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LIST OF TABLES

(b) (4) (PFIZER CHESTERFIELD)

QUERY 1

Please clarify what critical utilities are used during the (b) (4) process, and the microbial control for each critical utility (e.g., (b) (4) or routine monitoring).

RESPONSE 1

(b) (4) are the only critical utilities used during the (b) (4) process.

(b) (4)

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 2

The list provided in Table 3.2.A.1-1 does not include tubing, small parts, biological safety cabinets, and laminar flow hoods. Please update Table 3.2.A.1-1 to include all direct product contact equipment.

RESPONSE 2

Additional product-contact parts are listed in the table below. Biological safety cabinets and laminar flow hoods are not direct product contact and are not included in the table. Table 3.2.A.1-1 in Section 3.2.A.1 Facilities and Equipment (Chesterfield) has been updated.

Table 1. List of Critical Equipment/Materials Used in Manufacturing of the (b) (4) (b) (4)

Equipment/ Materials	Product Contact/ Use	Single Use / Multiuse/ Dedicated	Material of Construct (MOC)	Cleaned / Sterilized
(b) (4)				

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

3.2.A.1 Facilities and Equipment (Chesterfield)-Replaced

Previously submitted supporting documentation

None

QUERY 3

Regarding equipment cleaning validation, please provide the following information:

a. Provide the cleaning validation results (or rationale for lack thereof) for the following equipment (b) (4)

b. Specify the maximum clean hold times and provide clean hold time validation results for each equipment.

c. Specify the equipment cleaning verification frequency and the parameters to be tested (i.e., (b) (4)) during routine production.

RESPONSE 3

(b) (4)

(b) (4)

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

Section 3.2.A.1 Facilities and Equipment Cleaning Validation Summary (Chesterfield)- Replaced

Previously submitted supporting documentation

None

DRUG SUBSTANCE (PFIZER ANDOVER-(b) (4) AND (b) (4)

QUERY 4

Regarding environmental monitoring, please provide the following information:

a. Please define "at rest" and "in operation".

b. Please clarify if the total air particulate limits are for "in operation" conditions.

RESPONSE 4 a

"At rest" describes the status of a facility with all services functioning, standard processing equipment installed, and with no personnel or manufacturing activities being performed other than environmental monitoring.

"In operation" describes the status of a facility with all services functioning, standard processing equipment installed, but includes routine personnel and production-related activities being performed or simulated. A facility is considered to be in operation status from the time of the initial set-up to the start of final clean-up including set-up and production operations.

RESPONSE 4 b

The total air particulate limits are applied for both at rest and in operation monitoring. A footnote was added to the Table 3.2.A.1-4, in 3.2.A.1 Facilities and Equipment (Andover (b) (4) and Table 3.2.A.1-6, in 3.2.A.1 Facilities and Equipment ((b) (4) for clarification.

Literature References

None

SUPPORTING DOCUMENTATION

3.2.A.1 Facilities and Equipment (Andover (b) (4) -Replaced

3.2.A.1 Facilities and Equipment ((b) (4) -Replaced

Previously submitted supporting documentation

None

QUERY 5

Please supply the following information regarding the dirty and clean hold times of direct product contact equipment:

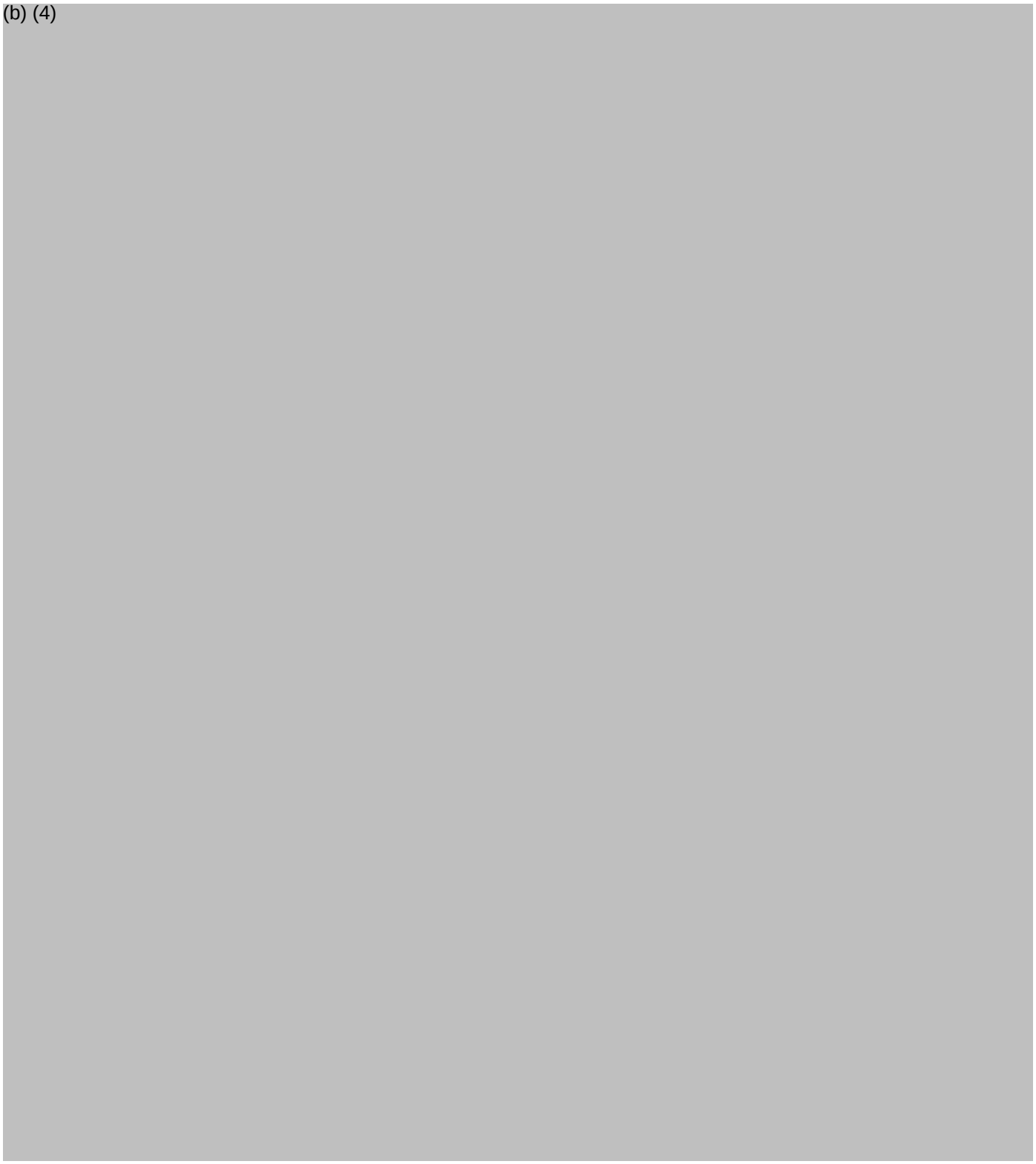
a. Please clarify if clean and dirty hold times were performed during process validation, and please provide the number of replicates performed.

b. Define the parameters tested at the end of the clean hold time to verify the equipment remained clean (i.e., (b) (4)).

RESPONSE 5

(b) (4)

(b) (4)



Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 6

Please clarify if the manufacturing areas and direct product contact equipment are product dedicated or campaign dedicated for BNT162b2 in both (b) (4) and (b) (4) , as there are the following inconsistencies:

a. In 3.2.A.1.1, you state, (b) (4)
(b) (4) However, in 3.2.A.1.8.1, you indicate that the (b) (4)
(b) (4)

b. Table 3.2.A.1-4 ((b) (4) indicates that (b) (4)
(b) (4)

c. Table 3.2.A.1-3 ((b) (4)) indicates that (b) (4)
(b) (4)

RESPONSE 6

The response applies to query 6 a, b and c.

(b) (4)

Literature References

None

SUPPORTING DOCUMENTATION

3.2.A.1 Facilities and Equipment (Andover (b) (4) -Replaced

3.2.A.1 Facilities and Equipment ((b) (4) -Replaced

Previously submitted supporting documentation

None

DRUG PRODUCT

QUERY 7

Please update Table P.3.1 with the specific analytical test methods for drug product release and stability testing to be performed at each facility.

RESPONSE 7

Section 3.2.P.3.1 Manufacturer(s) is updated to include the analytical test methods performed at each facility for release and stability. This information is also included within Section 3.2.R Summary of Analytical Procedures, Method Validation and Transfer Reports.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

3.2.P.3.1 Manufacturer(s), replaced

Previously submitted supporting documentation

3.2.R Summary of Analytical Procedures, Method Validation and Transfer Reports

QUERY 8

Please indicate what room and building the (b) (4) visual inspection line is located. Please explain when this inspection machine will be used for inspecting BNT162b2 filled vials manufactured on Filling Lines (b) (4).

RESPONSE 8

Inspection Line (b) (4) is located in the (b) (4) Building at Pfizer Puurs, room (b) (4). The Inspection Line is not intended for use under the commercial BLA and information is removed from the 3.2.A.1 Facilities and Equipment (Puurs).

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

3.2.A.1 Facilities and Equipment (Puurs), replaced

Previously submitted supporting documentation

None

QUERY 9

Regarding the container closure integrity testing, please submit the (b) (4) method validation protocol, summary report and assay performance procedure that is followed at Pfizer Puurs and Pfizer Kalamazoo.

RESPONSE 9

(b) (4)

For Pfizer Kalamazoo, the analytical method transfer/validation report along with the analytical procedure covering the (b) (4) method is found in Section 3.2.R Summary of Analytical Procedures, Method Validation and Transfer Reports. The protocol used for

(b) (4)

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

(b) (4)

Previously submitted supporting documentation

3.2.R Summary of Analytical Procedures, Method Validation and Transfer Reports

QUERY 10

Please submit the (b) (4) container closure integrity test method validation protocol, summary report and assay performance procedure that is followed at Pfizer Puurs and Pfizer Kalamazoo. Please explain when this method will be used as you have two container closure integrity methods for your drug product.

RESPONSE 10

Executed test method validation protocols for the (b) (4) analysis test method are provided in lieu of the protocols and summary reports (as all information is captured therein), covering container closure combinations from both Pfizer Puurs (USP-1207 Method Validation (b) (4) - Pfizer Puurs 2mL vial Rev 2.4_Final Report) and Pfizer Kalamazoo (USP-1207 Method Validation (b) (4) - Pfizer Kalamazoo 2mL vial Rev 1.2_Final Report).

(b) (4)

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

USP-1207 Method Validation (b) (4) Pfizer Puurs 2mL vial Rev 2.4_Final Report, new

USP-1207 Method Validation (b) (4) Pfizer Kalamazoo 2mL vial Rev 1.2_Final Report, new

3.2.P.3.1 Manufacturer(s), replaced

Previously submitted supporting documentation

3.2.P.2.4 Container Closure System

3.2.P.2.5 Microbiological Attributes

3.2.P.3.5 Shipping Validation

QUERY 11

Regarding a recent Information Request response (Response to FDA 26 Jul 2021) STN 125742/0.24, the Agency requires clarification to your Query 16a response regarding new equipment at Pfizer Kalamazoo. As stated in Table 5 of your 16a response, the (b) (4) (b) (4) tanks are not yet qualified. Please provide the following information regarding these (b) (4) tanks:

QUERY 11a

Please provide the equipment numbers and when qualification is expected to be completed (if not previously completed).

RESPONSE 11a

Equipment (ie, tank) numbers and qualification status are provided in Table 6. Based on procedures, equipment cannot be used in the process until it is qualified.

Table 6. (b) (4) Tank Qualification Status

Tank Size	Tank ID Number	Qualification Status	Anticipated Qualification Completion Date
(b) (4)			

Abbreviations: NA = Not Applicable

The (b) (4) tanks were not included in the BLA application and were submitted as an amendment to the EUA/IND (SN0426 submitted on 28 Jul 2021), which is currently under review by CBER.

QUERY 11b

Please explain whether these tanks were used in the process validation runs included in support of your BLA application. If not, please provide a justification to explain how the tanks are suitable for your process operation.

RESPONSE 11b

The (b) (4) tanks were not used for the process validation runs included in the BLA application.

(b) (4)

(b) (4)

QUERY 11c

Please address the discrepancy regarding the (b) (4) tanks qualification status with your recent IND amendment (SN0426), which you referenced in Table 5 of your response to Query 16a. According to your IND amendment, 2.3. Introduction to the Quality Overall Summary Section 2.3.1.1 you claim these (b) (4) tanks are qualified.

RESPONSE 11c

The (b) (4) tanks have been submitted as an amendment to IND 19736 (SN0426 submitted on 28 Jul 2021) and also included in Table 5 of response to Query 16a previously submitted to STN 126742/0.24. Query 16 indicated that it was in regard to the BNT162b2 major manufacturing equipment used at Pfizer Kalamazoo, therefore the (b) (4) tanks that were recently submitted, were added to the table to be complete.

As a clarification relative to the Quality Overall Summary Section 2.3.1.1 of IND 19736 SN0426 which states that the tanks are (b) (4) status is in reference to and in support of the (b) (4) tanks are (b) (4) although (b) (4) of the tanks (b) (4) been fully qualified for use. The remaining (b) (4) tanks will be qualified prior to being placed into service by (b) (4) .

QUERY 11d

Please address whether these tanks have been used in the manufacture of EUA BNT162b2 material prior to qualification.

RESPONSE 11d

None of the (b) (4) tanks have been used to manufacture EUA BNT162b2 material. (b) (4) of the (b) (4) tanks has been qualified for use. Change control records are utilized to document the qualification activities of each individual tank. Tanks can be placed into service following approval of the amendment to IND 19736 (SN0426 submitted on 28 Jul 2021) and after all change control activities have been completed.

QUERY 11e

Please provide summaries of your cleaning and sterilization validations for the (b) (4) tanks. If cleaning and/or sterilization validations are not complete, please provide a timeframe that you expect to complete the respective validations. Please provide a summary of your cleaning verification regime including acceptance criteria.

RESPONSE 11e

The sterilization validation for the (b) (4) tanks has been provided in the recent IND 19736 amendment (SN0426). An updated Section 3.2.P.3.5 Sterilization in Place (SIP) Validation [Kalamazoo] is also provided in this response. This updated document is fully aligned with the content submitted in IND 19736 SN0426, including a revised scope of (b) (4) tanks presented, which focuses only on tanks that contact the sterile drug product. Information has been removed for (b) (4) (b) (4) and do not contact the sterile drug product.

A cleaning assessment has been completed for the (b) (4) tanks which determined that the tanks are covered by existing cleaning validation. The cleaning validation summary for the (b) (4) tanks are covered by the data for the BNT162b2 (b) (4) Bulk Hold, and Sterile Tanks provided in 3.2.A.1 Facilities and Equipment Cleaning Validation Summary – Pfizer, Kalamazoo.

QUERY 11f

Please provide (b) (4) BNT162b2 hold time validations for the (b) (4) tanks including the microbial challenge results and criteria.

RESPONSE 11f

The hold time validations for the (b) (4) tanks have not yet been completed. The hold time validations will be completed by (b) (4) .

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

3.2.P.3.5 Sterilization in Place (SIP) Validation [Kalamazoo], Replaced

Previously submitted supporting documentation

3.2.A.1 Facilities and Equipment Cleaning Validation Summary – Pfizer, Kalamazoo

FOLLOW-UP TO FDA'S 26 JULY 2021 IR RESPONSE REGARDING MANUFACTURING AND EQUIPMENT: QUERY 16E

Regarding the recent Information Request response to the agency on 26 Jul 2021 (Response to FDA 26 Jul 2021) STN 125742/0.24, to Query 16e, the following Table 8 has been updated with additional information for portable tank (b) (4). Portable tank (b) (4) has been removed from the table as it was incorrectly added in the response to Query 16e. Minor formatting corrections were also made to the table.

Table 8. Drug Product Contact Equipment Summary

(b) (4)

Table 8. Drug Product Contact Equipment Summary

(b) (4)

Table 8. Drug Product Contact Equipment Summary

(b) (4)