From: Gottschalk, Laura
Sent: Monday, July 26, 2021 7:19 PM
To: Harkins Tull, Elisa <Elisa.HarkinsTull@pfizer.com>
Cc: Naik, Ramachandra <Ramachandra.Naik@fda.hhs.gov>; Smith, Michael (CBER) <Michael.Smith2@fda.hhs.gov>; Devlin, Carmel M <Carmel.Devlin@pfizer.com>; Aghajani Memar, Neda <Neda.AghajaniMemar@pfizer.com>; Rohlfing, Paul <Paul.Rohlfing@pfizer.com>
Subject: STN 125742/0 – COMIRNATY (COVID-19 Vaccine, mRNA) – Comments regarding manufacturing and equipment

Dear Ms. Harkins:

Our review of the information provided in your BLA STN 125742/0 for COMIRNATY (COVID-19 Vaccine, mRNA), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older, is ongoing. We have the following comments and requests for additional information:

(b) (4) ***(Pfizer,*** (b) (4)

1. Please clarify whether the (b) (4) 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.

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

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.

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

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

6. Please provide the shipping validation for shipments of (b) (4) (b) (4) (b) (4) Additionally, clarify if all shipments of (b) (4) (b) (4) will be temperature monitored and shipped via validated shipping methods.

Drug Substance (Pfizer, (b) (4)

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

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

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)

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.

Drug Product:

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

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.

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) 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) . This request is applicable to both drug product sites of Pfizer Puurs and Kalamazoo.

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) - (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.

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.

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

    a. 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.

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

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

    d. 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.

    e. 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.

    f. 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.

Please provide your response in an Amendment to STN 125742/0 by August 2, 2021. If you have any questions about this communication, please feel free to contact me.

Best regards,
Laura

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