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**LIST OF TABLES**

(b) (4)



**QUERY 1**

Please clarify whether the (b) (4) [redacted] can be stored. If so, please provide details regarding the container closure that is used for the storage of the materials and the maximum storage time.

**RESPONSE 1**

Both the (b) (4) [redacted] may be stored prior to further processing.  
(b) (4) [redacted]

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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**QUERY 2**

Please provide information on the container closure used for the (b) (4) as this material is shipped for further processing.

**RESPONSE 2**

The (b) (4) is stored in (b) (4) containers with a (b) (4)

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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**QUERY 3**

Please provide the maximum hold time for each manufacturing step of the (b) (4) (b) (4) and provide (b) (4) hold time study data for any hold greater than 24 hours.

**RESPONSE 3**

The manufacturing steps of the (b) (4) are routinely performed (b) (4) .

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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**QUERY 4**

Regarding (b) (4) manufacturing, please provide the in-process action limit for bioburden and endotoxin.

**RESPONSE 4**

In-process bioburden and endotoxin samples are evaluated at the steps as described in [Table 3.2.S.2.3-7. Process Flow for \(b\) \(4\)](#). If in-process bioburden results of (b) (4) are exceeded then an investigation is opened to determine product impact, identify root cause, and evaluate relevant preventative actions.

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

(b) (4)

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**QUERY 5**

Please clarify that bioburden sampling for the (b) (4) is taken at the (b) (4) (b) (4).

**RESPONSE 5**

In-process bioburden samples described in [Table 3.2.S.2.3-7. Process Flow for \(b\) \(4\)](#) (b) (4) are taken after the (b) (4) (b) (4).

The final (b) (4) is sampled (b) (4) (b) (4).

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

(b) (4)

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**QUERY 6**

Please provide the shipping validation for shipments of (b) (4) (b) (4)

Additionally, clarify if all shipments of (b) (4) will be temperature monitored and shipped via validated shipping methods.

**RESPONSE 6**

The shipping validation assessed the (b) (4) (b) (4) for shipment of (b) (4) from (b) (4) to (b) (4).

(b) (4)



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Analysis of the temperature monitor data for each of the shipments demonstrates that the temperatures of the (b) (4) were adequately controlled and remained below the (b) (4) (b) (4) when being transported in the (b) (4) shipper from (b) (4) to (b) (4)

All shipments of (b) (4) will be temperature monitored and shipped via validated shipping methods.

### **Literature References**

None

### **SUPPORTING DOCUMENTATION**

#### **New or Replaced Supporting Documentation**

None

#### **Previously submitted supporting documentation**

(b) (4)

**QUERY 7**

Regarding the (b) (4) hold time study, please clarify what (b) (4) (b) (4) media was tested, and how many replicates were performed.

**RESPONSE 7**

(b) (4)



**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

**QUERY 8**

Please include the acceptance criteria for (b) (4)  
(b) (4) study (applicable to both (b) (4)

**RESPONSE 8**

The acceptance criteria (applicable to both (b) (4) (b) (4)  
testing during (b) (4)  
respectively.

(b) (4)

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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**QUERY 9**

Please clarify how microbial control is verified during long term storage of the (b) (4) (b) (4) samples should be taken at the end of storage and prior to cleaning (applicable to both (b) (4) and (b) (4) )

**RESPONSE 9**

Membranes are stored long term in (b) (4) (b) (4) Therefore, samples cannot be taken and tested at the end of storage to demonstrate microbial control.

In order to demonstrate that the membranes are ready for production following long term storage, the following methodology is applied for both (b) (4) (b) (4) (b) (4)

[Redacted content]

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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**QUERY 10**

Please clarify if any drug substance direct product contact items (e.g., single-use system, tubing, gaskets, small parts) used in either (b) (4) are autoclave sterilized. If so, please provide the autoclave load validation summary report for the heat penetration studies. Ensure that the heat penetration information includes a detailed description of each autoclaved item (i.e., size and length of tubing, type of filter, size of container, wrapping in bag, etc.), thermocouple and biological indicator placement locations, cycle parameters used during validation and in normal production operations, validation acceptance criteria, results and any deviations.

**RESPONSE 10**

(b) (4)



**Literature References**

None

**SUPPORTING DOCUMENTATION**

Note: The unlinked supporting documents will be submitted to BLA 125742 the week of 02 August 2021.

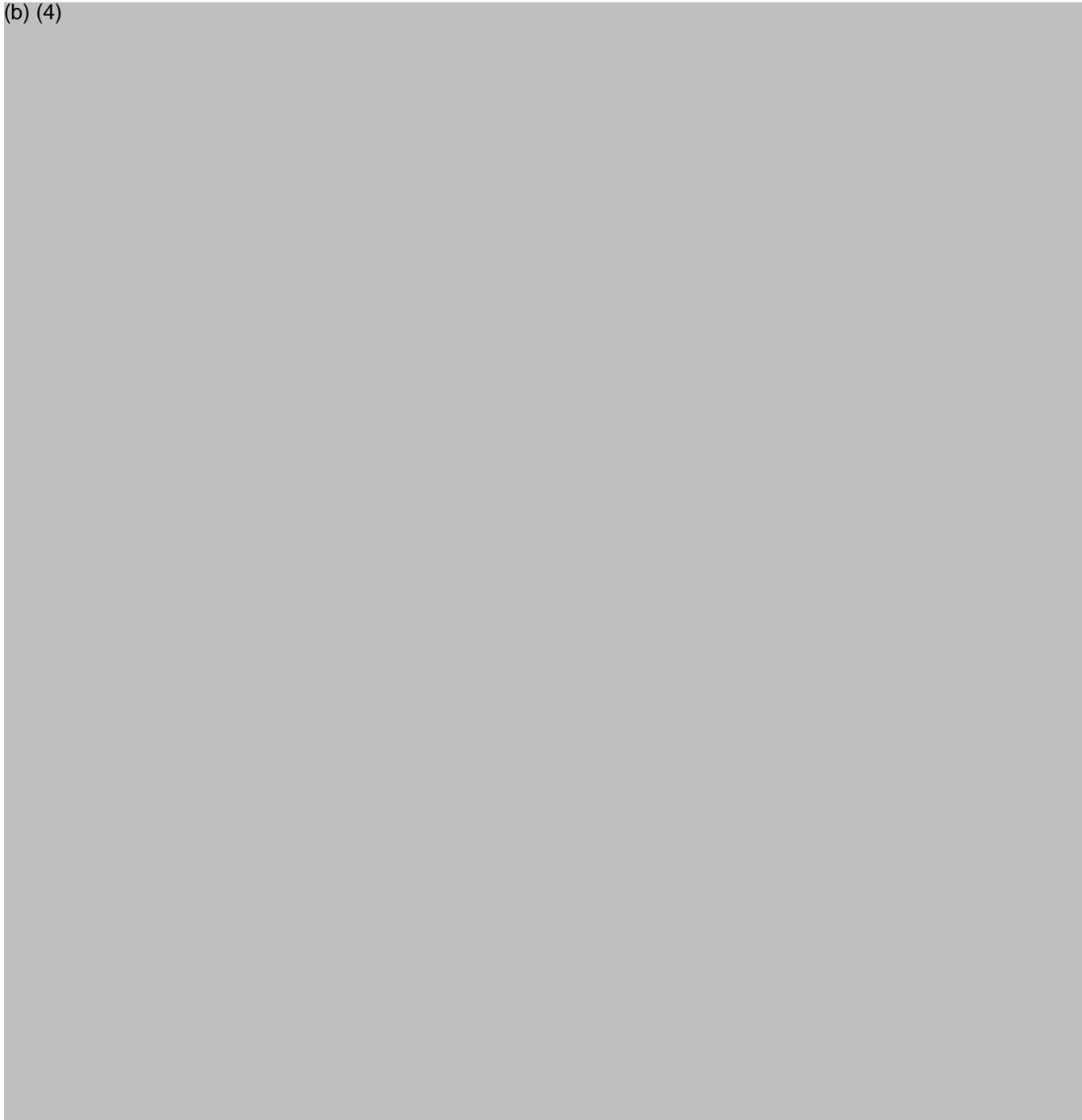
**New or Replaced Supporting Documentation**

(b) (4)



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(b) (4)



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### **QUERY 11**

Please provide the latest sterilization/depyrogenation revalidations for the stopper processors used to support the (b) (4) [REDACTED] were both performed in 2019. This request is specific to Pfizer Puurs.

### **RESPONSE 11**

The latest sterilization/depyrogenation revalidations are included in the updated Section 3.2.P.3.5 Stopper Depyrogenation and Sterilization [Puurs (b) (4) [REDACTED]] and Section 3.2.P.3.5 Vial Depyrogenation [Puurs (b) (4) [REDACTED]].

#### **Literature References**

None

#### **SUPPORTING DOCUMENTATION**

##### **New or Replaced Supporting Documentation**

[Section 3.2.P.3.5 Stopper Depyrogenation and Sterilization \[Puurs \(b\) \(4\) \[REDACTED\]\]](#), replaced

[Section 3.2.P.3.5 Vial Depyrogenation \[Puurs \(b\) \(4\) \[REDACTED\]\]](#), replaced

##### **Previously submitted supporting documentation**

None

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## **QUERY 12**

Regarding Section 3.2.P.3.5 for the (b) (4) sterilizing filter, you state “for batch sizes (b) (4) in markets where registered, a (b) (4) filter may also be used”. Please clarify if this statement was intended for BLA 125742. If this is the case, please supply the filter integrity test limits for the (b) (4) filter and the supporting validation report. This request is applicable to both drug product sites of Pfizer Puurs and Kalamazoo.

## **RESPONSE 12**

The applicant confirms that the referenced statement is not applicable to BLA 125742; as described in Section 3.2.P.3.2 Batch Formula, the intended commercial batch size range for BLA 125742 is (b) (4) Section 3.2.P.3.5 Sterilizing Filter Membrane Validation – (b) (4) has been updated to remove information related to the (b) (4) filter.

### **Literature References**

None

### **SUPPORTING DOCUMENTATION**

#### **New or Replaced Supporting Documentation**

[Section 3.2.P.3.5 Sterilizing Filter Membrane Validation – \(b\) \(4\)](#), replaced

#### **Previously submitted supporting documentation**

[Section 3.2.P.3.2 Batch Formula](#)

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**QUERY 13**

Regarding Section 3.2.P.3.5 for the (b) (4) sterilizing filter, the interim validation report for the (b) (4) filter in contact with BNT162b2 performed by the (b) (4) (b) (4) issued 06 Dec 2020 was submitted. Please submit the final report from (b) (4) and provide the supporting data for the integrity test parameters provided for (b) (4) (b) (4). This request is applicable to both drug product sites of Pfizer Puurs and Kalamazoo.

**RESPONSE 13**

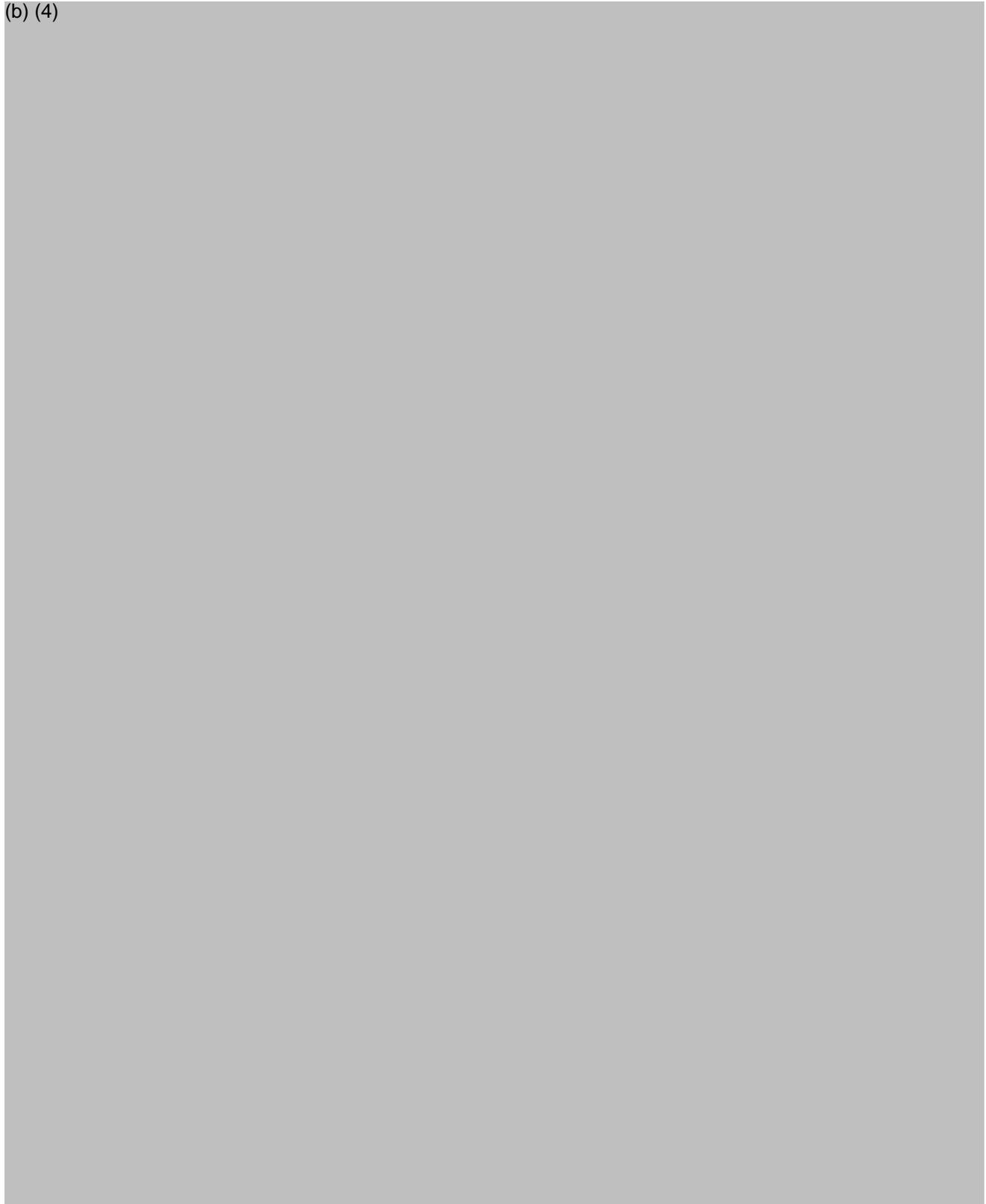
The final validation report for the (b) (4) filter is included, please refer to [INX100449287](#).

(b) (4)



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(b) (4)



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(b) (4)



**Literature References**

None

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COVID-19 Vaccine (BNT162, PF-07302048)

BLA 125742/0

Response to 26 Jul 2021 FDA queries – Comments regarding manufacturing and equipment

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## **SUPPORTING DOCUMENTATION**

### **New or Replaced Supporting Documentation**

[INX100449287](#), new

### **Previously submitted supporting documentation**

None

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#### **QUERY 14**

In Section 3.2.P.3.5 noting the shipping information, it is stated that you are currently qualifying a (b) (4) capable of maintaining BNT162b2 at (b) (4) and the transport inside a (b) (4). Please indicate if all shipments of BNT162b2 drug product transported via the (b) (4) and in the (b) (4) are continuously temperature monitored to confirm that the appropriate temperatures are maintained.

Please also provide an estimated time of completion for the ongoing shipping studies and the procedures that support these shipping methods. This request is applicable to both drug product sites of Pfizer Puurs and Kalamazoo.

#### **RESPONSE 14**

Pfizer confirms that all shipments of BNT162b2 drug product will be continuously temperature monitored to confirm that the appropriate temperatures are maintained via (b) (4) and in the (b) (4).

Pfizer has not yet operationalized shipment at (b) (4) from either Pfizer Puurs or Pfizer Kalamazoo and studies are still ongoing. Pfizer expects to complete qualification studies not later than November 2021 and commits to providing results of these studies prior to implementation.

#### **Literature References**

None

#### **SUPPORTING DOCUMENTATION**

##### **New or Replaced Supporting Documentation**

None

##### **Previously submitted supporting documentation**

None

**QUERY 15**

Please provide an update on the time frame for the completion of the microbial cleaning validation of BNT162b2 equipment in (b) (4)

(b) (4). This request is specific to Pfizer Puurs.

**RESPONSE 15**

The applicant confirms that Pfizer Puurs expects its microbial cleaning validation of BNT162b2 equipment to be completed by end of September 2021.

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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**QUERY 16**

Regarding the BNT162b2 major manufacturing equipment used at Pfizer Kalamazoo, the Agency requests the following information:

**QUERY 16a**

The qualification summaries including dates of completion for all new direct product contact equipment not included in the initial EUA submission relating to BNT162b2 manufacture.

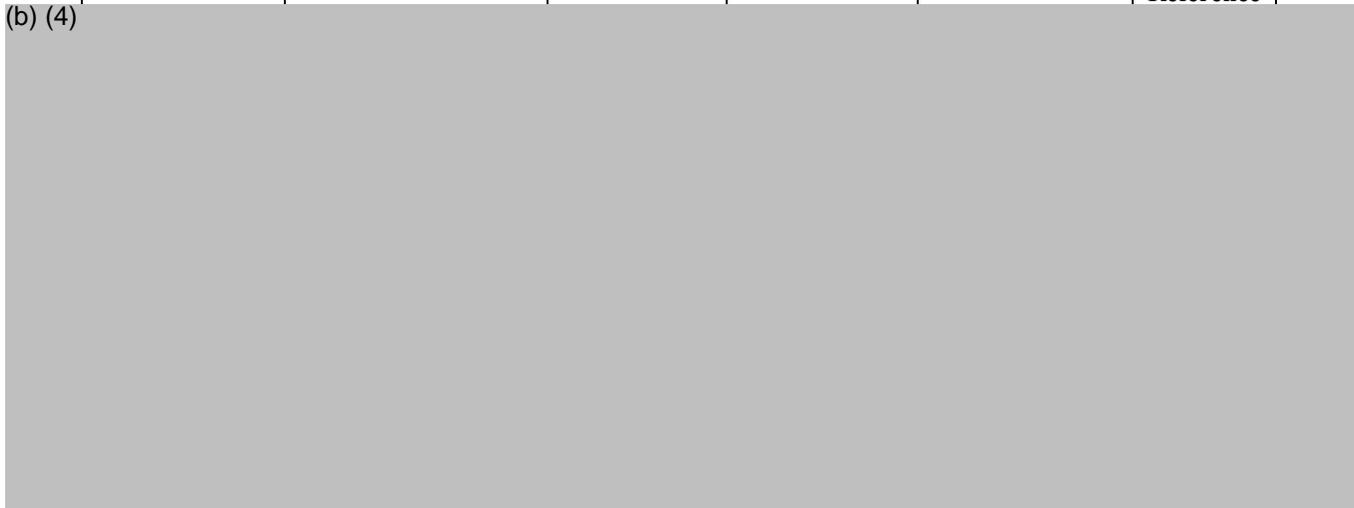
**RESPONSE 16a**

The qualification of all new direct product contact equipment not included in the initial EUA submission relating to BNT162b2 manufacture is summarized in Table 5.

**Table 5. Major Manufacturing Equipment Qualification Status**

<b>Equipment</b>	<b>Use</b>	<b>Status</b>	<b>Initial Qualification</b>	<b>Last Requalification</b>	<b>IND 19736 Submission Reference</b>
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(b) (4)



**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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**QUERY 16b**

It appears the (b) (4) . Please clarify the (b) (4) and provide the (b) (4) study protocol and summary, if available.

**RESPONSE 16b**

As described in Section 3.2.P.3.5 (b) (4) (b) (4) [Kalamazoo] (submitted in seq 0019 (b) (4))

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

PPQ Protocol for COVID-19 VX (b) (4) (b) (4), new

**Previously submitted supporting documentation**

Section 3.2.P.3.5 (b) (4) (b) (4) [Kalamazoo]

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**QUERY 16c**

Please confirm that all product contact equipment is dedicated to BNT162b2 manufacture.

**RESPONSE 16c**

It is confirmed that all product contact equipment is dedicated to BNT162b2 manufacture.

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

**QUERY 16d**

Please clarify if the dedicated product contact equipment used to manufacture BNT162b2 is product dedicated or campaign dedicated. If campaign dedicated, please identify the nature of the products with which it will be shared following the end of the campaign.

**RESPONSE 16d**

The dedicated product contact equipment used to manufacture BNT162b2 is product dedicated.

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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**QUERY 16e**

Please explain if the drug product contact equipment for BNT162b2 is new equipment or existing equipment which have been repurposed. If it has been repurposed, please identify the products used on the equipment previously and provide the changeover procedures for the equipment prior to dedication to BNT162b2.

**RESPONSE 16e**

The drug product contact equipment for BNT162b2 indicating if equipment is new or existing, identifying products using the equipment previously, and changeover procedure is summarized in Table 6. None of the previous products are considered potent compounds.

**Table 6. Drug Product Contact Equipment Summary**

<b>Equipment</b>	<b>Location</b>	<b>Equipment ID Number</b>	<b>New or Existing</b>	<b>Previous Product(s)</b>	<b>Changeover Procedure Prior to BNT162b2 Dedication</b>
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(b) (4)



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**Table 6. Drug Product Contact Equipment Summary**

Equipment	Location	Equipment ID Number	New or Existing	Previous Product(s)	Changeover Procedure Prior to BNT162b2 Dedication
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(b) (4)



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**Table 6. Drug Product Contact Equipment Summary**

Equipment	Location	Equipment ID Number	New or Existing	Previous Product(s)	Changeover Procedure Prior to BNT162b2 Dedication
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**Table 6. Drug Product Contact Equipment Summary**

Equipment	Location	Equipment ID Number	New or Existing	Previous Product(s)	Changeover Procedure Prior to BNT162b2 Dedication
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(b) (4)



**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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**QUERY 16f**

Regarding the cleaning validation summary for the direct product-contact equipment, please provide the rationale for not sampling bioburden or endotoxin for most of the equipment as part of your cleaning validations. In addition, please provide the necessary data that demonstrates the proposed cleaning cycles adequately remove bioburden and endotoxin from all product-contact equipment.

**RESPONSE 16f**

New equipment is evaluated per site Standard Operating Procedure to determine the cleaning validation requirements.

(b) (4)



[Table 7](#) presents bioburden and endotoxin data which supports the equipment used in the manufacture of BNT162b2 drug product.

**Table 7. Direct Product Contact Equipment Bioburden and Endotoxin Data**

	<b>Equipment</b>	<b>Indicator</b>	<b>Results</b>	<b>Limit</b>
(b) (4)				

**Literature References**

None

**SUPPORTING DOCUMENTATION**

**New or Replaced Supporting Documentation**

None

**Previously submitted supporting documentation**

None

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