From: Smith, Michael (CBER)
Sent: Thursday, August 5, 2021 1:48 PM
To: Harkins Tull, Elisa <Elisa.HarkinsTull@pfizer.com>; Aghajani Memar, Neda <Neda.AghajaniMemar@pfizer.com>; Devlin, Carmel M <Carmel.Devlin@pfizer.com>; Rohlfing, Paul <Paul.Rohlfing@pfizer.com>
Cc: Naik, Ramachandra <Ramachandra.Naik@fda.hhs.gov>; Gottschalk, Laura <Laura.Gottschalk@fda.hhs.gov>
Subject: STN 125742.0: 11 Facilities questions

Elisa,

The review team has the below 11 facilities questions, please respond as soon as possible but no later than COB Wednesday, August 11, 2021.

(b) (4) **(Pfizer, Chesterfield):**

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) (b) (4) or routine monitoring).

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.

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) (4) (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) (b) (4) (b) (4)) during routine production.

Drug Substance (Pfizer Andover; Both (b) (4) **and** (b) (4)

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.

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) , (b) (4)).

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. 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) (b) (4)

Drug Product:

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.

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) .

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

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.

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:
    a. Please provide the equipment numbers and when qualification is expected to be completed (if not previously completed).
    b. 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.
    c. 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.
    d. Please address whether these tanks have been used in the manufacture of EUA BNT162b2 material prior to qualification.

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

Regards,

Mike

- Please confirm receipt of this e-mail and let us know if you have any questions.

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