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QUERY 1

Regarding the computer systems, please provide the following:

a. A list of the critical BNT162b2 drug substance manufacturing steps that are computer-controlled with the computer system identified.

b. For each computer system identified in Part 1a, provide a narrative description of the validation process, certification that the installation and operational qualification (IQ and OQ) have been completed; explanation of the parameters monitored, and tests performed; and a validation data summary.

RESPONSE 1

1a.

The Critical steps in BNT162b2 drug manufacturing include (b) (4)

(b) (4)

Table 1. List of equipment with Automated Control using Computer Systems

Critical Step	Manufacturing Area	Equipment/System ID (Description)	Computer controlled Computer system	IQ	OQ	PQ

(b) (4)

Table 1. List of equipment with Automated Control using Computer Systems

Critical Step	Manufacturing Area	Equipment/System ID (Description)	Computer controlled Computer system	IQ	OQ	PQ
(b) (4)						

1b.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 2

For each cold room, freezer, and (b) (4) freeze/thaw system (b) (4) in (b) (4)(b) (4) in (b) (4) used in the manufacture of the BNT162b2 drug substance, please identify the equipment with its unique identifier and provide a concise description of the qualification (e.g., IQ, OQ, performance qualification (PQ)).

RESPONSE 2

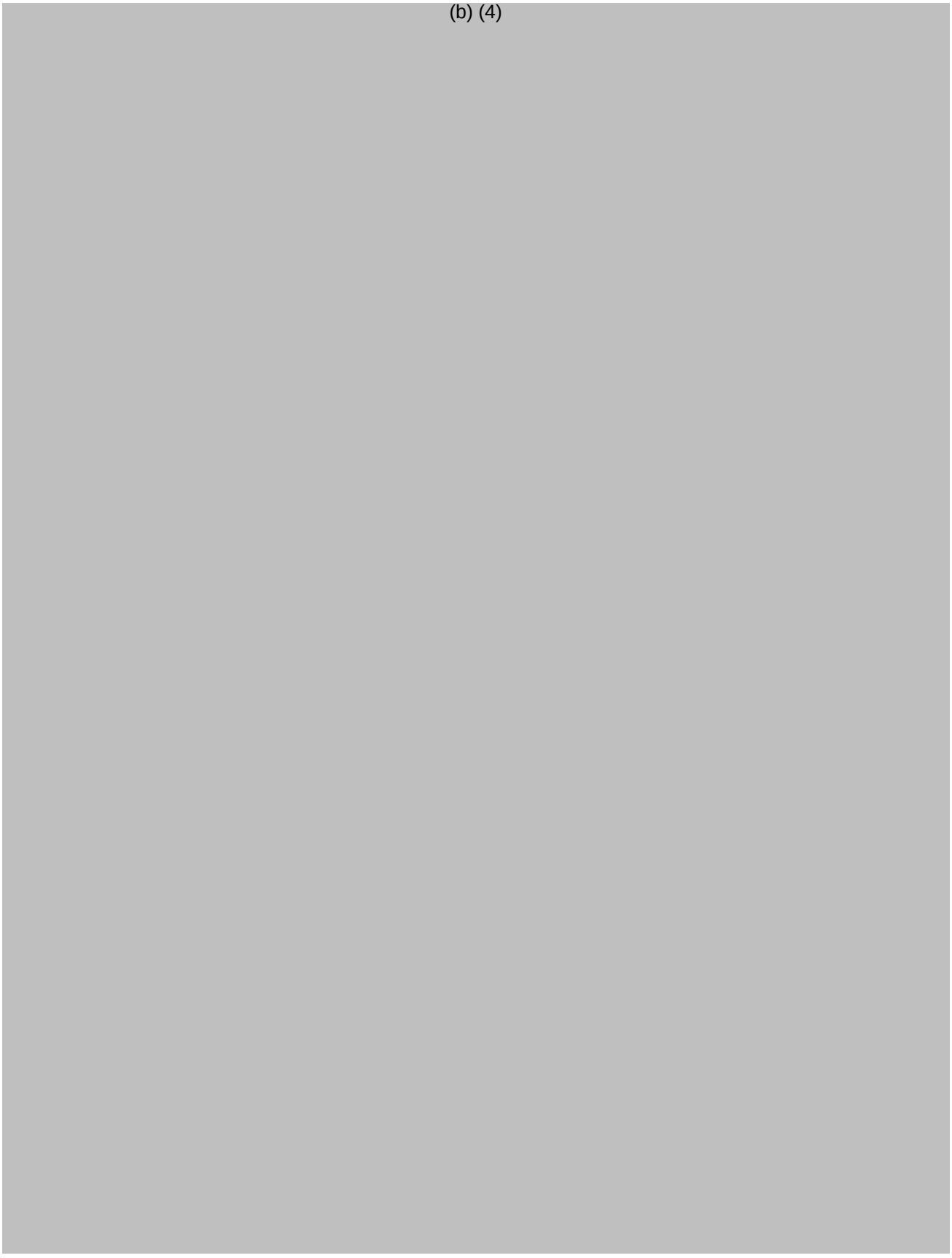
(b) (4)

Table 2 below lists the cold rooms, freezers, refrigerators, and the (b) (4) freeze/thaw systems associated with the manufacture of the BNT162b2 drug substance.

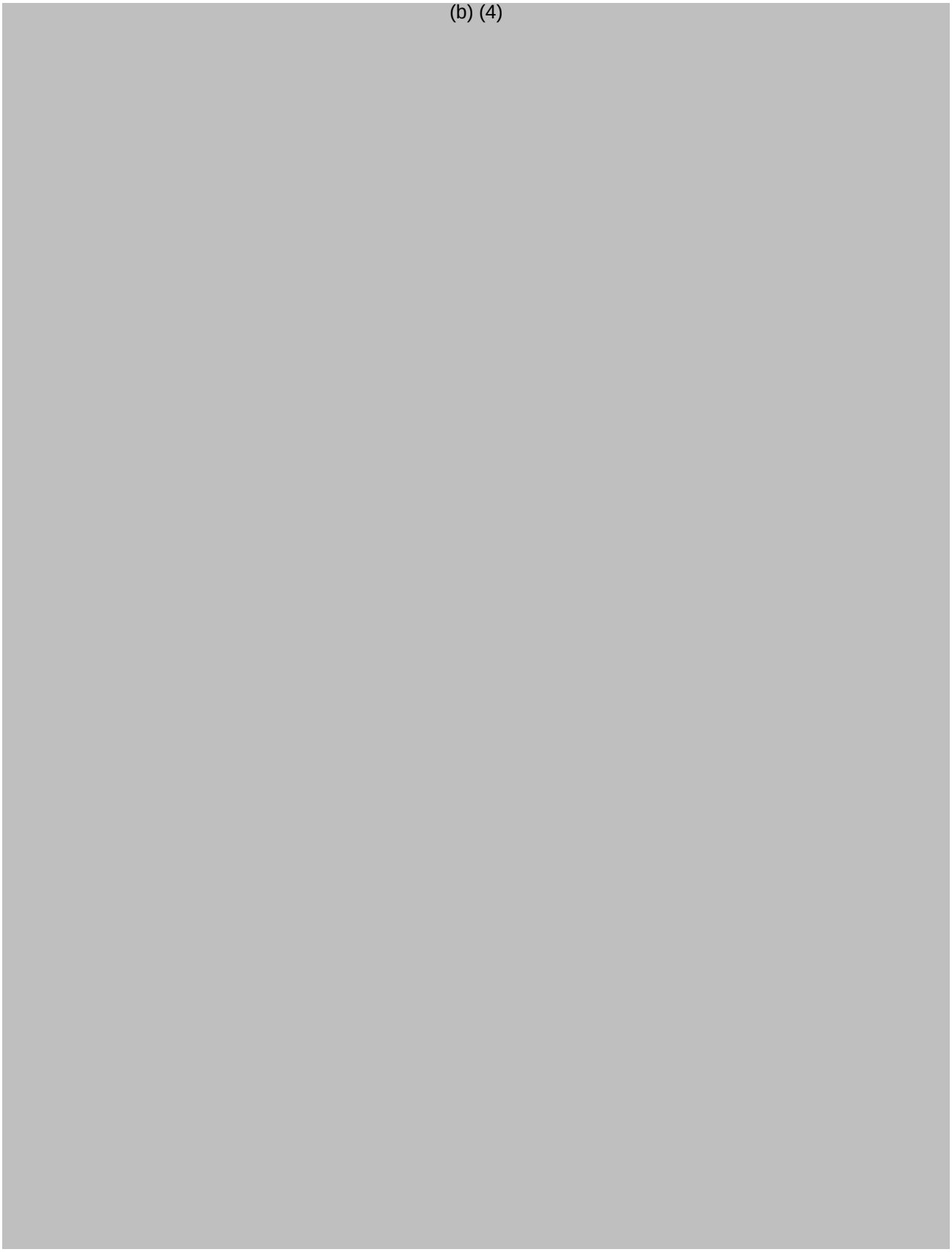
Table 2. (b) (4) Cold Rooms, Freezers, Refrigerators and the (b) (4) Freeze/Thaw Systems

Equipment	Description	IQ	OQ	PQ
(b) (4)				

(b) (4)



(b) (4)



(b) (4)

(b) (4)

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 3

Regarding the recent Information Request (IR) responses (Response to FDA 26 Jul 2021 and Response to the August 5, 2021 FDA IR) STN 125742/0.24 and STN 125742/0.43, the Agency has additional inquiries for the Kalamazoo facility. You provided Table 8 (appended in the Response to August 5, 2021 FDA IR), which lists the BNT162b2 product contact equipment. Please provide the operational and performance qualification (OQ/PQ) summary documents for all new pieces of equipment. In addition, please provide representative OQ/PQ summary documents for all families or groupings of tanks, regardless of whether they are existing or new.

RESPONSE 3

The operational and performance qualification (OQ/PQ) summary documents for the new equipment is contained in (b) (4) COVID Vaccine (b) (4) Formulation Umbrella Summary System Acceptance and Release Report and (b) (4) COVID Vaccine Formulation Tank (b) (4) System Acceptance and Release Report. The (b) (4) COVID Vaccine Formulation Tank (b) (4) System Acceptance and Release Report is a representative summary document for all groups of tanks, including existing tanks as the qualification strategy and testing is the same.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

(b) (4) COVID Vaccine (b) (4) Formulation Umbrella Summary System Acceptance and Release Report, New

(b) (4) COVID Vaccine Formulation Tank (b) (4) System Acceptance and Release Report, New

Previously submitted supporting documentation

None

QUERY 4

Regarding the equipment utilities at Pfizer-Kalamazoo please provide the following information:

a. Please provide the WFI/PW water quality criteria and a description of the monitoring program.

b. Please provide all uses of the compressed air and nitrogen specific to BNT162b2 manufacture. If the respective utility is used in the process, please provide the monitoring limits.

RESPONSE 4

a. The Water for Injection (WFI)/Purified Water (PW) water quality criteria are presented in Table 4.

Table 4. Water Quality Criteria

Test	Purified Water	Water for Injection
(b) (4)		

(b) (4)

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 5

Regarding the cleaning validation summary for the direct product-contact equipment at Pfizer-Kalamazoo, please provide the following information:

a. Please provide the data to support the validated clean hold times for all direct product-contact equipment.

b. Please explain why the acceptance criterion for residual cleaning agent is higher for the BNT162b2 (b) (4)) than it is for the other equipment (b) (4)).

RESPONSE 5

a. The data to support the validated clean hold times for all direct product contact equipment is provided in Table 5.

Table 5. Clean Hold Times for Product Contact Equipment

Equipment	Validated Clean Hold Time	Test	Results
(b) (4)			

(b) (4)

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 6

Regarding visual inspection of the BLA process validation lots of BNT162b2 filled vials at Pfizer-Kalamazoo, please provide the following information:

a. Please describe which PPQ/process validation lots were 100% visually inspected by automated inspection and which lots were 100% visually inspected manually.

b. Please provide the acceptance criteria for the allowable limit of rejects during visual inspection.

c. Please provide the defect/reject categories and the percentage of the rejects in each category for each BLA process validation lot.

RESPONSE 6

a. The inspection process for each PPQ/process validation lot is presented in Table 6.

Table 6. PPQ Lot Inspection Process

Drug Product Lot	Inspection Process
(b) (4)	

b. The allowable alert limit of rejects for visual inspection are (b) (4)

c. The defect categories and the percentage of defects in each category for each BLA process validation lot are presented in Table 7.

Table 7. Process Validation Inspection Results

Defect Type	Action Limit	Lot Number
		(b) (4)
(b) (4)		

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 7

Please update section 3.2 A.1 with the current cleaning validation status at Pfizer Puurs. Please update the status of your microbiological cleaning validation, outstanding manual cleaning and any cleaning validation deviation information, as applicable.

RESPONSE 7

The applicant confirms that cleaning validation for BNT162b2 will be completed by end of September 2021, including the microbiological cleaning validation, as committed via Response to FDA 26 July 2021 Information Request Regarding Manufacturing and Equipment, Query 15 (STN 125742.0/25 submitted 30 Jul 2021). As the cleaning validation approach is still being implemented, a cleaning verification is performed by visual check and the equipment remains dedicated to BNT162b2.

(b) (4)

An overview of the cleaning validation status is presented in Table 8.

Table 8. Overview Cleaning Validation Status for BNT162b2 in Puurs

Equipment	Cleaning Validation Status
(b) (4)	

No deviations impacting the cleaning validation have occurred. The Cleaning Validation Summary (Puurs) will be updated upon completion of the cleaning validation.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

Response to FDA 26 July 2021 Information Request Regarding Manufacturing and Equipment, Query 15 (STN 125742.0/25 submitted 30 Jul 2021)

A.1 Cleaning Validation Summary (Puurs)