. A complaint was opened with the vendor (b) (4) and the (b) (4) will be sent to the vendor for further analysis. Additionally, this lot is put on stability per (b) (4), and the feasibility of using (b) (4)

(b) (4)
will be updated as appropriate. No objectionable observations were identified.

Change Control Management

(This section written by KRJ)
On 07/20/2021, I discussed change control procedures with (b) (6), (b) (7)(C). We discussed (b) (4), (b) (4), effective 12/16/2020. I was told that Pharm Sci defaults to PGS's change control SOP. Change controls are documented and tracked in Quality Tracking System (QTS) for both Pharm Sci and PGS. Change control consists of the following steps:

- Change Identification Phase: Includes the business process steps to identify a change control.
- Change Development Phase: Includes recommended business process steps to plan and consult with stakeholders.
- Change Creation Phase: Includes determining scope of the change along with creating a draft change record.
- Change Assessment and Pre-Approval Phase: Includes evaluation of the change by the functional area impact assessors and quality. Change implementation cannot occur until QA has pre-approved the change control.
- Change Implementation Phase: Includes executing and documenting implementation activities including releasing for GMP use with a phased release approach.

- Change Post Approval and Closure Phase: QA approver verifies that all actions/deliverables have been successfully completed. The change is closed once any remaining activities have been verified as complete.

Temporary and permanent change controls are treated the same. Temporary change controls can incorporate multiple line items for such items as updated procedures, interim reports, or to reevaluate risk assessments. A temporary change control can operate in an implement/approval state and is considered closed when everything is reverted back to the original state. Any changes with potential multi-site impact are escalated to the Biotech Change Review Board (BCRB). The BCRB meets (b) (4), and all Pfizer affected sites are present and discuss the change. The implementation timing is decided during this meeting and is coordinated so that any lot manufactured in one area with the change will not be released until the change is implemented at both "sites". However, each individual "site" is responsible for their individual change control. No objectionable observations were identified.

Biotech Change Review Board (BCRB)
(This section written by KRJ)
I discussed the Biotech Change Review Board (BCRB) with (b) (6), (b) (7)(C) on 7/21/2021. There is only one (b) (4) (b) (4), effective 02/14/2017) that governs the BCRB as it is a Pfizer global board. Section 7.1 Background point B4 defines membership into the BCRB. This includes Quality Operations Product Leader(s) for product(s) covered, site(s) change control chairpersons, Global Chemistry, Manufacturing and Control personnel, Operations personnel, and a chairperson. This ensures that any change that would affect product manufactured in one Andover "site" would be communicated to and implemented by the other Andover "site". No objectionable observations were identified.

Change Control Review
(This section written by KRJ)
I discussed the temporary change control and risk assessment to manufacture BNT162b2 in (b) (4) with (b) (6), (b) (7)(C) on 7/19/2021 and 7/20/2021, as well as (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C) on 7/19/2021. The temporary change control ((b) (4)) contained 43-line items that include but not limited to updating standard operating procedures, implementation of cleaning validation, adding quality agreements. The line items associated with (b) (4) mitigated the risks identified in (b) (4), (b) (4), effective 03/02/2021 in order to bring BNT162b2 into (b) (4) No objectionable observations were identified.

Document Control Management

(This section written by KRJ)
On 07/20/2021 and 07/21/2021, I discussed document control with (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C) We discussed (b) (4), (b) (4), effective 03/01/2021 (PGS) and (b) (4) (b) (4), 06/22/2021. I was told that the processes are nearly identical, but the systems used in document control are different. In general, documents are created, reviewed, approved, effective, superseded, and obsoleted. Any document that impacts functional areas, has to be assessed if a regulatory affairs review is required. If so, then it would be reviewed by the BCRB. Documents are periodically reviewed every (b) (4) If a control print is required, then a reconciliation is also completed and reviewed at least (b) (4). If there is a red lined version as part of a temporary change control, Pfizer Global can see both documents in the system but it is clearly delineated. No objectionable observations were identified.

QA Batch Numbering

(This section written by KRJ)
On 7/21/2021, (b) (6), (b) (7)(C) from Pharm Sci and I discussed (b) (4), (b) (4), Effective 04/23/2021. Batch numbering for (b) (4) is (b) (4) generated. Batch numbers are a combination of letters (b) (4) and numbers (b) (4) and the formula is (b) (4) are the last (b) (4) of the production year. (b) (4) is the Suite Identifier (for BNT162b2 it is (b) (4) for (b) (4) (b) (4) are the product code. (b) (4) identifies the process step. (b) (4) is the batch number for campaign, and (b) (4) would be sequential process steps (e.g., three sequential see lab records for scale up). (b) (4) is used for multiple (b) (4).

I spoke with (b) (6), (b) (7)(C) from PGS on 7/21/2021 regarding batch number. We discussed (b) (4) (b) (4), effective 11/25/2020. Batch number can be (b) (4) generated batch numbers are created similarly as in (b) (4) (b) (4) assignment of batch records/batch number is performed Pfizer wide, so sequential batches may not have sequential batch numbers. No objectionable observations were identified.

QA Batch Release

(This section written by KRJ)
On 7/21/2021, I discussed batch release with (b) (6), (b) (7)(C) We discussed (b) (4)

(b) (4) effective date 06/03/2021 (PGS), and (b) (4) ((b) (4), effective 12/21/2020. Batch disposition starts with review of all batch records by QA, including raw materials and equipment status compliance. A check for open investigations, change controls, and CAPAs is performed. Open change controls are acceptable if they are implemented with restriction (QA approved). QA is responsible for providing final sign-off on the DS batch records to permit release for DP manufacture. No objectionable observations were identified.

Quality Agreements

(This section written by KRJ)

I reviewed (b) (4) , (b) (4) , effective 0202/2021 (Pharm Sci); (b) (4) (b) (4) , effective 06/30/2021 (PGS); and (b) (4) (b) (4) , effective 04/14/2021 (PGS). The general process is to determine if a quality agreement is required, determine the appropriate quality agreement template or form, customize the template, complete a cross-functional stakeholder review, negotiate responsibilities (may involve Quality), and sign/archive. Quality agreements are good for the lifetime of the product; however, the agreements undergo an (b) (4) review. Typical services covered in a quality agreement include, but are not limited to:

- Partial or full product manufacture
- Primary/Secondary Packaging
- Warehousing, Distribution
- Cell bank production and storage
- Testing associated with manufacture, product release, and stability
- Testing to support investigations or validations
- Sterilization

I discussed the quality agreement between the Pharm Sci and PGS quality units with (b) (6), (b) (7)(C) on 07/20/2021. The quality agreement between the (b) (4) quality units indicates that equipment validation, maintenance, calibration, change control systems, pest control, and cleaning validation (revalidation) are the responsibility of PGS system. It also denotes required cross talk between the (b) (4) quality units. Additionally, I reviewed the following quality agreements:

- Pharm Sci and PGS: delineating responsibilities between the (b) (4) Quality units
- Wyeth BioPharma Division LLC (Andover, MA) and Pfizer Manufacturing Belgium NV (Puurs, Belgium; drug product manufacturer)
- Wyeth BioPharma Division LLC (Andover, MA) and Pharmacia & Upjohn Company LLC (Kalamazoo, MI; drug product manufacturer)

No objectionable observations were identified.

Vender Qualification

(This section written by KRJ)

I spoke with (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C) on 7/19/2021 both from PGS ((b) (4) , and (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C) from Pharm Sci ((b) (4) on 7/21/2021 and 7/23/2021 about supplier qualification. We discussed the following documents:

Document number	Title	Version	Effective Date	Pharm Sci or PGS
(b) (4)			12/02/2020	PGS
			12/09/2020	PGS
			12/16/2020	PGS
			12/05/2019	PGS
			11/09/2020	Pharm Sci
			11/10/2020	Pharm Sci

New suppliers are selected via a change control and a cross functional team determines the criticality of material or service. The risk assessment and criticality of material determines the frequency of audits. Qualification of material includes establishing the material specifications and the testing requirements. The risk assessments are established at the time of supplier qualification, and all risk assessments are reviewed on a three-year schedule. However, individual supplier qualification reassessment is performed at a minimum of every (b) (4) , with high-risk suppliers requiring reassessment every (b) (4). Pfizer can request a for-cause audit at any time. (b) (6), (b) (7)(C) provided the gap assessment performed as part of the change control ((b) (4) and child action (b) (4)). The differences between the Pharm Sci and PGS groups was in the frequency of audit for different types of suppliers. All suppliers for Pharm Sci were also qualified for PGS, meaning all the suppliers had been qualified at the frequency of PGS (commercial standards). I reviewed the supplier qualifications for all bag suppliers: (b) (4) No objectionable observations were identified.

Annual Product Review

(This section written by KRJ)

I discussed the annual product quality review (APQR) with (b) (6), (b) (7)(C) on 7/20/2021. As the APQR is standard practice for manufacturing commercial products, Pharm Sci uses PGS's (b) (4) , (b) (4) , effective 07/14/2021). The annual product

review contains summaries from both Pharm Sci and PGS. This document is reviewed and signed by both the Pharm Sci and PGS's site heads and quality heads. The SOP defines roles and responsibilities, content for each chapter, and computer instructions to properly create, format, and enter the APQR into the QTS system. No objectionable observations were identified.

Biological Product Deviation Reporting

(This section written by DME)

The firm's document: (b) (4), (b) (4), (b) (4), effective 6/24/2020, was reviewed without comment. The procedure requires a Biological Product Deviation Report (BPDR) to be submitted to FDA within (b) (4) with regards to any event associated with the manufacturing, to include testing, processing, packing, labeling, storage, or holding of a licensed biological product in which the safety, purity, or potency of a distributed product may be affected. Per (b) (6), (b) (7)(C), there have been no BPDR's submitted for commercial products since the last inspection. The COVID-19 vaccine is authorized under an EUA and as such not subject to BPD Reporting at this time. Pfizer submitted a notification to FDA on 7/14/2021 about a stability failure of BNT162b2 drug substance batch (b) (4) which was manufactured in (b) (4) (b) (4) for a confirmed out-of-specification (OOS) for (b) (4) at the (b) (4) stability interval result: (b) (4). The specification for (b) (4) was initially (b) (4) and in May 2021 was revised to (b) (4) The BNT162b2 drug substance stability is currently (b) (4) . The BNT162b2 drug substance lot (b) (4) was used in (b) (4) drug product lots: (b) (4) drug product lots were manufactured at Pfizer Kalamazoo. Drug product lot (b) (4) has been distributed to the US Market and the lot has also been placed on the stability program for drug product. Drug product lot (b) (4) has been distributed to Japan. The investigation into the DS stability failure is in-progress.

Reprocessing/Rework

(This section written by AC)

(b) (4) establishes the requirements for reworking and reprocessing clinical and commercial current GMP materials manufactured in PGS. Any reworking or reprocessing shall be approved through the change control process per (b) (4) . All reworked or reprocessed materials shall meet all specifications and acceptance criteria prior to release and must have unique traceable batch numbers, be segregated, identified with the appropriate status, and controlled to prevent mix-ups.

A laboratory scale validation study was performed to demonstrate that a (b) (4) (b) (4) of the DS through the (b) (4) step has no adverse effects on the quality of DS. A (b) (4) step may be performed using a new and identical (b) (4) if a technical issue occurs that compromises the integrity of the system. This (b) (4)

validation study supports the (b) (4) process of DS lot (b) (4) under QAR report # (b) (4).

A separate DS batch (b) (4) that went through several reprocessed steps were discussed under the section of Deviation Review.

Training Program

(This section written by KRJ)

I spoke with (b) (6), (b) (7)(C) from PGS and (b) (6), (b) (7)(C) from Pharm Sci on 07/19/2021 and 07/20/2021 about training. We discussed the following documents:

Document number	Title	Version	Effective Date	Pharm Sci or PGS
(b) (4)			08/05/2020	PGS
			12/16/2019	Pharm Sci
			05/27/2021	Pharm Sci

The personnel explained the main difference in training between Pharm Sci and PGS are the systems that document the training. Training consists of (b) (4). There are general trainings, such as GMP training or (b) (4) GMP refresher, and job specific trainings. Job roles and subsequent trainings are reviewed (b) (4). Employees and managers can view training statuses at any time, and there are (b) (4) metrics that allow managers view outstanding training records. There is also an (b) (4) review of training status of all employees.

I reviewed the task related training records of employees performing (b) (4) operations in (b) (4) (b) (4) ((b) (6), (b) (7)(C)), and employees performing (b) (4) testing ((b) (6), (b) (7)(C)) and (b) (4) operations in (b) (4) (b) (4) (b) (4) ((b) (6), (b) (7)(C)). All training was complete. No objectionable observations were identified.

Returns/Salvage

(This section written by DME)

The procedure: (b) (4) (b) (4), effective 12/16/2020, was reviewed without comment. Per (b) (6), (b) (7)(C), the firm has received two shipments of Pfizer manufactured material under Returns. The first was for multiple lots of (b) (4) which

were returned from Puurs, Belgium. The (b) (4) was shipped back to Pfizer Andover using the same qualified shipper and Pfizer Andover provided training to Pfizer Puurs staff on how to properly pack the shipper. The second was for product Adalimumab which was made at Andover and sent to (b) (4) for "special projects" manufacturing. There were no shipping excursions for either return. Through records provided, Pfizer was able to confirm the storage temperatures of the material when at both facilities.

FACILITIES AND EQUIPMENT SYSTEMS
Environment Monitoring

(This section written by EA)

(b) (4) (b) (4)(b) (4) (b) (4)Room (b) (4), for manufacture of DS, was implemented in December 2020 by partitioning it from the existing manufacturing area ((b) (4) (b) (4) Some walls were removed to enlarge room (b) (4). Within room (b) (4), there are (b) (4) existing (b) (4) (relocated together with its utilities during the remodel to Southwest wall) and a new (b) (4) installed next to entry/exit to Gowning Room (b) (4) in Spring 2021. Supporting rooms (b) (4) remained the same and were not remodeled.

I discussed the Environmental Monitoring (EM) program with (b) (6), (b) (7)(C) , and (b) (6), (b) (7)(C) . The Subject Matter Experts (SMEs) explained that EM sites were assessed for (b) (4) and (b) (4) during the construction phase. The site selection was documented in initial (b) (4) (b) (4) (b) (4) (b) (4) which was modified to include (b) (4) after it was installed ((b) (4) effective 04/30/2021). The assessment covered room (b) (4) (ISO(b) (4) and the (b) (4) only, as the rest of the adjacent rooms were not remodeled. Risk assessment considered difficulty to clean, personnel flow/presence/ activity, material flow, proximity of open product or product contact material, and known risk for bacteriological host cell containment. Each risk factor was rated as (b) (4) for each of the areas being assessed (b) (4) was divided across in (b) (4) of similar area, each with a (b) (4) The total risk score (multiplication of all individual risk factor scores) was used to determine minimum sampling sites, e.g., (b) (4) sample for lower risk areas, no less than (b) (4) samples, (b) (4) for medium risk areas and no less than (b) (4) samples, (b) (4) for high-risk areas. (b) (4) were determined "high risk" and both (b) (4) were evaluated as critical non-aseptic processing area.

Based on the risk assessment, the routine EM sampling plan for (b) (4) (b) (4)includes (b) (4) sites, (b) (4) . I (EA) reviewed the locations and they appeared acceptable (however see **Discussion Item EA-2** regarding lack of sample location reevaluation post-commissioning of (b) (4) (b) (4) action limits were in line with ISO(b) (4) sample is collected); (b) (4) limits are (b) (4) except floor samples (b) (4)

sample. Sampling of ISO areas is performed on a (b) (4) basis. (b) (4) sampling using (b) (4) is performed (b) (4) . EM frequency and sample size (b) (4) are insufficient to ensure cleanrooms operate in the state of control given the room size and frequency of use in manufacture (b) (4) See **Observation 9b** and **Discussion Item EA-2** for more details.

(b) (4) are monitored (b) (4) for (b) (4) for (b) (4) are not monitored during or post-operation. Action limits are . According to Paige Persky, Manager DP Manufacturing, and (b) (6), (b) (7)(C) , monitoring in operation is not proceduralized and is MBR-driven instead. It is limited to (b) (4) sampling (b) (4) during (b) (4) activities per (b) (4) effective 06/30/2021. No personnel monitoring or monitoring post-operations is performed.

EM is proceduralized in (b) (4) (b) (4) (b) (4) (b) (4) effective 05/12/2021. The sampling sites/types described in this document match those determined in the risk assessment and described above. Additionally, (b) (4) samples are collected in Gown/Degown room (b) (4) and (b) (4) . No routine EM is performed for other areas adjacent to (b) (4), including Control Room/Storage (b) (4) (see **Observation 9c**).

According to (b) (6), (b) (7)(C) , growth promotion testing is performed on every lot of (b) (4) used for (b) (4) sampling upon receipt and (b) (4) thereafter. Media qualification is proceduralized in (b) (4) (b) (4) (b) (4) . The firm uses (b) (4) with (b) (4) as disinfectant neutralizers.

All EM excursions above alert level and any mold growth are identified. Isolate identification is performed to aid with root cause analysis, and to identify any unusual recoveries. EM data is trended (b) (4) along with changes in percent recovery. Limits are established statistically once sufficient data is acquired and trends can trigger investigation if alarm level excursions repeat. (b) (4) evaluation of isolate identification is also performed. Mold recoveries at any level trigger an investigation initiation (also required for any (b) (4) recoveries) and CAPA (facility sanitization with a sporicidal and visual inspection). Recoveries over alert level are identified and assessed for trends (mold and spore formers). For recoveries over action level QTS record is required, including product-impact analysis. Isolates are not retained past the amount of time required for identification; therefore, no facility isolates are available if trends emerge that require additional disinfectant effectiveness studies to be performed.

I reviewed the following EM trending reports covering (b) (4)

- (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) effective 03/31/2021
- (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) effective 05/27/2021

No above action level recoveries were reported for (b) (4) Isolated mold recoveries were reported in December 2020 and January 2021, none in the (b) (4)

EMPQ of (b) (4) was performed after (b) (4) of the facility and equipment with a sporicidal in December 2020 following (b) (4) effective 11/04/2020 (see). Per my (EA) discussion with (b) (6), (b) (7)(C), EMPQ consisted of (b) (4) of (b) (4) sampling, followed by (b) (4) of (b) (4) sampling, at which point the facility was released for operations. Increased (b) (4) sampling (b) (4) continued over (b) (4) at which point sampling switched to routine schedule. Sampling locations and volumes used for EMPQ were the same as those used for routine EM and described above. (b) (4) was included in EMPQ. EMPQ results were provided to me in a form of EM Trend Detail Report printout for rooms (b) (4) (including the (b) (4) for the period of (b) (4) (b) (4) sampling) and for (b) (4) (including the (b) (4) only for the period of 12/28/2020-01/02/2021 (extended sampling). (b) (4) was qualified upon its installation by performing (b) (4) sampling only on (b) (4). All results met the acceptance criteria. See also **Observation 9a** and **Discussion Item EA-2** regarding EMPQ design and (b) (4) qualification.

I reviewed environmental alarm configuration and an alarm data report for (b) (4) for the period from 01/01/2021 to 12/31/2021 (data only provided through inspection dates) and alarms with (b) (6), (b) (7)(C). Alarm limits for (b) (4) and adjacent rooms were defined during HVAC IOQ and are set as follows:

- Room temperature: outside of (b) (4) min delay.
- Humidity: outside of (b) (4) range; (b) (4) delay.
- Pressure differentials (relative to non-controlled corridor):
  (b) (4) Foyer: outside of (b) (4)
  (b) (4) Gown/Degown: outside of (b) (4)
  (b) (4) (b) (4) outside of (b) (4)
  (b) (4): outside of (b) (4)
  (b) (4) Sample Pass Through: outside of (b) (4)
  Pressure differential alarms are on (b) (4) delay.

If an alarm is triggered, personnel from an appropriate call list will be contacted by central monitoring system; however, routine EM data is not reviewed. The alarm response staff is

dedicated and is on call (b) (4). For the pressure differentials, there is also a local alarm (light and audible), which is on (b) (4) delay to ensure the doors are not propped open for example, (b) (4) delay on the alarm was set to ensure it is only triggered in case of an HVAC failure. Alarm monitoring and response is proceduralized in the following SOPs:

- (b) (4) effective 07/21/2021
- (b) (4) effective 04/14/2021

During review of the alarm data report for (b) (4) I (EA) noticed a number of pressure differential alarms on 03/31/2021 (status (b) (4) in rooms (b) (4) and on 03/18/2021 (status (b) (4) in room (b) (4). See **Observation 10** for further details.

(b) (4) *EMPQ and Routine Monitoring.* (b) (4) used for the DS manufacture is located on Level (b) (4) of Building (b) (4) (b) (4) facility also includes (b) (4) (b) (4), all accessed from clean corridor, and a return corridor. All classified areas were qualified under the same EMPQ documented in (b) (4) (b) (4) (b) (4) effective 09/04/2019. My assessment focused on (b) (4) ((b) (4) (b) (4)

I reviewed the study report and discussed it with (b) (6), (b) (7)(C). EMPQ of the facility was performed following the baseline EM study (for information only) followed by (b) (4) cleaning using (b) (4). EMPQ consisted of (b) (4) of (b) (4) monitoring followed by (b) (4) monitoring completed on (b) (4) and (b) (4); the scope of the study included (b) (4) used for reagent (b) (4) (b) (4) in (b) (4), ISO see **Observation 7c**) and (b) (4) in (b) (4) (b) (4) Activities during (b) (4) sampling included various representative in operation activities, including downstream manufacturing activities in (b) (4) Maximum personnel capacity was challenged for (b) (4) only. Sampling included (b) (4), and (b) (4). All (b) (4) sampling was performed after completion of operations using (b) (4) and (b) (4) only) (b) (4) with (b) (4) Cleanrooms were oversampled during EMPQ (e.g., number of (b) (4) samples was based on ISO recommendation).

Action limits (EMPQ and routine EM) for (b) (4) were per ISO ((b) (4) (b) (4), ISO (b) (4) for ISO ISO and ISO areas, respectively.

(b) (4) action limit was (b) (4) sampling; see **Observation 7b**). (b) (4) action limits were surface-dependent (in (b) (4) (ISO(b) (4) (ISO(b) (4) and (b) (4) (ISO(b) (4)

There was a trend identified for (b) (4) excursions (both (b) (4) conditions; all (b) (4) results within the limit). However, a root cause of failures in most cases was found to be (b) (4) spraying or similar activities. The counter was purged, and a second sample was collected immediately with a passing result in all cases. (b) (4) excursions were observed under (b) (4) conditions only: (b) (4) and (b) (4), (b) (4) (b) (4). Per the SME, acceptance criterion for the study was (b) (4) out of (b) (4) of passing results. There was no additional extended sampling as a follow up to the EMPQ excursions, instead all (b) (4) sampling locations with results over the action limit were incorporated into routine monitoring program. All growth over action limit and in (b) (4) was identified; of (b) (4) (entire facility).

Hazard/critical control point analysis of microbial control in the facility was performed and high hazards were determined to be critical (b) (4) and open critical processes/additions (include final (b) (4) activities, to be performed "in critical ISO(b) (4) per p.22 of the report (b) (4)). Monitoring of critical ISO(b) (4) to include EM of (b) (4) and (b) (4) and personnel monitoring. Non-critical ISO(b) (4) were deemed low hazard; their sampling is to exclude (b) (4) and personnel monitoring (see **Observation 7a**).

Upon completion of EMPQ sampling sites for routine EM were reduced by a cross-functional group based on the evaluation of EMPQ outcomes and location of potential hazard points to the manufacturing environment, process, and product. Contributing factors to sample site elimination were the size of the room, other sampling sites being more representative, historically low bioburden levels for similar surfaces (i.e., walls) at other sites. Routine EM sites in small non-production areas (airlocks and In-Process Lab) were reduced to (b) (4) samples. (b) (4) (b) (4) sampling was reduced to (b) (4) samples. (b) (4) sampling was reduced to (b) (4). (b) (4) (b) (4) sampling was reduced to (b) (4) samples. (b) (4) routine monitoring sites include (b) (4) samples (b) (4) of the worksurface).

Frequency of routine sampling is (b) (4) for critical ISO(b) (4) areas (except (b) (4) and personnel monitoring which are performed per batch record), (b) (4) for ISO(b) (4)

and non-critical ISO areas, and (b) (4) for ISO areas. All excursions over the action limit and all ISO recoveries are identified to (b) (4). Per the SME, bioburden recovered from ISO areas is saved until completion of next trending report. Routine EM program, including sampling locations, frequencies, methods, action limits, notifications and incidence reporting, etc. is proceduralized in (b) (4) effective 12/31/2020.

Routine EM results and isolates identified are trended (b) (4) contamination recovery rates action levels to be established as more data becomes available. I (EA) reviewed the following EM trending data covering DS manufacturing areas within (b) (4)

- Printout of Environmental Monitoring Summary – Andover (b) (4) Rooms (b) (4) for the period from 07/01/2020 to 08/31/2020
- Printout of Environmental Monitoring Summary – Andover (b) (4) Rooms (b) (4) for the period from 04/01/2021 to 07/23/2021
- (b) (4) (b) (4) (b) (4) (b) (4) approved on 05/27/2021

No objectionable observations were noted.

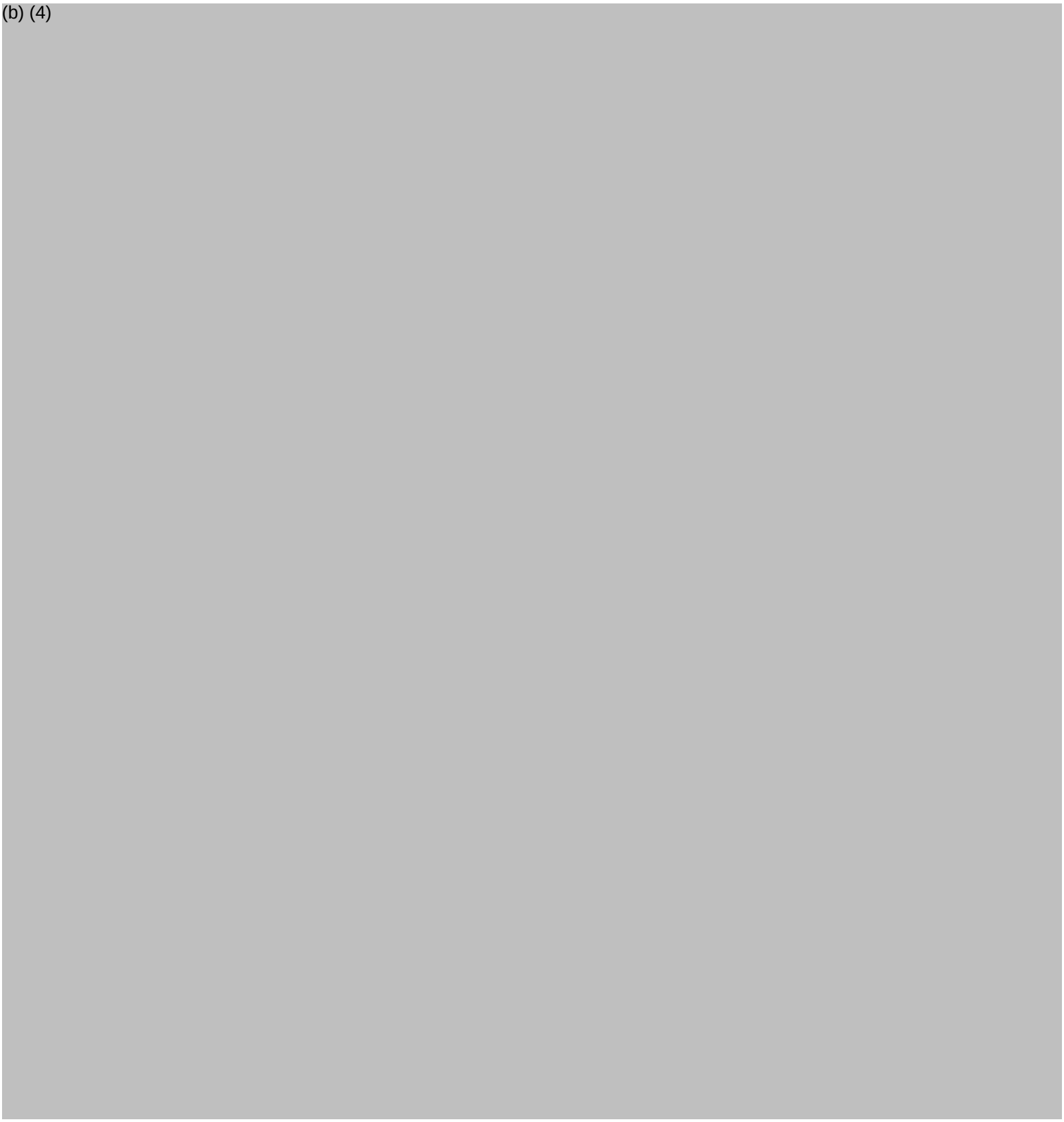
Water System

(This section written by EA)

(b) (4) *Water System.* (b) (4)

I (EA) discussed water monitoring with (b) (6), (b) (7)(C)., who explained that the routine (b) (4) monitoring is performed per (b) (4) (b) (4) (b) (4) (b) (4) effective 11/25/2020. (b) (4) sampling is performed (b) (4) for all (b) (4) within (b) (4) (b) (4) for ambient return, and (b) (4) for ambient supply. Source water prior to (b) (4) is monitored for (b) (4)

(b) (4)



(b) (4)

No objectionable observations were made. There appeared to be a decrease in frequency of (b) (4) excursions compared to 2019. It was noted that predominant (b) (4) in 2019 were those indicative of (b) (4) . However, their recoveries reduced dramatically in 2020: (b) (4) Note that the manufacture of BNT162b2 was initiated in 2020 following the reduction in the (b) (4) .

Compressed Air

(This section written by KRJ)

On 07/23/2021, I discussed compressed air qualification and monitoring of (b) (4) manufacturing areas with the following people:

- (b) (6), (b) (7)(C)
-
-
-
-

We discussed (b) (4) , (b) (4) (b) (4) (b) (4) approved on 08/28/2018 (**Exhibit KRJ-14**) and the report (b) (4) , (b) (4) (b) (4) (b) (4) approved on 04/23/2019 (**Exhibit KRJ-15**). The acceptance criteria are as follows:

ISO Class	Water/Oil Detection	Total Air Particulates ≥ 0.5 µm (particles/m^3)	Total Air Particulates ≥ 0.5 µm (particles/m^3)	Active Air Viable Particulates (CFU/m^3)
(b) (4)				
(b) (4)				

Facility Cleaning
(This section written by KRJ)
I discussed the facility cleaning of (b) (4) with (b) (6), (b) (7)(C) on 7/22/2021. We discussed (b) (4) (b) (4) effective 06/26/2021. (b) (4) is Area (b) (4) and BNT162b2 buffer prep is Area (b) (4) The floors and glass items are cleaned (b) (4), and the disinfectant (b) (4) between (b) (4) Walls, external equipment, and (b) (4) are cleaned (b) (4) with (b) (4) Surfaces are wiped down with (b) (4) after contact time with (b) (4) Cleaning is performed during (b) (4) . Rooms are cleaned starting at the (b) (4) . Cleaning is document in logbooks. Frequency deficiencies were identified, see **Observation 12a**.

(This section written by EA)
(b) (4) (b) (4) facility cleaning is performed per (b) (4) (b) (4) effective 06/09/2021. The SOP addresses cleaning frequency, methodology, agents, their preparation, rotation, expiry, and contact time, as well as documentation, suite status, and special sanitization requests. I discussed (b) (4) (b) (4) cleaning with (b) (6), (b) (7)(C) . He explained that facility cleaning occurs (b) (4) during the (b) (4) shift, regardless of whether the (b) (4) was used. (b) (4) (b) (4) is used for manufacturing operations (b) (4) It was noted that clean status of the room is not documented in batch record or verified prior to start of manufacture (see **Observation 10**).

Disinfectants, (b) (4), are used for (b) (4) cleaning (b) (4) is used on (b) (4) basis. (b) (4) is performed in foyer, gowning, and pass-through room. (b) (4) is used in all areas prior to scrubbing with (b) (4) and as needed). Otherwise, (b) (4) method is used. (b) (4) logbook is used to document room status, sanitization agent preparation (including lot and expiration date), cleaning type, method, agent used, and areas sanitized.

Training of cleaning personnel consists of a (b) (4) of reading SOPs followed by assessment of the following skills by a qualified trainer: sanitization, (b) (4) log, use and handling of (b) (4), gowning (no gowning qualification is performed). I reviewed (b) (4) (b) (4) Facility Sanitization Summary reports from 12/31/2020 to 2/28/2021. No objectionable observations were noted.

Periodic cleaning of outside surfaces of major equipment and cleaning/breaking down of (b) (4) is performed by operators using (b) (4) or (b) (4) down, respectively per (b) (4). See **Observation 11b** regarding outside cleaning of major equipment.

Disinfectant Efficacy
(This section written by KRJ)
I discussed disinfectant efficacy with (b) (6), (b) (7)(C) on 7/22/2021. We discussed (b) (4) (b) (4) effective 04/30/2015 (PGS; **Exhibit KRJ-11**) and (b) (4), approved on 04/28/2021 (Pharm Sci; **Exhibit KRJ-10**).

PGS: The surfaces tested in (b) (4) include (b) (4). The organisms tested include (b) (4) The disinfectants tested and the validated contact times include (b) (4) against all organisms tested with the exception of (b) (4)

(b) (4) The surfaces tested in a (b) (4) include (b) (4) The disinfectants tested and the validated

contact times include (b) (4)

See **Observation 6** regarding conflicting efficacy data in the two studies for (b) (4) with a contact time of (b) (4) .

Security
(This section written by EA)
(b) (4) (b) (4) Only authorized personnel are allowed in the manufacturing area, which is controlled via access (b) (4) . During the (b) (4) (b) (4) walkthrough (see "Walk through" section), I verified that the door to (b) (4) (b) (4) Foyer (b) (4) could not be opened with the (b) (4) of (b) (6), (b) (7)(C) , who does not have access to the area. No concerns were noted regarding security.

Containment
(This section written by EA)
I reviewed the following procedures governing personnel, material, equipment, and waste flows in (b) (4) (b) (4)

- (b) (4)
  (b) (4) effective 06/02/2021
- (b) (4)
  effective 04/07/2021

Both (b) (4) (b) (4) and (b) (4) airlocks have interlocking doors; the functionality of personnel airlocks was verified during the walkthrough.

Material, equipment, DS, and waste exits the suite via (b) (4) , which is operated as a (b) (4)

During the walkthrough of (b) (4) (b) (4) I discussed waste handling procedures with Haroon Beg. Mr. Beg explained that there are (b) (4) types of solid waste generated within the suite, (b) (4)
respective waste containers were observed within the suite. (b) (4) container was (b) (4) (allowed per (b) (4) for (b) (4) solid waste). Mr. Beg explained that operators remove waste at the (b) (4)

Per (b) (6), (b) (7)(C), waste is removed from (b) (4) (b) (4), during the (b) (4) shift as well as by operators and placed into a (b) (4) with a (b) (4), where it is picked up from (b) (4). See **Discussion Item EA-5**.

I explained that SOPs should be clear and specific enough to allow for consistent execution. There is also an increased risk of cross-contamination due to the waste handling procedures, such as not using (b) (4) or not temporally segregating waste from DS and materials that are transferred via the same (b) (4)

Pest Control

(This section written by DME)

The procedure (b) (4) Effective 7/7/2021, was reviewed without comment. The procedure provides the requirement for pest control of all Pfizer buildings at this location. Pfizer uses (b) (4) located in (b) (4) to provide (b) (4) and (b) (4) inspection and pest treatment for all buildings. The pest control includes (b) (4) inspection of (b) (4) inspection of (b) (4) inspection of (b) (4), and (b) (4) replacement of (b) (4). Pfizer staff inspect the external areas of all buildings for areas where bugs/rodents may enter, and work orders are opened to repair these facility concerns. Pfizer compiles a (b) (4) review of all pest control documents and an (b) (4) review of all pest control records that includes all buildings. The following reports were reviewed without comment:

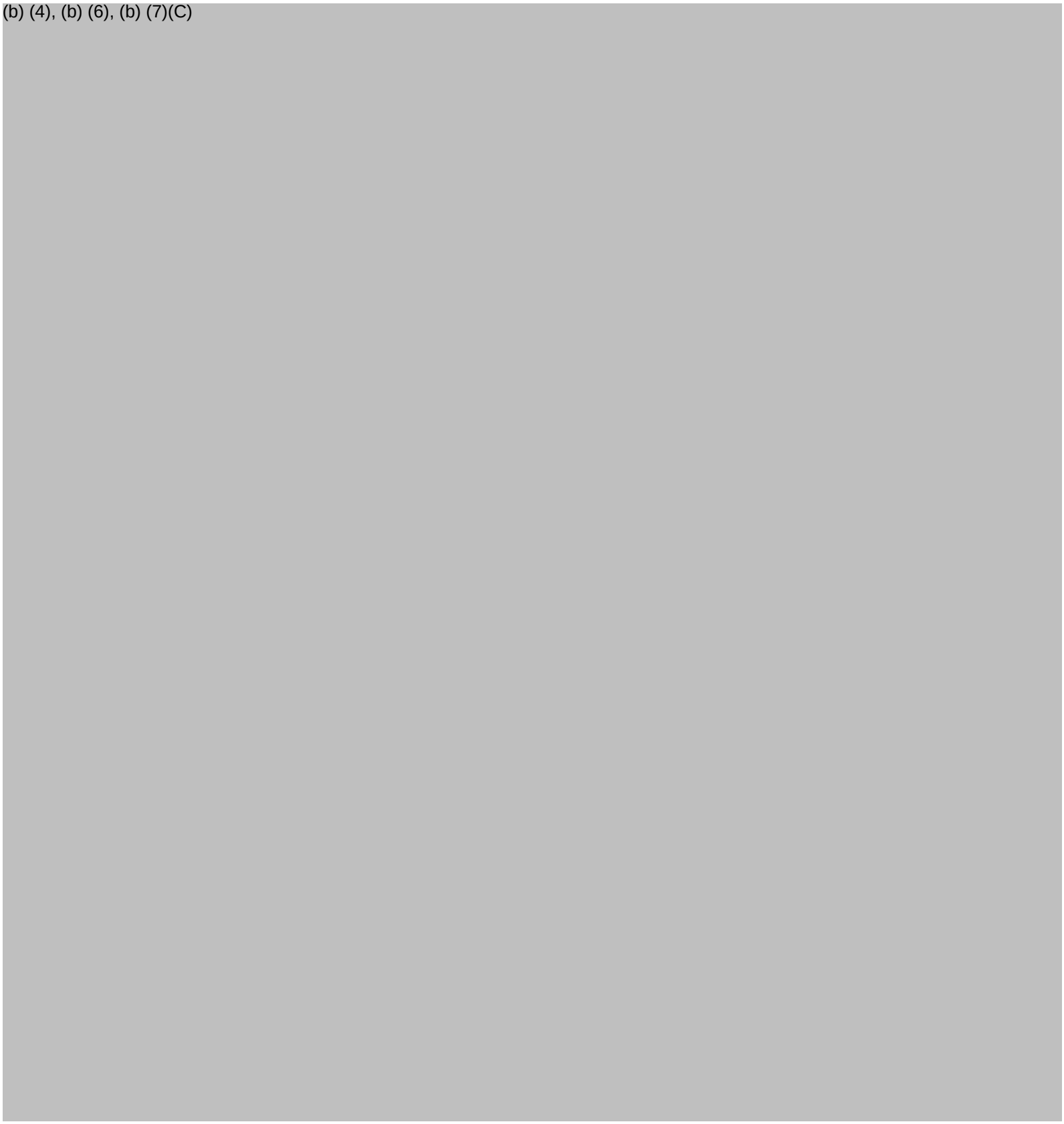
- (b) (4)
  (b) (4) effective 3/31/2021
- (b) (4)
  (b) (4) effective 5/25/2021

Equipment Qualification

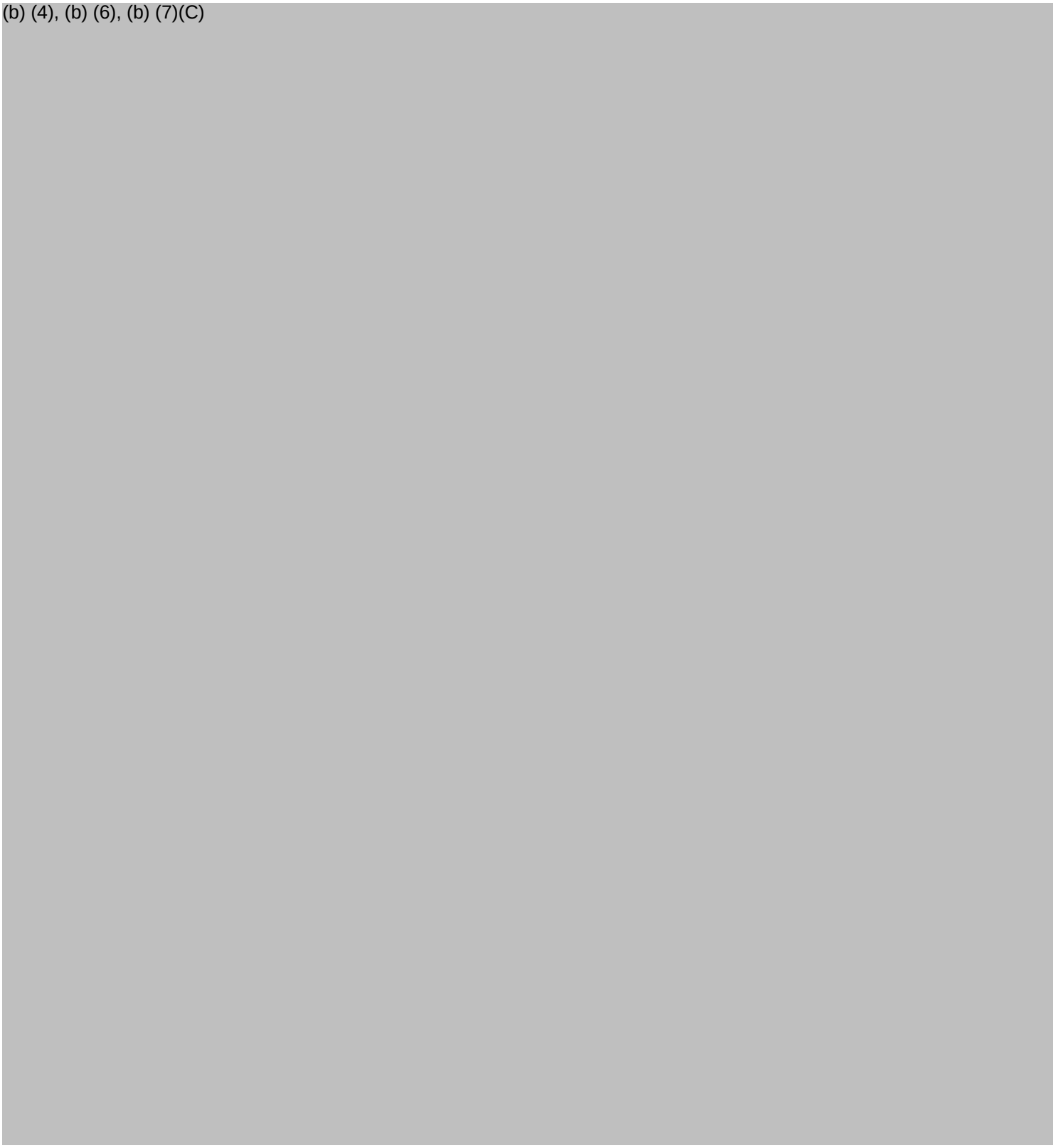
(This section written by KRJ)

(b) (4)

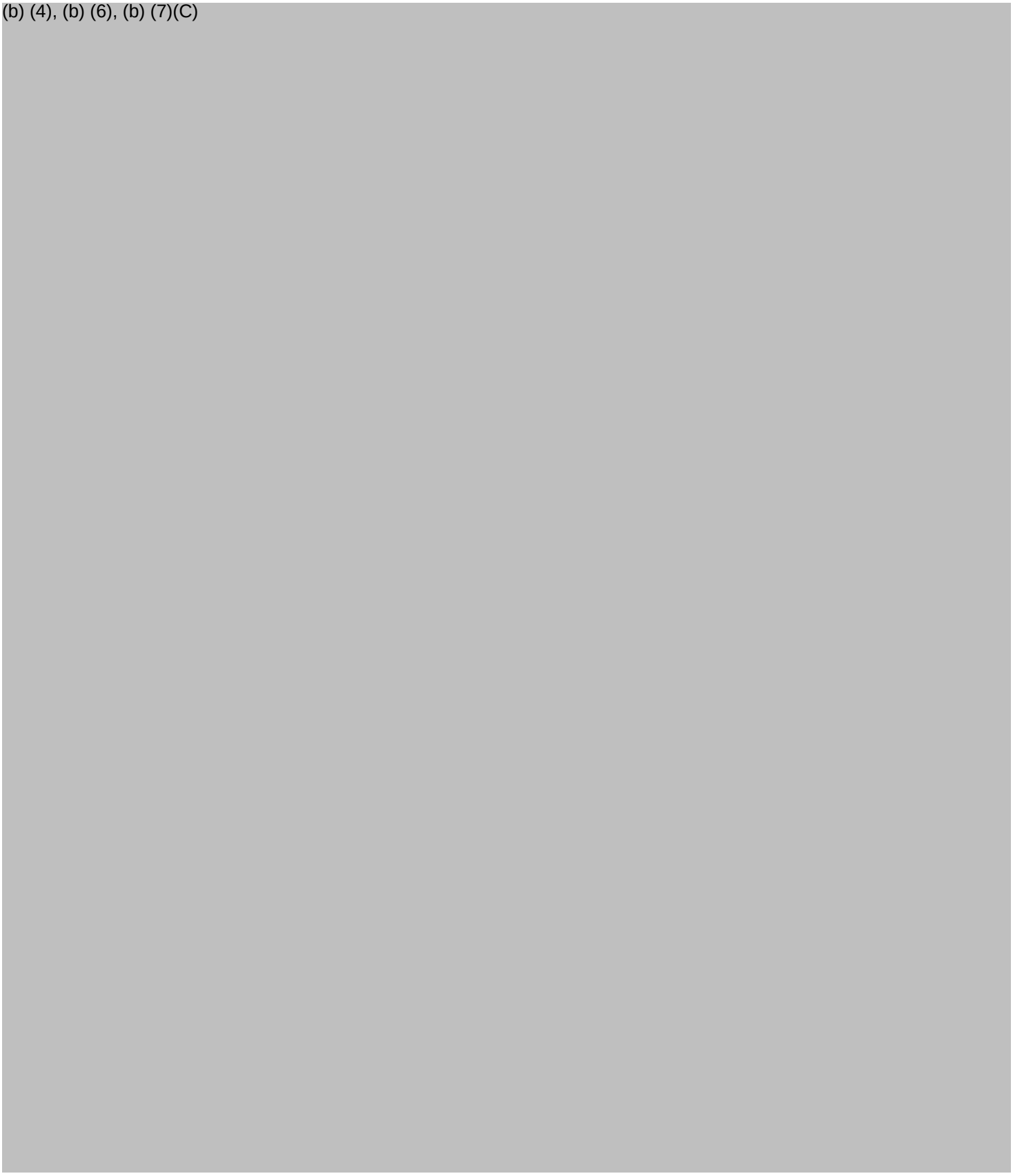
(b) (4), (b) (6), (b) (7)(C)



(b) (4), (b) (6), (b) (7)(C)



(b) (4), (b) (6), (b) (7)(C)



(b) (4), (b) (6), (b) (7)(C)

Equipment Maintenance/Calibration
(This section written by KRJ)
I reviewed Work order 1452715 for calibration of (b) (4) used during DS (b) (4) in (b) (4) This (b) (4) is calibrated every (b) (4) . The (b) (4) passed calibration without adjustment. This work order was completed on 01/26/2021. No objectionable observations were identified.

Calibration Program

(This section written by KRJ)

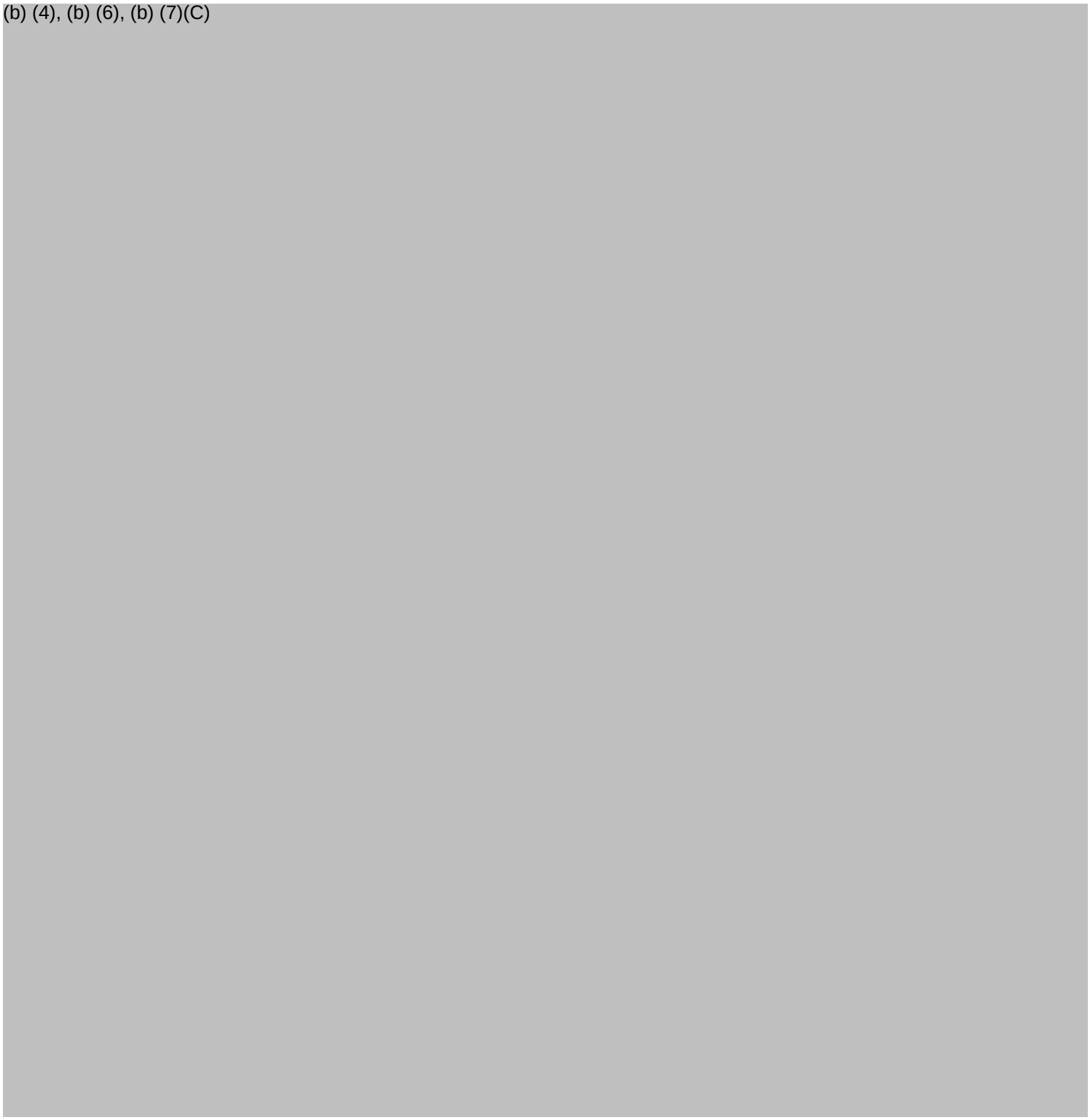
On 07/20/2021, I discussed calibration out of tolerance (OOT) procedures with (b) (6), (b) (7)(C) [redacted]. Per the Quality Agreement PGS is responsible for oversight of calibration and validation in (b) (4) We discussed (b) (4) effective 03/10/2021 (PGS); (b) (4) (b) (4) (b) (4) effective 04/16/2021(Pharm Sci); and (b) (4) (b) (4) (b) (4), effective 07/15/2020 (Global Workplace Solutions (laboratories)). Calibration OOT investigation process for GMP critical instruments is documented on the EAMS work order when the condition is first identified. The responsible person documents the investigation and sends it to Quality. Quality will either approve the investigation or will initiate a deviation. Laboratory calibration OOT are documented in the work order. The equipment owner is notified, corrective actions are implemented and recorded in the work order, work order is approved by a secondary reviewer, and equipment owner performs an impact assessment and routes for quality approval. No objectionable observations were identified.

Equipment Cleaning Validation

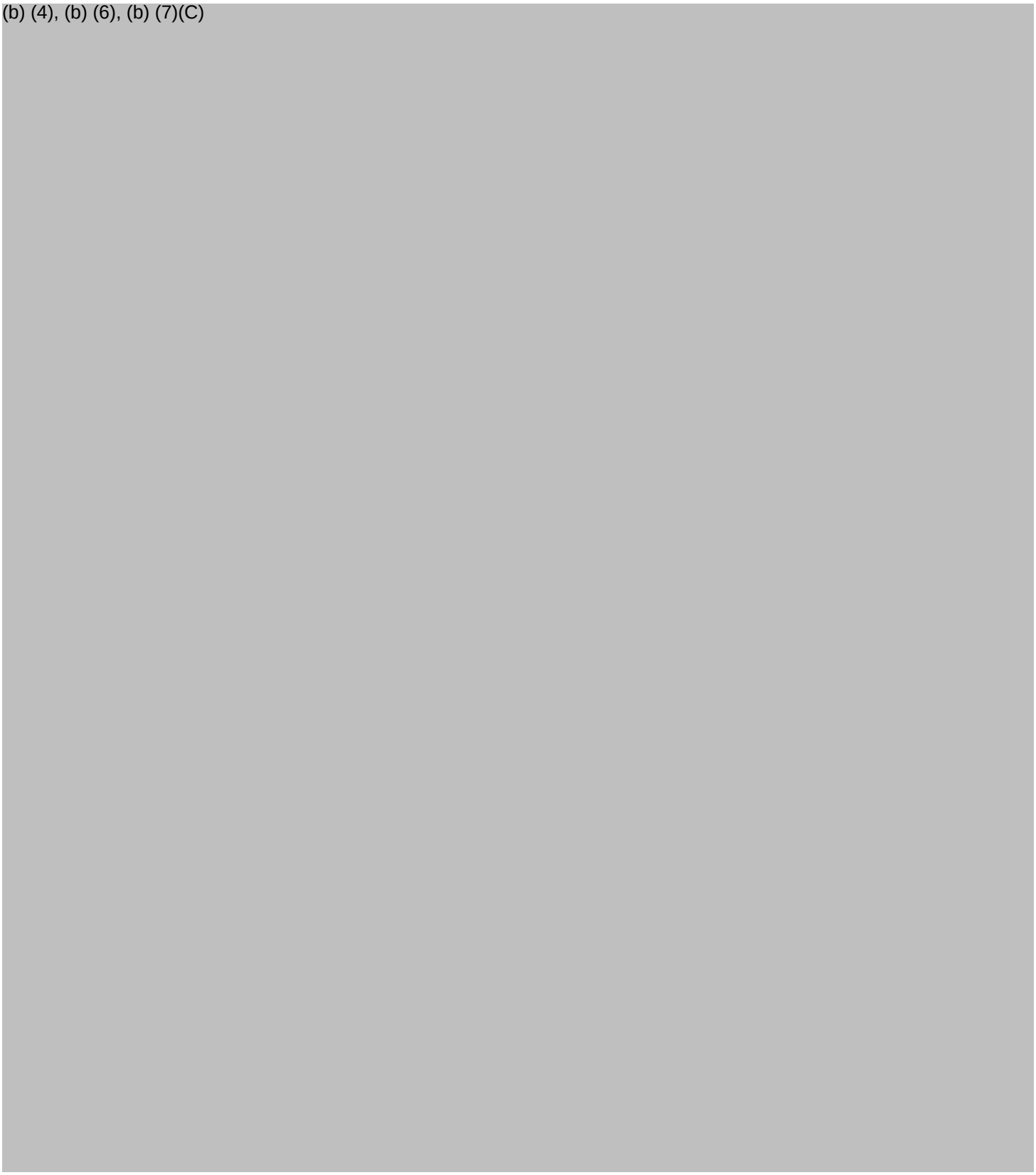
(This section written by KRJ)

(b) (4), (b) (6), (b) (7)(C) [redacted]

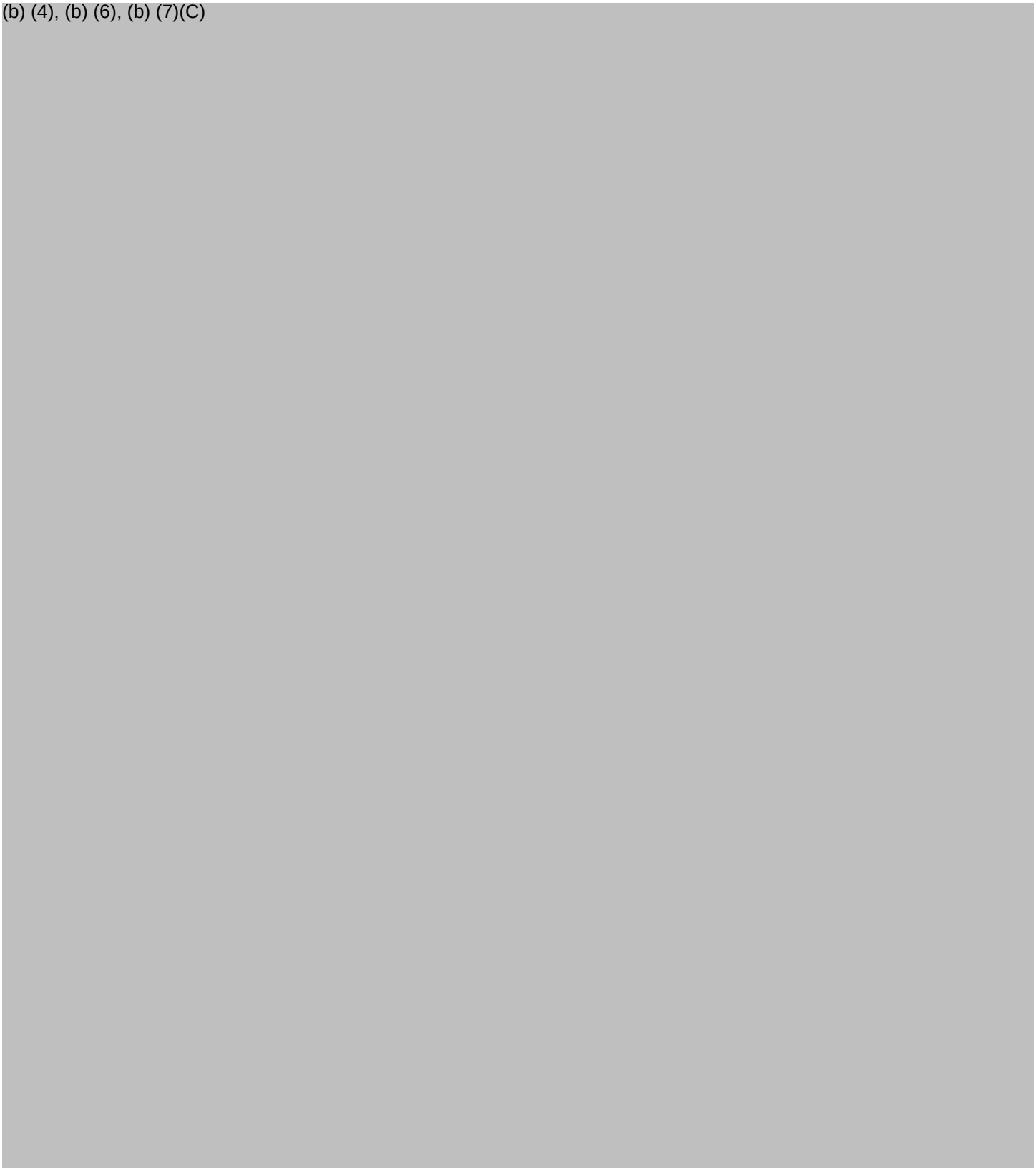
(b) (4), (b) (6), (b) (7)(C)



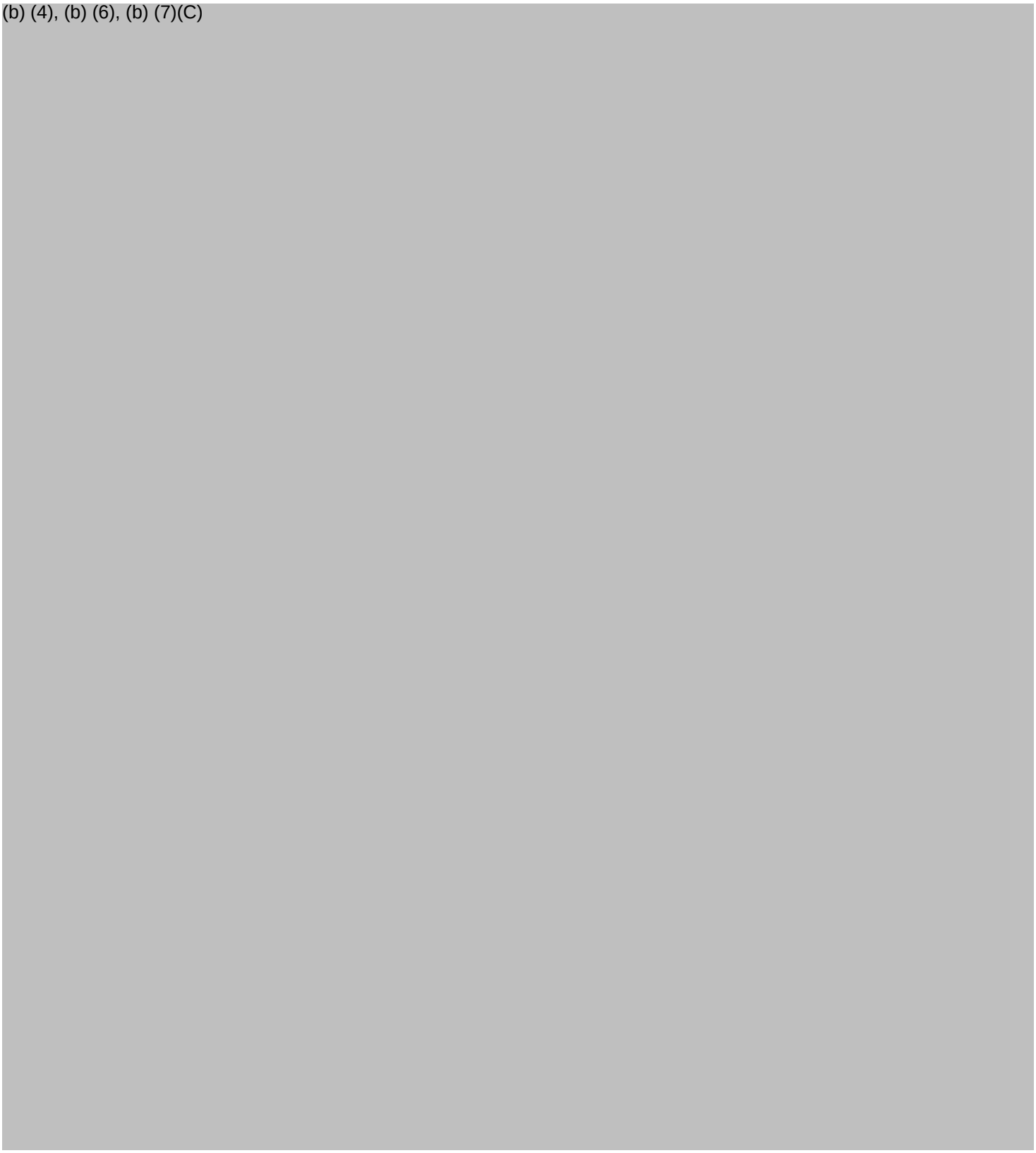
(b) (4), (b) (6), (b) (7)(C)



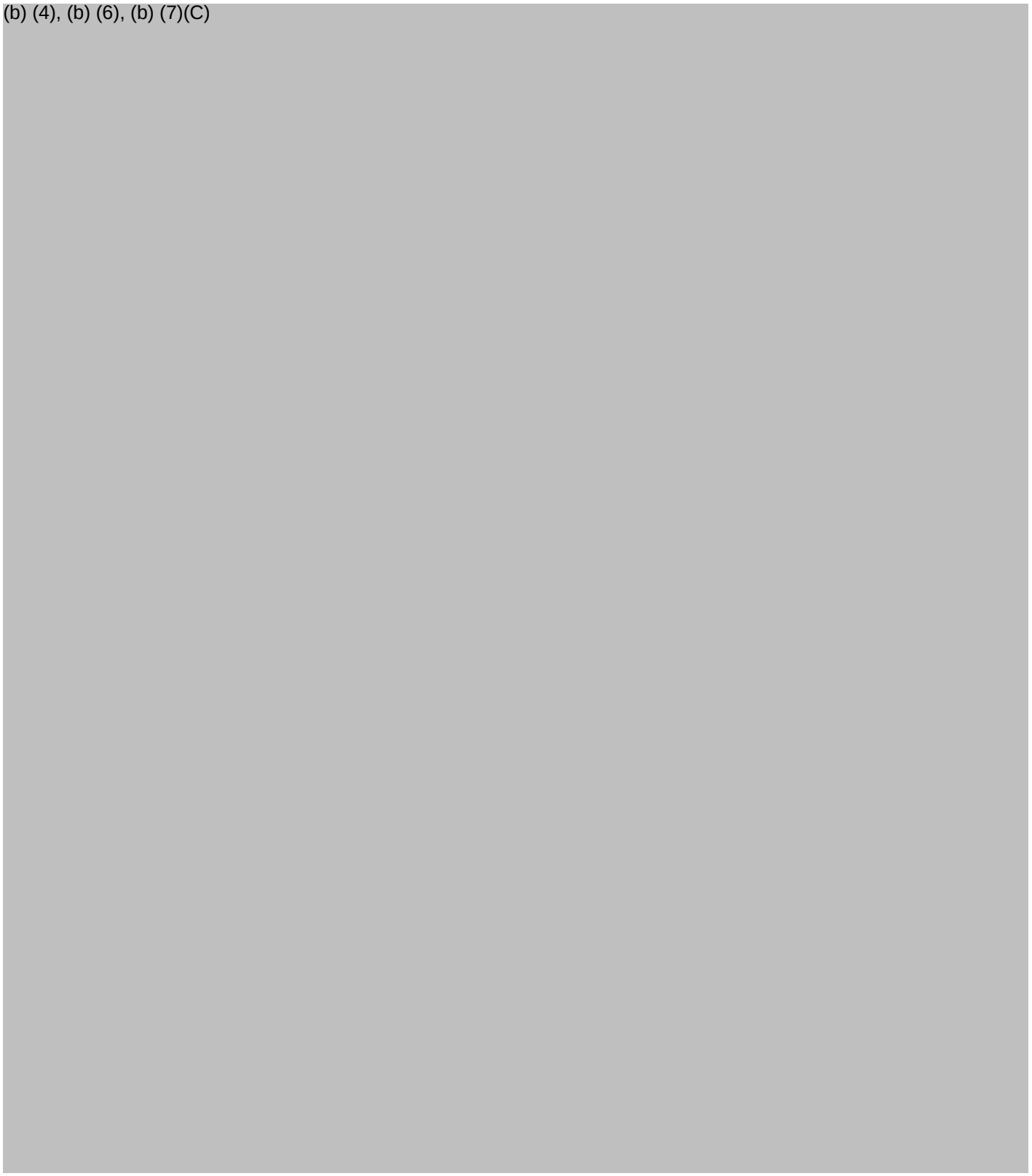
(b) (4), (b) (6), (b) (7)(C)



(b) (4), (b) (6), (b) (7)(C)



(b) (4), (b) (6), (b) (7)(C)



(b) (4)

Waste

(This section written by DME)

The procedure for the flow and removal of waste in Building (b) (4) ((b) (4) was reviewed without comment. The procedure: (b) (4) (b) (4), effective 6/25/2021, was reviewed along with schematics for the flow of waste without comment. Building (b) (4) is a multi-product/multi-host GMP clinical manufacturing building. The following waste products exist in Building (b) (4)
(b) (4)

Specific waste from (b) (4) (b) (4)

The procedure for the flow and removal of waste in Building (b) (4) (including (b) (4) (b) (4) was reviewed without comment. Procedure: (b) (4) (b) (4) effective 4/7/2021, was reviewed along with schematics for the flow of waste without comment. Building (b) (4) is a multi-product commercial manufacturing building.

MATERIALS SYSTEM

Material Control

(This section written by EA)

I discussed single use material management as it relates to DS manufacture with (b) (6), (b) (7)(C), and (b) (6), (b) (7)(C). Receiving of raw materials is proceduralized in (b) (4) (b) (4) effective 07/21/2021. Briefly, before materials are (b) (4) See **Discussion Item EA-7** regarding lack of periodic sampling of incoming lots of product-contact materials (b) (4) suppliers.

Warehouse ((b) (4)

(This section written by DME)

I reviewed the procedure: (b) (4), effective 12/21/2020, (**Exhibit DME 1**) without comment. The procedure speaks to transfer of materials into the warehouse, storage of materials in the warehouse, the issuance of materials to process areas, handling of damaged or defective materials and includes a floor diagram for the (b) (4) warehouse (**Exhibit DME 1** p. 8) and a diagram of the room used for drug substance (b) (4) and shipping of materials and the associated walk-in units used for storage of drug substance (**Exhibit DME 1** p. 9).

On 7/19/2021, I met (b) (6), (b) (7)(C) (b) (6), (b) (7)(C), and he walked me through the receipt of materials, storage of incoming materials, and shipping out of drug substance. I observed a gap along the side of the mobile platform at the overhead shipping door, see FDA **Observation 12d** below for additional information.

Raw Materials

(This section written by DME)

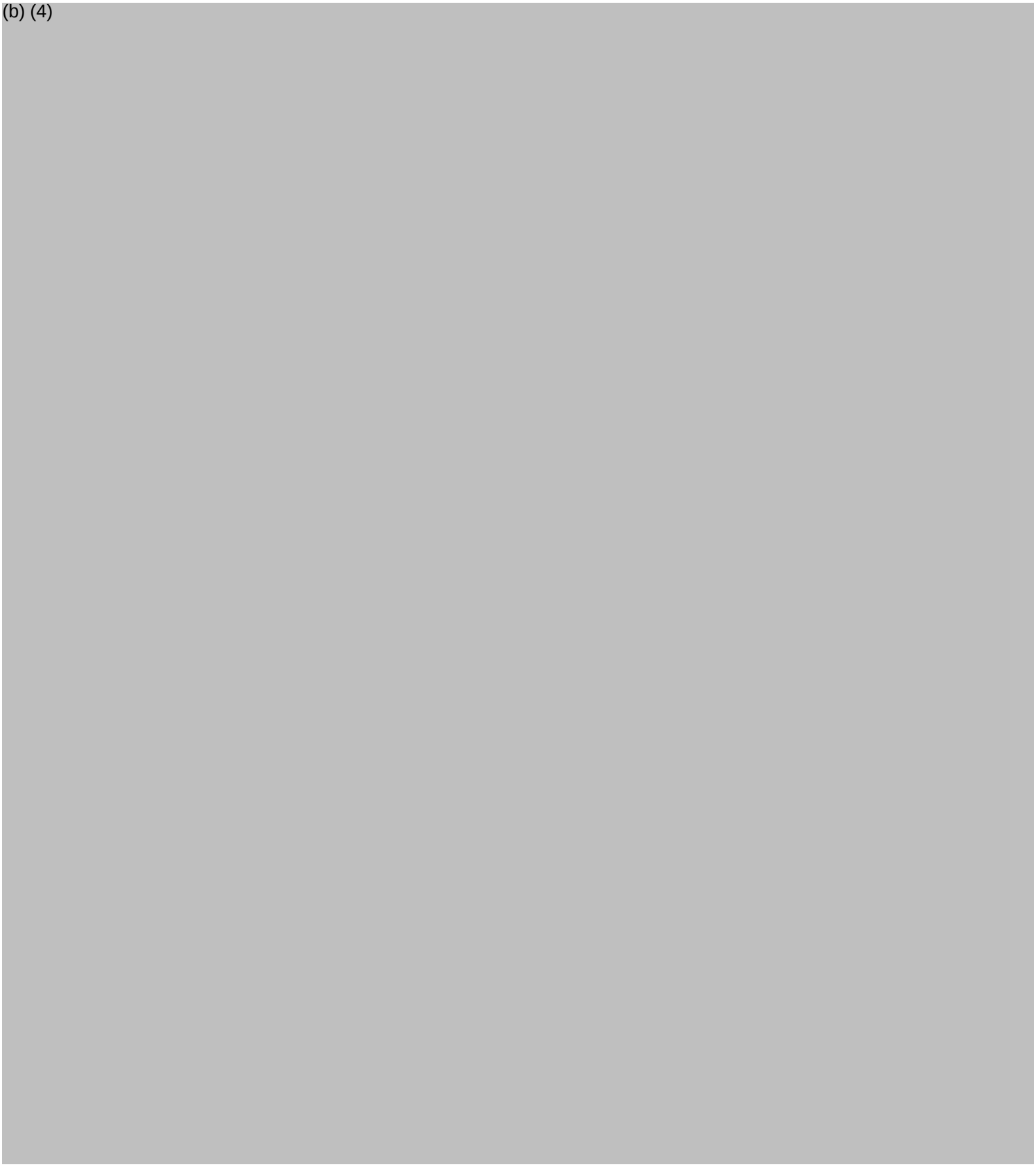
On 7/22/2021, I observed operator (b) (6), (b) (7)(C) (b) (6), (b) (7)(C), performing (b) (4) operations for (b) (4) solutions that will be used in the manufacture of the BNT162b2 drug substance. (b) (6), (b) (7)(C) was observed opening a new container of (b) (4). He (b) (4) the material into a (b) (4). The (b) (4) is connected to the (b) (4) system that contains the

(b) (4) . (b) (6), (b) (7)(C) explained that he calculates the amount of (b) (4) (b) (6), (b) (7)(C) explained the calculation is (b) (4) . (b) (4), (b) (7)(C) brought in a container with the wrong lot code and (b) (6), (b) (7)(C) , retrieved another container with the same lot code. The container that (b) (6), (b) (7)(C) retrieved was partially opened. (b) (6), (b) (7)(C) took the cover off the container, opened the (b) (4) and began adding (b) (4) There was no documentation on the container to identify that it had been opened or when, see FDA **Observation #13** for additional details.

I looked into the large pass thru on the wall of the (b) (4) area and residue was observed along the sided and bottom of the pass thru, see FDA **Observation 12c** for additional details.

(b) (4)

(b) (4)



(b) (4)

(b) (4), (b) (6), (b) (7)(C)

Changeover
(This section written by KRJ)
I discussed (b) (4)
(b) (4)
(b) (4)
effective 03/31/2021 with (b) (6), (b) (7)(C)
on 07/20/2021. I was told that an area can be
(b) (4)

(b) (4) No objectionable observations were identified.

I discussed (b) (4) shutdown and new product introduction on 7/22/2021 with (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C). We broadly discussed (b) (4) (b) (4) effective 03/23/2020; (b) (4) (b) (4) effective 03/04/2021; and (b) (4) (b) (4), effective 12/16/2020. I was told that an area can be (b) (4) No objectionable observations were identified.

(This section written by EA)

I discussed line clearance and changeover procedures for (b) (4) (b) (4) with Paige Persky. Ms. Persky stated that changeover was only required for multiproduct manufacture and line clearance was not proceduralized, but rather MBR-driven. I reviewed line clearance documentation in the following batch records:

(b) (4)

It was noted that (b) (4) does not document area clearance. Ms. Persky explained that (b) (4). Other MBRs document removal of previous batch-specific documentation, samples, and solutions prior to the respective operations, but not upon their completion. Verification of waste removal is not documented. I (EA) explained that it is typical and advisable to perform line clearance before and after the operation to provide additional assurance.

Computerized Systems

(This section written by DME)

Pfizer utilizes (b) (4) systems in the manufacture of BNT162b2 drug substance which includes (but not limited to) the (b) (4) and the (b) (4) processes. In (b) (4) (b) (4) the (b) (4) is used to perform these operations. In Building (b) (4) ((b) (4)), the (b) (4) system is used to perform these operations.

It was explained that for the (b) (4) process, there are (b) (4) which can be performed either (b) (4) . The target for each (b) (4) . It was explained that if (b) (4) process to account for the discrepancy. Pfizer staff provided a list of all deviations associated with the (b) (4) (**Exhibit DME 7**). There were 7 deviations in Building (b) (4) ((b) (4)) and 3 deviations in (b) (4) (b) (4) It was explained by Pfizer staff that the process validation batches included (b) (4) Some of the deviations are discussed below:

Building (b) (4) ((b) (4)):

- Deviation (b) (4) (**Exhibit DME 8**) was opened for lot (b) (4) , when the volume of the (b) (4) It was explained by (b) (6), (b) (7)(C) , that there was a download which created a glitch in the system and the (b) (4) was not connecting to the logic communication. As the (b) (4) was above the control limits, the decision was made to change from (b) (4) When I reviewed the batch record, there is documentation for (b) (4) (**Exhibit DME 9 p. 17**). There is no (b) (4) printout in the batch record from (b) (4) to document that the (b) (4) was given through (b) (4) . There is no documentation in the batch record that the (b) (4) was given via (b) (4) . I asked (b) (6), (b) (7)(C) why the operators did not document the events in the batch record, and he said because it is documented in the deviation (**Exhibit DME 8 p. 4**). I asked how Quality would be aware that the (b) (4) even though the batch record has (b) (4) listed and (b) (6), (b) (7)(C) stated that Quality would be aware from the deviation. Release testing indicated no impact to (b) (4) . The batch record was reviewed by manufacturing and quality (**Exhibit DME 9 p. 21-22**).

- Deviation (b) (4) (**Exhibit DME 10**) was opened for lot (b) (4) when the (b) (4) did not begin as planned because the (b) (4) . When the operator realized the issue, the operator switched the (b) (4) began. However, due to timing for the (b) (4) The issue was found to be the (b) (4) mode and should have been set on (b) (4) when running on the (b) (4) When I reviewed the batch record, there is documentation for (b) (4)

(**Exhibit DME 11 p. 12**). There is no (b) (4) printout in the batch record from (b) (4) to document that the (b) (4) was given through (b) (4). There is no documentation in the batch record that the (b) (4) was given via (b) (4). As a corrective action, they added a step in the batch record to ensure that the operators program the (b) (4) correctly. The batch record was reviewed by manufacturing and quality (**Exhibit DME 11 p. 16-17**).

- Deviation (b) (4) (**Exhibit DME 12**) was opened for lot (b) (4) when (b) (4) was (b) (4) and an (b) (4) was given. The (b) (4) time frame. I asked (b) (6), (b) (7)(C) if the process validation exceeded the (b) (4) timeframe for (b) (4) and he said no. I asked if the process validation included (b) (4) and he said no. When I reviewed the batch record, there is documentation for the (b) (4) (**Exhibit DME 13 p. 126**). However, there is no documentation in the batch record for the time taken to administer (b) (4). I asked why and (b) (6), (b) (7)(C), stated that it can be seen in the (b) (4). This data for (b) (4) is not on the (b) (4) printout provided by (b) (6), (b) (7)(C) (**Exhibit DME 13 p. 126**). In addition, when the operator changes from (b) (4), they need to set the (b) (4). This information is not documented in the batch record. In talking with (b) (6), (b) (7)(C), I stated that there are insufficient details in the batch record for the critical process parameters defined by the firm. The batch record was reviewed by manufacturing and quality (**Exhibit DME 13 p. 99-100**). The batch met release specifications. The lot was released for use under the EUA on 3/18/2021 **(Exhibit DME 14**).

- Deviation (b) (4) (**Exhibit DME 15**) was opened on (b) (4) after staff realized that the time for the (b) (4) was incorrect in the batch record. The parameter in the batch record was documented as (b) (4) (**Exhibit DME 16 p. 75**). A review of all batch records was performed and (b) (4), was found to have a deviation in the (b) (4) time. All (b) (4) (**Exhibit DME 16 p. 75**). This record was reviewed by Operations and QA (**Exhibit DME 16 p. 97 -98**). See **Observation #2c** for additional details.

(b) (4) (b) (4)

- Deviation (b) (4) was opened for (b) (4) (which became DS lot (b) (4) as (b) (4) did not meet the control limits. The operators added a (b) (4) into the control limit, but this addition did not account for

the (b) (4) that was missing between (b) (4). I asked why the operators did not add the (b) (4) as (b) (4) and no answer was provided. It was explained that as the (b) (4) did not meet the target because the (b) (4) with the (b) (4) was (b) (4). The corrective action was to (b) (4) the (b) (4). I asked if there was an investigation with documented impact and (b) (6), (b) (7)(C) said no. The lot was interim released on (b) (4) to (b) (4) and the full release occurred (b) (4). When I asked (b) (6), (b) (7)(C) if the lot was placed on stability, she explained that stability is not part of the release program. The lot was placed on stability on 7/22/2021. The firm determined no product impact as all data is within acceptance criteria. The batch is only allowed to be distributed in the US and Canada. See **FDA Observation #1** for additional details.

- Deviation (b) (4) was opened when the (b) (4) (b) (4) was exceeded. The (b) (4) was within the control limits. It was determined that the (b) (4) was (b) (4) because the (b) (4) system had not been cleared from the deviation discussed above (where too little of a (b) (4) was given for (b) (4). An emergency change control (b) (4) was opened to correct the code in the (b) (4) system to reset the parameters for each new batch. I asked if they notified the staff working in the (b) (4) building about the code issue with (b) (4) and I was told no. (b) (6), (b) (7)(C), checked the (b) (4) system and confirmed that the (b) (4) is set to clear before beginning a new batch, therefore this error would not occur in the (b) (4) building.

- Deviation (b) (4) (**Exhibit DME 18**) was opened for BNT162b2 drug substance lot (b) (4) (**Exhibit DME 19**), as the (b) (4), and the operator switched from (b) (4). The operators performed a calculation for (b) (4) and this calculation is not recorded in the batch record. I asked Paige Persky, Manager of Drug Product Manufacturing, why the calculation for (b) (4) is not in the batch record and she stated that per their documentation procedures, the operators should have recorded the calculation for the (b) (4). The (b) (4) printout from the (b) (4) system documents (b) (4) (**Exhibit DME 19 p. 54-56**) yet the batch record documents (b) (4) (**Exhibit DME 19 p. 22-33**). I asked Ms. Persky why there are (b) (4) recorded under the (b) (4) as well as (b) (4) and she said that she cannot speak to this. The record was reviewed and approved by QA on (b) (4) (**Exhibit DME 19 p. 47**). See **Observation 2b** for additional details.

Gowning

(This section written by DME)

Building (b) (4)

The procedure: (b) (4) effective 12/30/2020, was reviewed without comment. This procedure provides gowning and de-gowning requirements for all personnel and visitors entering and exiting (b) (4) Manufacturing Areas at the Pfizer Andover, MA facility; and it describes the pathways for personnel, equipment, and materials that are entering moving through, and exiting (b) (4) manufacturing area at the Pfizer Andover, MA facility. Personnel are to wear safety glasses, hair cover, beard cover (if applicable), face mask, plant shoes or shoe covers, high density polyester (HDP) coverall is worn over street clothes, gloves with sanitization, and a bump cap. I spoke with (b) (6), (b) (7)(C) (b) (6), (b) (7)(C) about the gowning process on 7/22/2021. She confirmed that there is training for gowning which includes a performance assessment by a qualified trainer. She explained that the operators are qualified by ensuring that the staff can perform the gowning independently and this is documented in skills check.

Building (b) (4)

The document: (b) (4) (b) (4) effective 1/4/2019, was reviewed without comment. This procedure defines the process for gowning required of personnel flowing into, out of, and throughout the Clean Environmental Areas (CEA) within the (b) (4) (b) (4) during production and facility non-production periods. All personnel enter either the Women's or Men's locker room, wash their hands and apply covers over their street shoes. Then they remove all outer street clothes and change into plant provided blue scrubs. Staff wear plant dedicated shoes (which are changed (b) (4) and visitors wear their shoes with covers. Then safety glasses, masks, head covers, beard covers (if applicable), and disinfection of hands occurs. This gowning allows access to the controlled non classified areas. To enter (b) (4) (b) (4) media prep or buffer prep (where BNT162b2 is manufactured), a frock is added with shoe covers, and gloves with sanitization. The gowning was confirmed upon entry into the (b) (4) areas. I spoke with (b) (6), (b) (7)(C), about the gowning process on 7/22/2021. She confirmed that there is training for gowning which includes a performance assessment by a qualified trainer. She explained that the operators are qualified by ensuring that the staff can perform the gowning independently and this is documented in a skills check.

LABORATORY CONTROL SYSTEM

Laboratory Investigation (Out of Specification (OOS), Out of Limit (OOL), and Questionable Result (QR))

(This section written by KRJ)

On 07/20/2021 I discussed compressed laboratory investigations with the following people:

- (b) (6), (b) (7)(C)
-
-
-
-
-
-

Laboratory investigations (LIR) include out of specification (OOS), out of limit (OOL), and questionable results (QR). OOS applies to release specifications excursions in PGS and any filed specification, including in-process action limit excursions in Pharm Sci. OOL includes alert limit excursion in PGS or target limit excursion in Pharm Sci. QRs applies to any questionable result, especially in comparison to historical data. We discussed (b) (4) (b) (4) effective 03/24/2021 (PGS), and (b) (4) effective 04/20/2020 (Pharm Sci). All OOS, OOL, or QRs must be documented and notification to management needs to be initiated if applicable within (b) (4) of discovery. Records should be closed within (b) (4) days from date of discovery, and if records exceed (b) (4) timeline, an interim report shall be issued prior to the (b) (4) due date. PGS has a category for Readily Apparent Assignable Cause (RAAC). Examples of RAAC are incorrectly executed test method, instrument failure during a run, or standard curve failure. In the case of a RAAC, the original result is invalidated, and a repeat test is performed. QTS RAAC-LIR are approved by the lab manager and site quality authority. LIR workflow include initial investigation, investigation measurements protocol (IMP), further analysis, retest, and conclusion. Retesting can be performed once QA concurs. Retest protocol followed per procedures (b) (4) replicates for PGS and (b) (4) replicates for Pharm Sci). During the LIR conclusion, the scope is reassessed following determination of root cause, review for trends, and any applicable CAPAs are implemented. If the assignable cause is not lab related, a MIR/QAR must be opened. A MIR/QAR may be opened with QA concurrence at any stage of the LIR if there is concern the assignable cause is not a laboratory error. LIR and RAAC-LIRs are trended at least (b) (4) . No objectionable observations were identified.

Review of OOS Investigations

(This section written by AC)

More than 40 product- or process-related deviations were reviewed by Inspector Cheung. Majority of them were adequately addressed and appropriate CAPAs were implemented if

necessary. A few deviations were discussed more extensively with the firm and are described below.

1. QAR (b) (4) was created on (b) (4) regarding to a batch (b) (4) that had a (b) (4) at the (b) (4) stage. The recorded (b) (4) concentration was (b) (4) and the acceptable range is (b) (4) . The operator escalated the problem to area management and final decision was made to further process to (b) (4) . However, the (b) (4) of the final DS batch (b) (4) was (b) (4) which was outside the specification of (b) (4) , but the other DS release attributes including (b) (4) were all within specifications. The root cause of this deviation was due to the (b) (4) sample collection. The firm created a Change Request (6093257) to reprocess the DS batch (b) (4) and was governed per (b) (4) . As part of the reprocessing, they re-execute the (b) (4) of the DS lot. To perform these reprocessed steps, (b) (4) was documented to ensure that it was within the recommended time duration. During the inspection, only a portion of the release tests for this reprocessed batch (b) (4) were completed and the (b) (4) was within specification at (b) (4) . The reprocessed batch will have the original batch expiration date. The reprocessed DS batch and the corresponding formulated DP batches will be placed on stability to monitor product quality during long-term storage. The firm already enrolled (b) (4) on stability with a base date on July 19, 2021 and the first pull date will be on (b) (4) that is also the expiry date for (b) (4) . Pfizer put this reprocessed lot under quarantine in their warehouse and will wait for the full release results before making further decision. I did not identify issues of concerns for this deviation.
2. A total of four deviations related to the OOS of the (b) (4) in DS lots were created between May 24, 2021 and June 30, 2021. Two deviations (QAR (b) (4) and QAR (b) (4)) associated with DS batches (b) (4) ((b) (4) and (b) (4) ((b) (4) had confirmed OOS results, therefore the DS batches were discarded. No root cause was identified for the (b) (4) for the above (b) (4) investigations. After about a (b) (4), another two deviations for the OOS (b) (4) (LIR (b) (4) and LIR (b) (4)) associated with DS batches (b) (4) ((b) (4) (b) (4) ((b) (4) and (b) (4) ((b) (4) (b) (4) were raised, and the firm has an ongoing investigation. During the review on these deviations with (b) (6), (b) (7)(C) they shared that the (b) (4) was first observed in (b) (4) by the (b) (4) Process Verification program prior to any OOS results. Pfizer started a proactive meeting on May 26, 2021 to establish a clear problem definition and have a better

understanding on the process. As more data from the raw materials, operation parameters, and stability/validation data were collected, in addition, more deviations were created due to the (b) (4) OOS, the (b) (4) was confirmed, and the investigation was escalated to (b) (4) for further analysis and root cause identification. During the inspection, the firm has not identified any root cause, but they believe the raw materials may be the potential root cause. They are expediting the investigation effects to identify the root cause and implement solutions and control plan if necessary.

Sample Handling

(This section written by KRJ)

I reviewed a sampling handling presentation of samples from (b) (4) and (b) (4) to ARD laboratories. The general flow for chemical analysis samples is as follows:

(b) (4)

Sample flow from (b) (4) to ARD-MST (microbiology lab) is similar; only samples are delivered to sample port (b) (4), and either Sample Handling or MST lab personnel inspect the samples and retrieves the sample from the (b) (4) Samples from (b) (4) to PGS laboratories is as follows:

(b) (4)

The microbiology laboratory personnel run queries at least (b) (4) for time sensitive assays (b) (4)

I spoke with (b) (6), (b) (7)(C) PGS) and (b) (6), (b) (7)(C) PGS) on 7/22/2021 about sampling handling of DP samples. I

was told that Andover is not performing testing on drug product from Pfizer Manufacturing Belgium NV. (b) (4), (b) (4), effective 05/26/2021 defines what drug product testing will be performed from samples from Pharmacia & Upjohn Company LLC and Hospira Inc. Quality Control Biological Shipping and Receiving (QCBSR) receives shipment and examines it for damage. The container is opened, and the temperature monitoring device is stopped. The contents are compared against the invoice, packing list, and internal Pfizer form (b) (4). The temperature monitoring data reviewed and QSM is notified. QSM reviews (b) (4) and temperature monitoring data. QSM creates a lot in LIMS, generates labels, inspect vials, affix LIMS labs, transfer samples to appropriate laboratory chambers, and changes the location of samples in LIMS. No objectionable observations were identified.

Review of Analytical Methods for Drug Substance

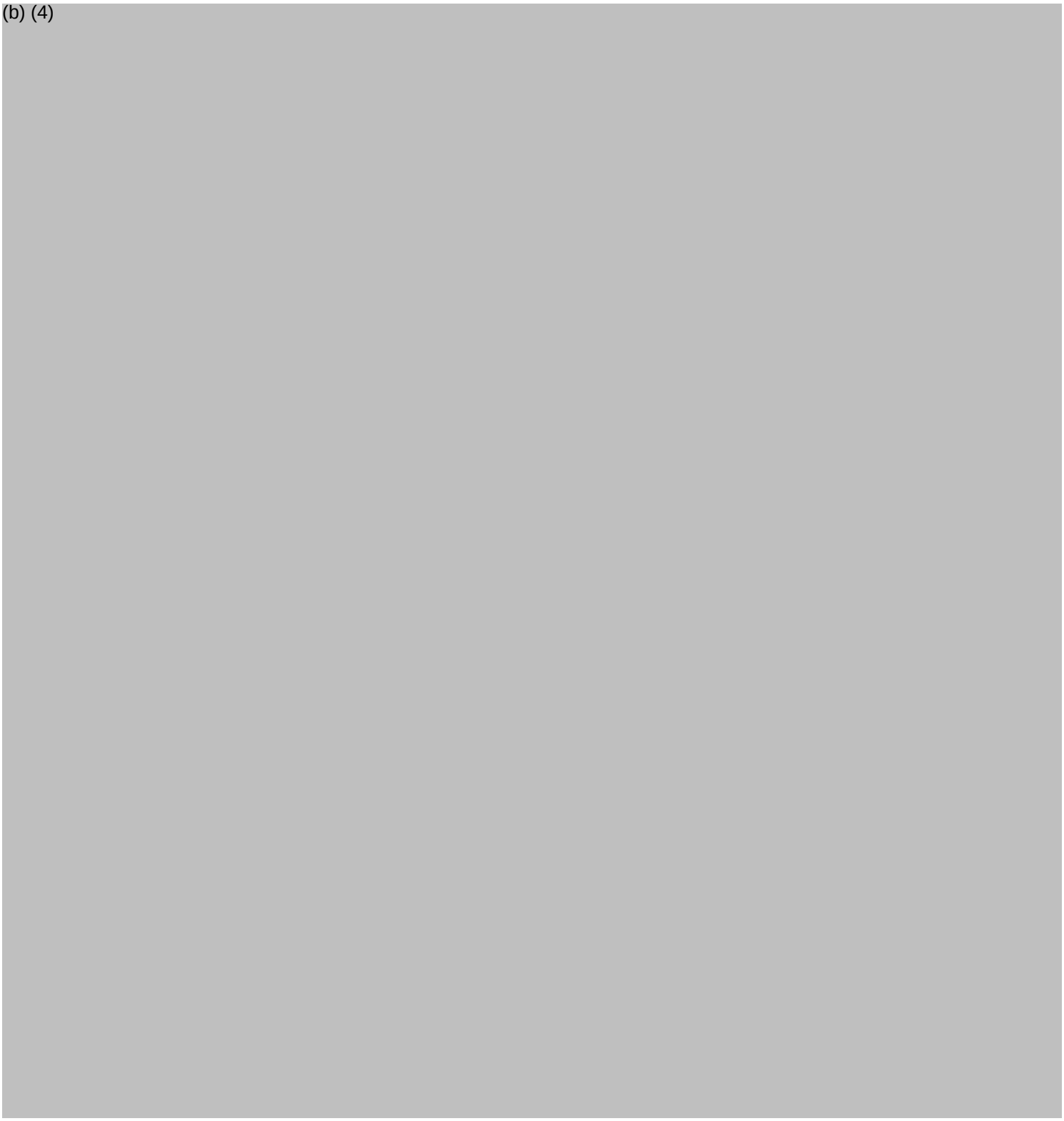
(This section written by AC)

Currently, all release and stability testing of DS lots manufactured at (b) (4) and (b) (4) (b) (4) are performed at either PharmSci or PGS analytical laboratory at Andover except the (b) (4) for DS lots manufactured at (b) (4) (**Exhibit AC-6**). However, the firm stated that all these analytical assays will be performed only at PGS-Andover eventually and the transition date will be in the (b) (4) of this year. The approach of transferring the analytical assays from PharmSci to PGS is based on data generated either from the co-validation/qualification studies or method transfer exercise.

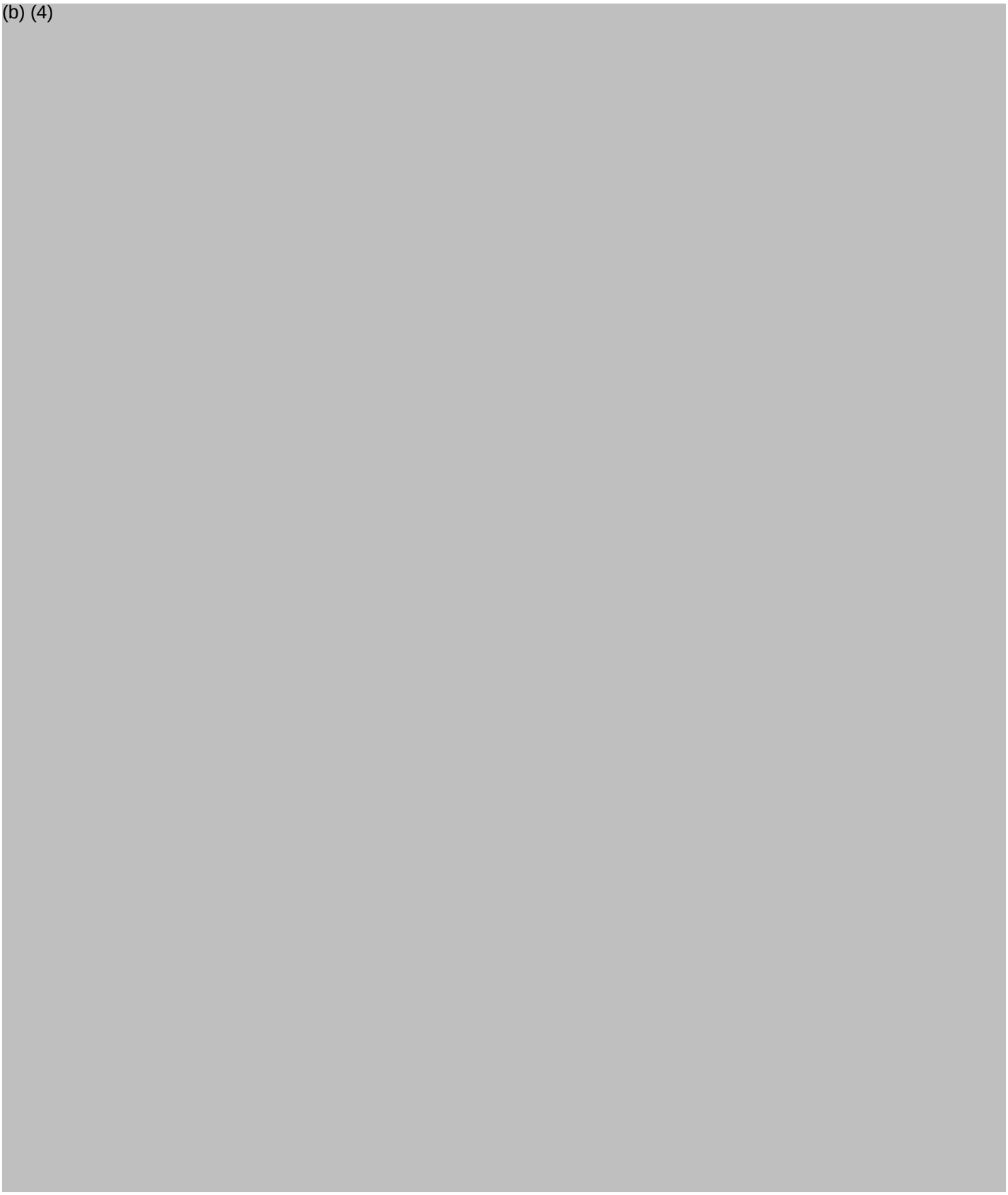
During review of the (b) (4) assay validation report, I found that no data was generated to validate the assay range. (b) (6), (b) (7)(C) reminded me that (b) (4) is a limit test, and the specification is (b) (4), so the assay range is not required to be validated. However, an absolute percentage of (b) (4) was reported on the CoA of each DP batch. I discussed with SMEs that if a quantitative % is being reported rather than a positive/negative result, data to validate the assay range is needed to support that the quantitative % reported on the CoA is accurate. (b) (6), (b) (7)(C) explained that this assay had been validated for multiple times and they may have data to define the linear range. On July 21, 2021 (b) (6), (b) (7)(C) presented validation reports for the (b) (4) assay from (b) (4) different analytical laboratories: (b) (4), and the data from these studies support that concentrations at (b) (4) is the lowest concentration that meets (b) (4) linearity criteria.

(b) (4), (b) (6), (b) (7)(C)

(b) (4)



(b) (4)



(b) (4)

Tour of the QC Chemical Laboratory

(This section written by AC)

(b) (6), (b) (7)(C) accompanied me on the tour of the Bioassay laboratory located in Building 1 room (b) (4) on July 19, 2021. The analytical assay that I observed was (b) (4) assay. This is an assay to (b) (4) for BNT162b2 DP. The entire assay takes (b) (4) to complete, and I only observed the initial sample preparation step. The operator (b) (4) .

(b) (6), (b) (7)(C) showed me the raw data generated by the (b) (4) and demonstrated how the software performing the data analysis. The negative control (b) (4), positive control ((b) (4) and test samples were run (b) (4). For a (b) (4)

The technician is responsible to create the (b) (4) assay record under (b) (4) (b) (4)

(b) (4) . I did not identify issues of concerns regarding the execution of the assay and analyses of the raw data.

Tour of Microbiology Laboratories

ARD Micro Laboratory:

(This section written by DME)

On 7/19/2021, I inspected the ARD microbiology laboratory. I inspected the storage area for incoming samples. There are (b) (4) one is used for bioburden testing of (b) (4) and one is used for bioburden testing of (b) (4) product samples. The firm uses a (b) (4) to test (b) (4) samples for (b) (4). This laboratory has (b) (4) areas identified for (b) (4). During the inspection, (b) (4) stations were empty, and an operator was observed to be (b) (4) in an area marked (b) (4) ". I asked why the operator (b) (6), (b) (7)(C) was (b) (4) in the area marked (b) (4) " and (b) (6), (b) (7)(C) , stated that the other (b) (4) stations were being used earlier today so the analyst used a different area. I observed (b) (6), (b) (7)(C) (b) (4) . These (b) (4) were for new lots of (b) (4)

Environmental (b) (4) are (b) (4) . (b) (6), (b) (7)(C) explained that the (b) (4) is the primary equipment used for identification of organisms. If the (b) (4) is unsuccessful in generating an identification, then the (b) (4) is used. The (b) (4) is currently out of service as it is being upgraded to (b) (4)

GMP Micro Laboratory

(This section written by DME)

On 7/19/2021, I inspected the GMP microbiology laboratory. I inspected the refrigerated storage area (b) (4) for incoming samples. There is a refrigerator in the laboratory that is used (b) (4) (b) (6), (b) (7)(C) , explained the (b) (4) are stored in case an investigation is needed. The laboratory is currently qualifying a (b) (4) identification. Freezer (b) (4) is used to store (b) (4) reagents. Freezer (b) (4)) is used to store (b) (4) reagents. The stability samples for drug substance are stored in (b) (4) Pfizer Kalamazoo is responsible for the stability samples and stability program for drug product. However, some samples are sent to Pfizer Andover for stability testing.

I observed (b) (6), (b) (7)(C) performing a (b) (4) It was explained that the (b) (4) method was being concurrently validated. I observed the analyst touch the (b) (4) . I asked why the analyst was touching the (b) (4) and (b) (6), (b) (7)(C) , explained that this is a (b) (4) (b) (6), (b) (7)(C) , explained that the analyst is (b) (4) and that the analysts implemented this type of (b) (4) to allow the material to (b) (4) . I was provided a printout for the (b) (4) samples processed by the analyst on 7/19/2021 (**Exhibit DME 3**). I reviewed the following procedures: (b) (4) effective 6/9/2021 (**Exhibit DME 4**); and (b) (4) (b) (4) (b) (4) effective 6/23/2021 (**Exhibit DME 5**) and both were silent as to the (b) (4) by the analyst observed on 7/19/2021. (b) (6), (b) (7)(C) explained later during the inspection that she has spoken with the analysts performing the (b) (4) testing and they will revise the method to have the analyst consult management for issues during (b) (4) testing, see Discussion Points with Management.

COMPLAINTS
(This section written by DME)
The firm's document: (b) (4) , (b) (4) effective 5/19/2021 was reviewed without comment. I discussed the complaint process with (b) (6), (b) (7)(C) . Complaints are received by Pfizer US Drug Safety Unit at 100 Route 206 N, Peapack, NJ 07977, and sent to Andover through the Pfizer Quality Tracking System (QTS). (b) (6), (b) (7)(C) stated that since the last FDA inspection, Pfizer has received one request to perform an investigation as the result of a complaint.

Complaint parent document in QTS (b) (4) was received on 12/21/2020 for COVID drug product lot (b) (4) drug substance lot (b) (4) . A child record (b) (4) was opened for Pfizer Andover to perform a batch record review for COVID drug substance lot (b) (4) This investigation was reviewed and was uploaded into QTS once complete. No concerns noted.

ADVERSE EVENTS
(This section written by DME)
The firm's document: (b) (4) , (b) (4) , effective 5/19/2021 was reviewed without comment. I discussed the adverse

event process with (b) (6), (b) (7)(C). Adverse events are received by Pfizer US Drug Safety Unit at 100 Route 206 N, Peapack, NJ 07977, and sent to Andover through the Pfizer Quality Tracking System (QTS). (b) (6), (b) (7)(C) stated that since the last FDA inspection, Pfizer has not received any request to perform an investigation as the result of an adverse event. (b) (6), (b) (7)(C) (b) (6), (b) (7)(C) stated that this includes the COVID-19 vaccine (which is authorized under an EUA) as well as other commercial drug products manufactured onsite.

Reports of complaints and/or adverse events can be received through:

E-mail: USA.AEReporting@pfizer.com
Phone: 1(866) 635-8337 or 1(800) 438-1985
Website: https://www.pfizersafetyreporting.com

RECALL PROCEDURES

(This section written by DME)
The firm's procedure: (b) (4), effective 7/10/2019, was reviewed without comment. This document describes the process and procedures to be followed in determining and acting on a decision to execute a Market Action for distributed commercial product. The Market Action Coordination Committee (MACC) is responsible for determining the need for and executing a Market Action. A Market Action is a general reference embracing a potential product recall, market withdrawal, field correction, or Dear Healthcare Provider Letter. A Market Action also includes notification to authorities regarding remedial actions, urgent public health threats, corrective actions, and field safety notices. As part of the Market Action Procedure, a mock Market Action will be tested annually to confirm effectiveness of the program. If a Market Action has occurred in the past 12 months for the Pfizer Andover site, a mock Market Action is not required. There have been no Market Actions of biologic product to date.

OBJECTIONABLE CONDITIONS AND MANAGEMENT RESPONSE

Observations listed on form FDA 483

Below in bold type are the inspectional observations as they appear on the Form FDA 483. Beneath each observation is a discussion of the supporting evidence and relevance. Relevant discussions with Management are also included.

OBSERVATION 1

There is insufficient data to support product quality prior to the release of BNT162b2 drug substance (DS) batch (b) (4) manufactured at (b) (4) (b) (4) Pfizer Andover on (b) (4) (b) (4) (b) (4) was derived from (b) (4) batch (b) (4), and a deviation ((b) (4)) was initiated due to the multiple control limit excursions

during the (b) (4) of (b) (4). The (b) (4) were below the control limits and the (b) (4) between (b) (4) and overall (b) (4) (b) (4) both exceeded the control limits. The affected batch (b) (4) was manufactured with a process that deviated from the validated process parameters, and your firm planned to put this batch on stability to further assess product quality. However, DS batch (b) (4) was not put on stability until July 22, 2021. The affected DS batch was released on (b) (4) and formulated into (b) (4) drug product (DP) lots (b) (4) at (b) (4) on (b) (4). All three DP lots were released on (b) (4).

Supporting Evidence, Relevance, and Discussion with Management:
(Written by AC)
Deviation (b) (4)) was initiated on (b) (4) due to the multiple control limit excursions during the (b) (4) of DS batch (b) (4) ran on (b) (4). The (b) (4) [redacted]. CAPA (b) (4) was opened on (b) (4) to facilitate the enrollment of this batch into the stability program per Protocol (b) (4); however, (b) (4) has not been placed on stability as of July 22. CAPA (b) (4) was only executed on July 23, 2021 after the inspectors discussed the deviation with the firm (**Exhibit AC-8**). It is acceptable for the firm to release the affected DS batch (b) (4) for formulation based on the DS release data; however, the firm should place the affected batch on stability in a timely manner, so they will have data to support the degradation profile of the affected DS batch is not significantly different from the regular DS batches prior to the release of final DP batches (b) (4) on (b) (4) (**Exhibit AC-9**).

OBSERVATION 2

There is inadequate quality oversight in that:

a. **The electronic data/reports from (b) (4) associated with the (b) (4), and (b) (4) process used in the manufacture of BNT162b2 drug substance are not reviewed by Quality during batch record review or prior to batch release.**
b. **During processing of BNT162b2 drug substance lot (b) (4), the (b) (4) were (b) (4), and the operator switched from (b) (4) The operators performed a calculation for (b) (4), and this calculation is not recorded in the batch record. The (b) (4) printout from the (b) (4) system documents (b) (4) per (b) (4) yet the batch record documents (b) (4) were performed (b) (4). The record was reviewed and approved by QA on (b) (4).**
c. **BNT162b2 drug substance lot (b) (4) was manufactured in (b) (4). The record was reviewed by Operations in (b) (4) and by Quality on (b) (4). All (b) (4) were (b) (4). There was no notation in the batch record until (b) (4) that (b) (4) exceeded the allowable (b) (4).**

Supporting Evidence, Relevance, and Discussion with Management:
(Written by DME)

a. It was explained by (b) (6), (b) (7)(C), that the (b) (4) reports associated with the (b) (4) and the (b) (4) process are not reviewed by QA as they do not have access to the system to review this data. In addition, these reports are not always part of the batch record.

   It was explained by Paige Persky, Manager of Drug Product Manufacturing, that the (b) (4) printouts are not required to be part of the batch record. (b) (6), (b) (7)(C), stated that QA staff will access a computer terminal (b) (4) the manufacturing (b) (4) to review the data in (b) (4). I did not go to the terminal to confirm that QA does review this data. It is not known if this electronic review by QA is documented.

b. During processing of BNT162b2 drug substance lot (b) (4), the (b) (4), **Exhibit DME 19 p. 54-56**), and the operator switched from (b) (4) (**Exhibit DME 19 p. 22-33**). The operators performed a calculation for (b) (4) and this calculation is not recorded in the batch record. I asked Paige Persky,

Manager of Drug Product Manufacturing, why the calculation for (b) (4) is not in the batch record and she stated that per their documentation procedures, the operators should have recorded the calculation for the (b) (4). The (b) (4) printout from the (b) (4) system documents (b) (4) (**Exhibit DME 19 p. 54-56**) yet the batch record documents (b) (4) were performed (b) (4) (**Exhibit DME 19 p. 22-33**). I asked Ms. Persky why there are (b) (4) recorded under the (b) (4) as well as (b) (4) for (b) (4) and she said that she cannot speak to this. I spoke with (b) (6), (b) (7)(C), who stated that the (b) (4) system was running in the background while the (b) (4) were added. It was not fully explained why the (b) (4) documents (b) (4) (**Exhibit DME 19 p. 54-56**) and the (b) (4) (**Exhibit DME 19 p. 22-33**). The record was reviewed and approved by QA on 7/15/2021 (**Exhibit DME 19 p. 47**).

c. BNT162b2 drug substance lot (b) (4) was manufactured in (b) (4). The record was reviewed by Operations in (b) (4) (**Exhibit DME 16 p. 97**) and by Quality on (b) (4) (**Exhibit DME 16 p. 98**). All (b) (4) were (b) (4) (**Exhibit DME 16 p. 75**). There was no notation in the batch record until (b) (4) that (b) (4) exceeded the allowable (b) (4) of (b) (4) (**Exhibit DME 16 p. 75**). The batch record target was (b) (4) and the (b) (4) added was over (b) (4) (**Exhibit DME 16 p. 75**). I explained to Mr. Tucker and other management in the room that during the batch record review it should identify when allowable parameters have been exceeded. The batch was released by QA on (b) (4) (**Exhibit DME 17**). A memo dated 3/4/2021, was added to the deviation that there is no product impact as the batch met release specifications (**Exhibit DME 15 p. 5**).

During review of the (b) (4) deviations it was explained that the (b) (4) systems are validated. The validations associated with these systems was not reviewed. I asked if the data has been restored from the system to ensure it is accurate and it was explained that this was done as part of validation of the system but no restore has been performed since.

OBSERVATION 3

The following deviation investigations were found deficient. Deviation (b) (4), (b) (4) (b) (4) (COVID): (b) (4) (b) (4)) and (b) (4), (b) (4) (COVID): (b) (4) (b) (4) : (b) (4) was found in (b) (4)

(b) (4) during its visual inspection (b) (4) On both occasions the (b) (4) was cleaned and released into manufacture. No (b) (4) sampling of (b) (4) and no cleaning verification was performed or is required after re-cleaning.

Supporting Evidence, Relevance, and Discussion with Management:
(Written by EA)

There were two deviations opened for (b) (4) (b) (4) post cleaning (b) (4)

- (b) (4) "(b) (4) (b) (4) (COVID): (b) (4) (b) (4) " created (b) (4) (**Exhibit EA-32**)
- (b) (4) "(b) (4) (b) (4) (COVID): (b) (4) (b) (4) " created (b) (4) (**Exhibit EA-32**)

Investigations of these deviations were limited to (b) (4) to determine whether the (b) (4) ; no (b) (4) sampling was performed to ensure (b) (4) Per the deviation reports and my discussion with (b) (6), (b) (7)(C) , and (b) (6), (b) (7)(C) , the (b) (4) was recleaned, visually inspected with passing results, and released for manufacture. Visual inspection of the (b) (4) is performed per (b) (4) (b) (4) effective 04/23/2021 (**Exhibit EA-33;** also see **Discussion Item EA-1**). No cleaning verification (i.e., (b) (4) or product impact assessment was performed or is required for (b) (4) deviations.

OBSERVATION 4

Per (b) (4) cleaning validation has not been performed on the (b) (4) (Building (b) (4) (b) (4) The (b) (4) is stored in a (b) (4) and as a result, a (b) (4) trend occurred in (b) (4) ((b) (4)); noted by identification of (b) (4)

Supporting Evidence, Relevance, and Discussion with Management:
(Written by KRJ)
Per (b) (4) , effective 04/15/2021 (**Exhibit KRJ-07**), cleaning validation was not performed on the (b) (4) trend (seven incidences) in (b) (4) commissioning, (b) (4) samples occurred prior to the (b) (4) results of (b) (4) in October. The (b) (4) results for batches (b) (4) led the rejection of the (b) (4) batches (**Exhibit KRJ-08**).

I explained my observations to Mr. Tucker and other management in the room at the time. There were no additional discussions during the close.

OBSERVATION 5

Cleaning of reusable product-contact parts using (b) (4) is not validated. Cleaning verification of such parts is inadequate as it is limited to testing of (b) (4) . Verification of surface and final rinse (b) (4) testing is not performed routinely.

Supporting Evidence, Relevance, and Discussion with Management:

(Written by EA)

In (b) (4) (b) (4) is used for cleaning of a range of miscellaneous small product-contact parts (**Exhibit EA-36**). According to (b) (6), (b) (7)(C) , and as confirmed by others (see SMEs below), validation of (b) (4) process was not performed. Instead, cleaning verification on (b) (4) sample (visual inspection and (b) (4) per (b) (4) specification) is performed for each load per (b) (4) (b) (4) effective 07/14/2021 (**Exhibit EA-37**). (b) (4) testing of (b) (4) sample is performed (b) (4) per (b) (4) (b) (4) (b) (4) effective 03/31/2021 (**Exhibit EA-38**). No (b) (4) sampling was performed to verify cleaning effectiveness.

According to (b) (6), (b) (7)(C) the rationale for not validating (b) (4) was the (b) (4) nature of the process and associated high variability of the outcome. Developmental coupon studies were performed using the same materials, (b) (4) as soil and worst-case process parameters (b) (4) to determine dirty hold time for (b) (4) . Flat surface coupons do not present the same level of challenge for the cleaning process, and although cleaning verification rather than validation could be more suitable for a (b) (4) process, it is insufficient to perform (b) (4) testing only as it does not inform of (b) (4) or (b) (4)

(Written by KRJ)

(b) (4) (b) (4) , effective 07/16/2021 is used to (b) (4) clean small parts and hoses via (b) (4) in (b) (4) This SOP only requires visual inspection and testing for (b) (4) , and not (b) (4) . There is no cleaning validation performed on small parts and hoses in (b) (4) as this is a (b) (4) process and can be operator dependent. There are direct product contact small parts and hoses, that could contribute (b) (4) contamination to the drug substance if not appropriately monitored.

I explained my observations to Mr. Tucker and other management in the room at the time. There were no additional discussions during the close.

OBSERVATION 6

Cleaning efficacy studies are inadequate (Building (b) (4) (b) (4) in that the firm has not demonstrated consistent efficacy with (b) (4) and a contact time of (b) (4) (b) (4) ; (Building (b) (4) demonstrates efficacy on all surfaces, however, (b) (4) ; (Building (b) (4) (b) (4) (b) (4) demonstrates a lack of efficacy on all surfaces except (b) (4) with a contact time of (b) (4) .

Supporting Evidence, Relevance, and Discussion with Management:
(Written by KRJ)
(b) (4) , approved on 04/28/2021 (**Exhibit KRJ-10**) demonstrates that a (b) (4) is effective with a contact time of (b) (4) . (b) (4) , (b) (4) , effective 04/30/2015 (**Exhibit KRJ-11**) demonstrates that (b) (4) is not effective with a contact time of (b) (4) except on (b) (4) All disinfectants used are the same between PGS and (b) (4) These studies overlap on (b) (4) The (b) (4) that overlap between the (b) (4) studies include (b) (4) .

I explained my observations to Mr. Tucker and other management in the room at the time. There were no additional discussions during the close.

OBSERVATION 7

The ISO-(b) (4) are not monitored to ISO (b) (4) standards. Specifically,

- **a. (b) (4) monitoring is not routinely performed.**
- **b. (b) (4) monitoring limit is set a (b) (4) instead of (b) (4) .**
- **c. (b) (4) (Building (b) (4) (b) (4) (b) (4) (b) (4) is within an ISO (b) (4) room.**

Supporting Evidence, Relevance, and Discussion with Management:
(Written by KRJ)
I reviewed BLA section 3.2.A.1 for (b) (4) (**Exhibit KRJ-12**). It states that (b) (4) meet ISO (b) (4) standards and are used for critical operations. It includes (b) (4) and room backgrounds. On 7/22/2021, I was told by (b) (6), (b) (7)(C)

(b) (6), (b) (7)(C) that monitoring during critical operations did not include (b) (4) monitoring. (b) (6), (b) (7)(C) informed me on 7/23/2021 that (b) (4) (b) (4) (b) (4) effective 02/10/2021 is the only SOP governing monitoring of (b) (4) during critical operations. (b) (4) does not require (b) (4) monitoring.

I explained my observations to Mr. Tucker and other management in the room at the time. There were no additional discussions during the close.

OBSERVATION 8

Routine monitoring of the compressed air of Building (b) (4), (b) (4) does not adequately represent all points of use. Only (b) (4), specifically (b) (4) listed in (b) (4) (b) (4) (b) (4), are routinely monitored.

Supporting Evidence, Relevance, and Discussion with Management:
(Written by KRJ)
On 07/23/2021, I was told by (b) (6), (b) (7)(C) (b) (6), (b) (7)(C) that testing of the compressed air has never been performed on all (b) (4). That only (b) (4) were qualified and monitored, as these points are the (b) (4) of distribution and therefore representative. However, there is no data to support that these (b) (4) points are representative of all the (b) (4). Additionally, (b) (4) qualified and monitored are in ISO-(b) (4) rooms (**Exhibit KRJ-16**). There are (b) (4) located in ISO (b) (4) rooms (**Exhibits KRJ-14** and **KRJ-15**), which has different acceptance criteria based on the room classification.

I explained my observations to Mr. Tucker and other management in the room at the time. There were no additional discussions during the close.

OBSERVATION 9

The environmental program (EM) program in (b) (4) (b) (4) is deficient in ensuring that the cleanrooms are operating in a state of environmental control:

a. **No prospective EM performance qualification (PQ) of classified areas or PQ of (b) (4) was performed to ensure EM specifications in operation are met.**
b. **Routine monitoring of ISO (b) (4) area is performed on a (b) (4) basis.**
c. **During a walkthrough on 7/22/2021, the door to the Control Room (b) (4) was observed opened to manufacturing (b) (4) (b) (4) (ISO (b) (4) through the duration of the walkthrough. Room (b) (4) is classified as controlled not classified and is not monitored.**

Supporting Evidence, Relevance, and Discussion with Management:
(Written by EA)
No prospective EMPQ protocol or EMPQ report for (b) (4) (b) (4) was provided by the firm immediately upon request. According to (b) (6), (b) (7)(C) , and (b) (6), (b) (7)(C) , instead of following such protocol, EMPQ was performed based on (b) (4) (b) (4) effective 11/04/2020 **(Exhibit EA-14**). The SOP does not contain sufficient detail and provides only general EMPQ requirements. Furthermore, section 4.1.3.1 of the SOP states that EMPQ activities following suite modifications and new construction "will be run per protocol". The study report (b) (4) (b) (4) effective 07/23/2021 (**Exhibit EA-15**) was provided to me during the close-out of the inspection (see **Discussion Item EA-2**).

The initial EMPQ study summarized in the report was performed in December 2020, prior to installation of (b) (4) , which was qualified upon its installation by performing (b) (4) sampling on (b) (4) . Qualification of this (b) (4) under (b) (4) was not performed and no PQ report was generated. Instead, a printout of EM Trend Detail Report for this sampling location for the dates stated above was provided (**Exhibit EA-16).**

Routine environmental monitoring of (b) (4) (b) (4) is described in (b) (4) (b) (4) effective 05/12/2021 (**Exhibit EA-12**). Sampling of ISO areas are performed on a (b) (4) basis, which can fail to detect excursions impacting multiple lots of product manufactured in (b) (4) (b) (4) which is currently operating (b) (4) days a (b) (4) (see **Discussion Item EA-2**).

The SMEs referred to Table 2 of (b) (4) (**Exhibit EA-11**) to support sampling frequency. However, it is stated in the footnote of the table that "these recommendations do not apply to production areas for non-sterile products or other classified environments in which fully aseptic gowns are not donned". Aseptic gowning is not used in (b) (4) (b) (4) it was observed during the walkthrough on 7/22/2021 and confirmed by (b) (6), (b) (7)(C) , that street clothes are allowed underneath overalls in (b) (4)

Per (b) (4) (b) (4) (b) (4) effective 05/12/2021 (**Exhibit EA-12**), no routine EM is performed in Control Room/Storage (b) (4). (b) (6), (b) (7)(C), and (b) (6), (b) (7)(C), explained that the room is not monitored because it is Controlled Not Classified (CNC). Door between (b) (4) and (b) (4) (ISO (b) (4) was observed opened (i.e., not alarmed and with no pressure differential as would be required between rooms of different classification) throughout the walkthrough of the (b) (4) (b) (4)

OBSERVATION 10

On (b) (4) the HVAC supplying (b) (4) was shut down for preventive maintenance, which resulted in pressure differential of room (b) (4) to drop to (b) (4) relative to the outside non-controlled non-classified corridor at 2:25 AM. The room was not cleaned until (b) (4) and environmental monitoring (EM) of the room was not performed to ensure that the room returned to ISO (b) (4) state until (b) (4). Between (b) (4) the room was used for processing of drug substance batches (b) (4) all of which were processed into drug product and released to US and international markets.

Clean status of the room is not verified or documented in the batch record. The firm allows up to (b) (4) of HVAC shutdown time until an additional cleaning needs to be performed. There is no data to support that (b) (4) room continuously meets its EM specification for any time after HVAC shutdown. No product impact assessment was performed.

Supporting Evidence, Relevance, and Discussion with Management:
(Written by EA)

According to the alarm data report for (b) (4) (b) (4) for the period from 01/01/2021 to 12/31/2021 (**Exhibit EA-18**), the pressure in room (b) (4) on (b) (4) was (b) (4) relative to the non-controlled corridor, while rooms adjacent to (b) (4) remained over pressurized relative to the same corridor (no alarm was recorded). Given that the pressure differential alarms are setup with (b) (4) delay (**Exhibit EA-17**) and the time of the alarm ((b) (4)), duration of the pressure differential excursion was approximately (b) (4). According to the work orders 1500905 and 1523038 (Exhibit **EA-20**), the cause of the alarm was a planned HVAC shut down for maintenance. Post-HVAC shutdown cleaning requirements are proceduralized in (b) (4)

(b) (4) effective 07/21/2021 (**Exhibit EA-19**), which does not require additional cleaning unless loss of airflow duration exceeds (b) (4).

I also reviewed facility sanitization log reports (**Exhibit EA-21**), EM trend detail report (**Exhibit EA-22**) and manufacturing schedule for (b) (4) (b) (4) **Exhibit EA-23**) covering the event and established the following sequence of events:

- (b) (4): (b) (4) sanitization of (b) (4) performed
- (b) (4): HVAC shut down, pressure differential in (b) (4) below the limit
- (b) (4): HVAC alarm triggered; pressure differential is (b) (4)
- (b) (4): HVAC alarm off; pressure differential returned to normal
- (b) (4): (b) (4) of batch (b) (4)
- (b) (4): (b) (4) sanitization of (b) (4) performed

No EM of the suite was performed from the time of the event until (b) (4) (b) (4) only) and (b) (4) (Room (b) (4). Batches were processed (b) (4) in (b) (4) between (b) (4) DS batches (b) (4) (manufactured from (b) (4) (manufactured from (b) (4)), and (b) (4) (manufactured from (b) (4)) processed within the timeframe when the (b) (4) (b) (4) EM status could not be assured were manufactured into DP batches and released between (b) (4) to the US and the international market (**Exhibit EA-24**). No impact assessment on the product was performed.

According to (b) (6), (b) (7)(C) , no study had been performed to determine room recovery rate after HVAC shutdown with respect to air and surface viables. There is also no procedure to ensure that any required additional or routine cleaning was performed as clean status of the room is not verified prior to start of manufacture in (b) (4) (b) (4)

The SMEs brought up the following documents to support the existing procedure for the HVAC shutdown response:

- (b) (4) effective 03/29/2021 (**Exhibit EA-25**)
- (b) (4) (b) (4) effective 04/07/2021 (**Exhibit EA-26**)

As part of HVAC qualification, a room recovery test was performed on 12/11/2020. Recovery time for (b) (4) was determined to be (b) (4) as determined by (b) (4)

reduction of (b) (4). The study included a (b) (4) and does not address room recovery with respect to (b) (4) contamination.

The risk assessment justifies the (b) (4) time window based on the lack of EM incidents, events, and deviations with HVAC air loss as a root cause. There were (b) (4) HVAC outages ranging from (b) (4), including (b) (4) event of a sitewide outage with alarm durations of (b) (4). Lack of such deviations is not informative given lack of EM sampling requirement (b) (4)-HVAC shutdown and the infrequent and limited EM sampling in (b) (4) (b) (4) see **Observation 9** and **Discussion Item EA-2**).

OBSERVATION 11

Standard operating procedures are not followed. For example,

a. On 7/22/2021 during observation of (b) (4) operations, cleaning of (b) (4), and dispensing of drug substance, the following was observed in deviation from (b) (4) (b) (4) (b) (4) and (b) (4)

- **An alarm went off (b) (4) due to operator (b) (4) to introduce (b) (4). (b) (4) prohibits work in a (b) (4) if it is in alarm condition.**
- **(b) (4) operators were (b) (4) over the (b) (4) of the (b) (4) blocking the (b) (4).**
- **(b) (4) did not cover all surfaces of the (b) (4) and was (b) (4) set contact time required per (b) (4).**

b. (b) (4) cleaning of the (b) (4) in (b) (4) (b) (4) was not performed in the (b) (4) of July 2021 in deviation from (b) (4).

Supporting Evidence, Relevance, and Discussion with Management:
(Written by EA)
During the walkthrough of (b) (4) (b) (4) on 7/22/2021, I observed the following:
During the setup for (b) (4) operations the (b) (4) were brought into (b) (4). The items were too large to fit under the (b) (4), which had to be (b) (4) each time triggering an alarm. (b) (4) (b) (4) (b) (4) effective 02/24/2021 (**Exhibit EA-4**) states "never work in a (b) (4)…if it is in alarm condition".

The (b) (4) operator was observed (b) (4) on the (b) (4) while monitoring the filtration. This is in violation of (b) (4) (**Exhibit EA-4**) section 9.6.1 General Behaviors stating "In (b) (4), do not (b) (4) the (b) (4) Same (b) (4) operator behavior was observed during (b) (4) walkthrough (see **Discussion Item EA-3**).

During cleaning of (b) (4) the operator used (b) (4) in a (b) (4) to cover surfaces of the (b) (4), including the (b) (4). Approximately (b) (4) area along the bottom of the (b) (4) was not completely covered and streaking of (b) (4) could be observed. Surfaces (b) (4) out before (b) (4) timer was up; some portions of (b) (4) surfaces were (b) (4) . Similarly, during (b) (4) setup surfaces of the (b) (4) , which was (b) (4) with (b) (4) left undisturbed inside the (b) (4) for (b) (4) contact time, (b) (4) out before the (b) (4) timer was up. On both occasions, the disinfectant was not reapplied to maintain the contact time. Contact time is specified in Section 9.1.4 Disinfectant Guidance of (b) (4) (**Exhibit EA-4**).

During the walkthrough of (b) (4) (b) (4) on 7/22/2021, the outside of major equipment appeared dusty, streaky, and had dried out residue (i.e., (b) (4) , **Exhibit EA-5**). Periodic cleaning of outside surfaces of major equipment and cleaning/breaking down of (b) (4) is performed by operators using (b) (4) down, respectively per (b) (4) (b) (4) (b) (4) effective 06/09/2021 (**Exhibit EA-6**). According to Section 17.2 of the procedure, (b) (4) sanitizations are to be performed "within each of the following dates of the month: (b) (4) Upon review of (b) (4) (b) (4) effective 03/05/2018 for (b) (4) (b) (4) equipment sanitization (**Exhibit EA-8)**, it was noted that in deviation from the (b) (4) , surface sanitization was not performed on (b) (4) .

OBSERVATION 12

The following deficiencies were observed within buildings used to produce BNT162b2 drug substance:

- **a. In Building (b) (4) preparation area:**
  - **(b) (4) was observed on multiple walls.**
  - **(b) (4) was observed in the hallway.**
  - **(b) (4) were observed with dust and debris on the (b) (4) and streaking/raised residue down the sides and bottom of multiple (b) (4)**
- **b. In Building (b) (4) (b) (4) (b) (4)**
  - **(b) (4) was observed on multiple walls inside room (b) (4)**

- (b) (4) **was observed in room** (b) (4)

c. **Residue was observed on the sides and base of multiple sample pass throughs to include** (b) (4) **preparation,** (b) (4) (b) (4) **and** (b) (4) **.**
d. **A gap to the outside was observed on the side of the mobile platform at the receiving dock in Building** (b) (4)

Supporting Evidence, Relevance, and Discussion with Management:
(Written by DME)

a. On 7/19/2021, while looking through the hallway windows into the (b) (4) production rooms in Building (b) (4) I observed streaking residue on the outside of multiple (b) (4).

On 7/21/2021, I observed dust and debris on (b) (4). The status of (b) (4) was clean. I observed streaking down the outside of (b) (4). The status of (b) (4) was clean. It was explained that the exteriors of the (b) (4) are cleaned (b) (4), and they were last cleaned in June 2021. A picture was taken which shows the streaking down the side of the (b) (4) (**Exhibit DME 2 p. 7**).

On 7/21/2021, I observed areas of (b) (4) that were in excess of 6 inches in length on multiple walls which included the wall behind (b) (4), the base of the wall near the floor scale, (b) (4) on the wall near the shower, the wall by the sink, and the wall above the outlets. Pictures were taken to show the concern (**Exhibit DME 2 p. 1 to 6**) however the pictures do not clearly show the (b) (4)

In addition, I observed a ring around the inside of the (b) (4) at about (b) (4) and a ring around the inside of the (b) (4) at about (b) (4) up (b) (4). I was later provided a technical report for the ring: (b) (4) (b) (4), (b) (4), effective 1/6/2017, which states that the ring is due to the slip agents inside the (b) (4) of some raw materials. It was explained that Pfizer has a process for monitoring the (b) (4) with these rings and will remediate the residue from the (b) (4) when appropriate. Due to the time constraints, I was unable to assess if this is being done for the (b) (4) in (b) (4)

I observed white residue streaking down the inside of the (b) (4) at 10 and 11 o'clock positions through the site glass. The (b) (4) was in a clean status. I asked about the residue, but no information was provided before the close of the inspection.

On 7/23/2021, I was provided with pictures (**Exhibit DME 20**) which demonstrate corrective actions to walls in (b) (4) preparation in (b) (4)

I spoke with Mr. Tucker and other management staff in the room and explained my concerns and I showed him the photos which were taken. Mr. Tucker stated that they have a robust program where the facility is inspected (b) (4) for damage, equipment issues, leaks, or areas of concern. During the close, (b) (6), (b) (7)(C) , stated that the facility is an operational/working facility. There were no additional discussions during the close.

(Written by EA)

b. During the walk through of (b) (4) (b) (4) I observed (b) (4) on walls inside room (b) (4) (behind equipment, (b) (4) from the floor) and (b) (4) in Control Room/Storage (b) (4) (**Exhibit EA-7**), by the entrance (see **Observation 12b**).

(Written by DME)

c. On 7/19/2021, while looking through the hallway windows into the (b) (4) production rooms in Building (b) (4) I observed residue on the base of the pass through into (b) (4).

On 7/22/2021, while inside the (b) (4) room, I looked into the large pass through, and residue was observed. I went with (b) (6), (b) (7)(C) to the hallway where the pass-through exits and (b) (6), (b) (7)(C) explained that the pass through is used for the transfer of samples out of (b) (4). I looked into the pass through and residue, some of which was raised and dark in color, was observed on multiple sides and the base of the pass through. I asked the firm to take pictures of the residue observed. Pictures were provided by the firm of this pass through, but the pictures were not clear (**Exhibit DME 2 p. 10-13**).

(Written by EA)
During (b) (4) walkthrough I observed dried up residue (splatter and pools of liquid) on the bottom surface of the sample pass through. No cleaning of the pass through was performed (or is required) before or after its use by the operator (b) (4) effective 08/25/2020 (**Exhibit EA-2**)]. Per (b) (4) effective 06/26/2019 (**Exhibit EA-3**), pass throughs are cleaned (b) (4) by "saturating" interior and exterior surfaces with disinfectant. The SOP does not instruct to wipe the surfaces after the contact time is achieved.

(Written by DME)
I explained my observations to Mr. Tucker and other management in the room at the time. No response was provided by the firm as to what the material was inside any of the pass throughs. There were no additional discussions during the close.

(Written by DME)

d. On 7/19/2021, while walking through the warehouse in Building (b) (4) I observed a gap (approximately ½ to 1 inch in size) to the outside, on the side of the mobile platform at the receiving dock. I explained to Mr. Tucker and other staff in the room that the gap on the side of the mobile platform is large enough to allow bugs and possibly small rodents into the facility. There were no additional discussions during the close.

OBSERVATION 13

During (b) (4) activities observed on 7/22/2021, an operator was observed to (b) (4) and subsequently (b) (4) material from a full and previously opened container of (b) (4) . The previously opened container of (b) (4) had a lid which was not fully closed, the (b) (4) within the container was not closed, and there was no documentation as to when the container had been initially opened.

Supporting Evidence, Relevance, and Discussion with Management:

(Written by DME)

On 7/22/2021, I observed operator (b) (6), (b) (7)(C) , performing (b) (4) operations for (b) (4) solutions that will be used in the manufacture of the BNT162B2 drug substance. He brought in one container with the wrong lot code in error and the system would not allow him to proceed with the (b) (4) operation.

(b) (6), (b) (7)(C) , retrieved a different another container with the same lot code. The container that (b) (6), (b) (7)(C) retrieved was partially open. (b) (6), (b) (7)(C) (b) (6), (b) (7)(C) took the cover off the container, opened the (b) (4) and began adding (b) (4) to the (b) (4) that was being (b) (4) . There was no documentation on the container to identify that it had been opened or when. It was explained by (b) (6), (b) (7)(C) (b) (6), (b) (7)(C) that they are not required to make note on the containers when they are initially opened or by whom. (b) (6), (b) (7)(C) explained that he retrieved this container from a specific area of the warehouse for partial containers. (b) (6), (b) (7)(C) took me to a storage area in the warehouse which is labeled “In-Process Materials Only Below This Sign”. A picture was of the sign and to show the two pallets of materials which were stored in this area (**Exhibit DME 2 p. 14**). None of the (b) (4) containers stored on either pallet had a date on the container to identify when the material had been opened. In review of procedure: Warehouse Storage and Movement of Materials in the (b) (4) (b) (4) effective 12/21/2020, (**Exhibit DME 1 p. 3**) provides some instruction for partial containers as far as checking the expiration date and (b) (4) down prior to entry into the (b) (4) . The procedure does state “ensure all partial containers are appropriately closed, sealed, and contained before moving back to

(b) (4) Warehouse" (**Exhibit DME 1 p. 3**). There were no additional instructions for sealing/closing the containers.

I explained to Mr. Tucker and other management in the room that at a minimum, the containers should be dated so that staff know when the container had been opened. I explained that some materials are sensitive to moisture and if not properly closed it could impact the potency and/or stability of the raw material. There were no additional discussions during the close.

REFUSALS
(Written by DME)

We encountered no refusals during the current inspection.

GENERAL DISCUSSIONS WITH MANAGEMENT
We discussed various issues with Management during the inspection which may require their attention including the following:

(Written by KRJ)

Discussion Item KRJ-1
On 7/21/2021, I discussed with management the crowded appearance of the (b) (4) with the (b) (4) in the room and the spatial area for the (b) (4) analysts to maneuver. I also discussed the set-up for the (b) (4) testing, as there is substantial empty space in (b) (4) (b) (4). By not being able to place the (b) (4) on the cart completely, there is a risk that the (b) (4) could fall off the cart and crack.

(Written by EA)
Discussion Item EA-1
Visual Inspection of Process Equipment – I discussed the following issues related to visual inspection of process equipment:

- Procedure (b) (4) (b) (4) effective 04/23/2021 (**Exhibit EA-33**) is deficient in that residue sample retrieval is not described. During investigation of (b) (4) (b) (4) (COVID): (b) (4) (b) (4) (**Exhibit EA-31**) (b) (6), (b) (7)(C) used (b) (4) (clean room brand towel) attached to a (b) (4) to avoid scratching the (b) (4). As a result, the sample was contaminated with adhesive (presumed to originate from tape used for tool wrapping).
- Per (b) (4) (**Exhibit EA-33**) opening deviations/investigations is not required for particulate deemed to be "native to the process", such as (b) (4). During (b) (4)

(**Exhibit EA-31**) investigation the residue was identified as (b) (4) and deviation was closed without further follow-up. Per list of parts used in (b) (4) with (b) (4) (**Exhibit EA-34**), (b) (4)

Solution incompatibility with (b) (4) material was not considered or investigated as a potential root cause of shedding.

Discussion Item EA-2
EMPQ and Routine EM – I discussed the following issues related to design of EMPQ and routine EM of (b) (4)

- It could not be confirmed that EMPQ was performed under (b) (4) conditions. Per (b) (6), (b) (7)(C), and (b) (6), (b) (7)(C), there is no requirement that any manufacturing activities are performed during (b) (4) sampling; presence of personnel at the time of sampling could not be confirmed.
- EMPQ was not performed under the worst conditions. Specifically, the firm did not define or challenge maximum occupancy during EMPQ.
- EMPQ/routine EM sampling is deficient in sample size and locations. First, locations of EM sample sites determined per risk assessment (b) (4) (**Exhibit EA-9)** and implemented per (b) (4) (**Exhibit EA-12**) were selected during construction phase and were not reevaluated after the (b) (4) was commissioned based on the actual personnel traffic. It was observed during the walkthrough that certain areas of the suite (i.e. around (b) (4) have unexpectedly high traffic, which had not been considered by the initial risk assessment. Second, the air sample volume (i.e. (b) (4), would not be representative of (b) (4) given the room size ((b) (4), especially given that only (b) (4) air samples of each type are collected on a (b) (4) basis (see **Observation 9b)**. (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C) referred to ISO (b) (4) standard (**Exhibit EA-10**) to support the sample size. However, ISO (b) (4) requires collection of (b) (4) samples rather than (b) (4) samples based on the size of (b) (4)

(b) (4) **-** I discussed the following issues related to (b) (4) use:

- During (b) (4) (b) (4) walkthrough the (b) (4) operator was observed (b) (4) (b) (4) the (b) (4) of the (b) (4) impeding the (b) (4). (b) (4) (**Exhibit EA-1**) prohibits placing items on the (b) (4).
- During a walkthrough of (b) (4) (b) (4) (b) (4) was observed crowded with various items during (b) (4) of (b) (4) reagent. For example, a (b) (4), an opened set of (b) (4) were observed stacked on top of each other inside the (b) (4) (b) (4)

(b) (4) effective 08/23/2019 (**Exhibit EA-1**) prohibits piling items on top of each other inside of a (b) (4).

- During (b) (4) walkthrough the (b) (4) operator was observed (b) (4) and using the (b) (4) for multiple strokes across (b) (4) surfaces. This is in violation of Attachment 7 (b) (4) Methodology" of (b) (4) (**Exhibit EA-6)**
- Utility of (b) (4) was discussed given that the equipment was not adequately qualified (see Observation 9a), monitored, or used (see also Observation 11a). According to Paige Persky, Manager DP Manufacturing, and (b) (6), (b) (7)(C), (b) (4) monitoring in operation is limited to (b) (4) activities per (b) (4) effective 06/30/2021 (**Exhibit EA-13**). No personnel monitoring or (b) (4) monitoring post-operations is performed.

Facility and Equipment Design - I discussed the following issues related to the facility and equipment design:

- As a result of stationary and mobile equipment/cart placement in (b) (4) and spatial limitations that it created, operators were observed kneeling on the floor and reaching under a cart to plug a (b) (4) into an electrical outlet, placing paper MBRs, printed SOPs and pens on top of SUMs being used in manufacture.
- The (b) (4) in (b) (4) appeared to have insufficient size for the operations being performed: during DS (b) (4) the entire space was occupied with a (b) (4) The operator had to rearrange the items inside the (b) (4) to bring in necessary equipment. The newer (b) (4) is used interchangeably and is smaller than (b) (4).
- (b) (4) testing was setup in the corner of the (b) (4) behind a mobile staircase adjacent to (b) (4) (**Exhibit EA-5**). During the setup, one of the operators was observed attaching a hose to the (b) (4) in the utility panel located on the wall behind the staircase while the other operator was assembling tubing on the surface of a cart located in front of the staircase. To help with the tubing assembly, the operator had to initially hold the hose over the rail of the staircase and eventually let it hang over the rail. Then operators squeezed past each other between the wall and the staircase to the utility panel where they proceeded to setup the filter on (b) (4) for (b) (4).

Discussion Item EA-5

Containment – The following issues related to containment were discussed:

- Per Haroon Beg and (b) (6), (b) (7)(C), operators close biohazardous waste (b) (4) by (b) (4)

- (b) (4) (**Exhibit EA-27**) governing transfer of solid waste is not detailed or specific enough to allow for consistent execution. For example, (b) (4) waste (b) (4) glove sanitization after waste handling, or placing waste (b) (4) into a secondary container inside (b) (4) is not described. The SOP appears to require (b) (4) of solid process waste, a practice that is not in place at the facility.
- Waste flow is not temporally segregated from flow of DS, materials, and equipment through (b) (4). It is typically placed in the (b) (4) at the end of each production shift (b) (4) and picked up from the (b) (4) (not on schedule) by Environmental Health & Safety (**Exhibits EA-28** and **EA-29**).

Discussion Item EA-6
(b) (4)

Discussion Item EA-7
Material Management - I discussed the following issues related to management of single use product-contact materials:

- (b) (4) status of product-contact materials sterilized by suppliers is not verified through periodic sampling of incoming lots. According to the SMEs, no testing is required for release of any product-contact single use materials, all of which are released solely based on suppliers' CofC/CofA and their (b) (4) claims.
- According to the provided lists of product-contact materials (**Exhibits**
- **EA-39** and **EA-40**) there are several direct product-contact materials for which no (b) (4) claim is provided by supplier.

(Written by AC)
Discussion Item AC-1
(b) (4)

(b) (4)

Discussion Item AC-2
PPQ Lots Stability -

- To demonstrate manufacturing process consistency at (b) (4) (b) (4) PPQ lots were executed. Nevertheless, only one PPQ lot, (b) (4) , was put on stability, and this DS lot failed the (b) (4) specification at (b) (4) time point at real-time storage conditions (**Exhibit AC-3**). I strongly recommended the firm to put at least (b) (4) PPQ lots on stability to assure that sufficient data will be available to support the proposed shelf life. The firm acknowledged the recommendation and stated that at least (b) (4) PPQ lots will be placed on stability for the (b) (4) size DS manufacturing process.

(Written by DME)
Discussion Item DME-1

(b) (4)

EXHIBITS COLLECTED
Exhibits collected by Inspector Jones are identified by "KRJ", Inspector Allen are identified by "EA", Inspector Cheung are identified by "AC", and Inspector Emerson are identified by "DME".

KRJ Exhibits

KRJ-01	Opening Meeting Attendees/Quality Oversight Presentation Attendees (3 pages)
KRJ-02	Close-out Meeting Attendees (1 page)
KRJ-03	Subject Matter Experts Interviewed (22 pages)

KRJ-04 Opening Meeting/Quality Meeting Presentations (51 pages)
KRJ-05 (b) (4) (b) (4) Quality Organization Charts (5 pages)
KRJ-06 (b) (4) Quality Organization (b) (4) (16 pages)
KRJ-07 (b) (4) (62 pages)
KRJ-08 (b) (4) trend deviation (b) (4) and (b) (4) deviation (b) (4) (7 pages)
KRJ-09 (b) (4) 3 pages)
KRJ-10 (b) (4) approved on 04/28/2021 (b) (4) (9 pages)
KRJ-11 (b) (4) , (b) (4) , effective 04/30/2015 (PGS) (26 pages)
KRJ-12 Section 3.2.A.1 (b) (4) (28 pages)
KRJ-13 (b) (4) (40 pages)
KRJ-14 (b) (4) (Plan) (6 pages)
KRJ-15 (b) (4) (Executed) (10 pages)
KRJ-16 (b) (4) (12 pages)

EA Exhibits

EA-1 (b) (4) effective 08/23/2019 (12 pages)
EA-2 (b) (4) effective 08/25/2020 (12 pages)
EA-3 (b) (4) effective 06/26/2019 (20 pages)
EA-4 (b) (4) effective 02/24/2021 (65 pages)
EA-5 Photos of (b) (4) , front view and (b) (4) surface (2 pages)
EA-6 (b) (4) effective 06/09/2021 (66 pages)
EA-7 Photos of (b) (4) in (b) (4) (b) (4) (3 pages)
EA-8 (b) (4) Sanitization Log pages 32 and 37 (2 pages)
EA-9 (b) (4) effective 04/30/2021 (24 pages)
EA-10 International Standard ISO (b) (4) (44 pages)
EA-11 (b) (4) , official on 07/14/2021 (12 pages)

EA-12 (b) (4) effective 05/12/2021 (28 pages)
EA-13 (b) (4) (b) (4) effective 06/30/2021 (49 pages)
EA-14 (b) (4) effective 11/04/2020 (10 pages)
EA-15 (b) (4) effective 07/23/2021 (11 pages)
EA-16 EM Trend Detail Report printout for room (b) (4) location (b) (4) for the period of 05/12-14/2021 (5 pages)
EA-17 Environmental alarm configuration in (b) (4) (b) (4) (11 pages)
EA-18 Environmental alarm data report for (b) (4) for the period from 01/01/2021 to 12/31/2021 (6 pages)
EA-19 (b) (4) ffective 07/21/2021 (26 pages)
EA-20 Pfizer maintenance work orders 1500905 and 1523038 (10 pages)
EA-21 (b) (4) (b) (4) sanitization log report for (b) (4) (2 pages)
EA-22 (b) (4) EM Trend Detail Report from 2/18/2021 to 05/12/2021 (8 pages)
EA-23 (b) (4) Manufacturing Schedule from 03/17/2021 to 04/01/2021 (1 page)
EA-24 Disposition declaration for DS and associated DP batches (1 page)
EA-25 (b) (4) effective 03/29/2021 (108 pages)
EA-26 (b) (4) effective 04/07/2021 (12 pages)
EA-27 (b) (4) effective 06/02/2021 (42 pages)
EA-28 (b) (4) (b) (4) effective 04/07/2021 (27 pages)
EA-29 EH&S Memorandum: Frequency of Waste Removal (1 page)
EA-30 Major manufacture equipment summary table (5 pages)
EA-31 (b) (4) (b) (4) *(COVID):* (b) (4) (b) (4) created (b) (4) (11 pages)
EA-32 (b) (4) (b) (4) (b) (4) *(COVID):* (b) (4) (b) (4) created (b) (4) ; (b) (4) (b) (4) (b) (4) *COVID):* (b) (4) (b) (4) created (b) (4) (63 pages)
EA-33 (b) (4) (b) (4) effective 04/23/2021 (32 pages)
EA-34 Lists of items and parts used in (b) (4) (b) (4) (2 pages)
EA-35 (b) (4) (b) (4) (b) (4) effective 05/18/2021 (13 pages)
EA-36 List of product-contact equipment cleaned via (b) (4) (1 page)

EA-37 (b) (4) effective 07/14/2021 (30 pages)
EA-38 (b) (4) (b) (4) (b) (4) effective 03/31/2021. (74 pages)
EA-39 List of product-contact materials (2 pages)
EA-40 List of product-contact materials (with supplier (b) (4) claims); List of Stock Room Supplied Parts (with supplier (b) (4) claims) (16 pages)
EA-41 List of Direct Contact/Indirect Contact Parts (1 page)

AC Exhibits

AC-1 RNA Manufacturing Process Flow Diagram, 1 page
AC-2 (b) (4) , 22 pages
AC-3 Stability Data (Long-term and Accelerated Storages) for Drug Substance PPQ batches at Andover (b) (4) (b) (4) and (b) (4) 12 pages
AC-4 Additional DS Batches from (b) (4) (b) (4) enrolled on Stability Program, 1 page
AC-5 Product Quality Data for Validation of COVID-19 Vaccine Drug Substance Shipping, 3 pages
AC-6 Analytical Testing Lab for the Release of COVID-19 Vaccine Drug Substance and Drug Product, 3 pages
AC-7 Manufacturing Batch Record for Reprocessed DS Lot (b) (4)
AC-8 Manufacturing Investigations-Action Item Detail Report (b) (4) , 3 pages
AC-9 Release Dates of COVID-19 Drug Product Associated with DS Batch (b) (4) , 1 page

DME Exhibits

DME 1 (b) (4) effective 12/21/2020, 10 pages
DME 2 Pictures from the facility, 14 pages
DME 3 Printout of the (b) (4) samples tested on 7/19/2021, 5 pages
DME 4 *Procedure:* (b) (4) , effective 6/9/2021, 57 pages
DME 5 *Procedure:* (b) (4) (b) (4)

	(b) (4), (b) (4) (b) (4) effective 6/23/2021, 13 pages
DME 6	List of BNT162b2 drug substance (b) (4), 13 pages
DME 7	List of (b) (4) deviations. 3 pages
DME 8	QAR (b) (4) deviation, 7 pages
DME 9	Pages from batch record lot (b) (4), 26 pages
DME 10	QAR (b) (4) deviation, 13 pages
DME 11	Pages from batch record lot (b) (4), 22 pages
DME 12	QAR (b) (4) deviation, 6 pages
DME 13	Pages from batch record lot (b) (4), 126 pages
DME 14	Release packet and Certificate of Analysis for batch (b) (4), 5 pages
DME 15	PR ID (b) (4), 6 pages
DME 16	Batch record for lot (b) (4), 105 pages
DME 17	Release packet for lot (b) (4), 5 pages
DME 18	QAR (b) (4), 29 pages
DME 19	Batch record (b) (4), 56 pages
DME 20	Pictures of repaired areas, 13 pages

ATTACHMENTS

Form FDA 482, Notice of Inspection Dated 07-19-2021

Form FDA 483, Inspectional Observations Dated 07-23-2021

The signatures of the FDA representatives are on the following page.

Signature Page

Kathleen R. Jones, Biologist, CBER/OCBQ/DMPQ/MRB1

Ekaterina Allen, CSO, CBER/OCBQ/DMPQ/MRB2

Anissa Cheung, CSO, CBER/OVRR/DVP

Debra M. Emerson, CSO, Team Biologics