From: Smith, Michael (CBER)
Sent: Tuesday, August 3, 2021 4:55 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: CMC-related questions

Elisa,

Our review of the information provided in your BLA STN 125742 for COMIRNATY (COVID-19 mRNA Vaccine), 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 CMC-related comments and requests for additional information.

1. In Section 3.2.S.2.5 Process Validation and/or Evaluation – Shipping Performance Qualification, you stated that the expected transit time for shipment of the (b) (4) DS from the Pfizer Andover DS manufacturing site to the Pfizer Kalamazoo and Pfizer Puurs DP manufacturing sites is (b) (4), respectively. Please provide supportive data to demonstrate that the physicochemical and biological attributes of the DS are not impacted after exposure to the shipping hazards (e.g., shock, vibration, pressure, thermal hazards, etc.). Please note that the data should be able to support the worst-case transit time of (b) (4) (b) (4) DS.

2. Please update the Table 3.2.S.2.5-2 "Performance Tests for Commercial Scale (b) (4) Validation and Routine Batches" in Section 3.2.S.2.5 Process Validation and/or Evaluation – Additional Process Evaluation to include the acceptance criteria/action limit for the (b) (4) performance-related parameters based on the results from the initial validation studies and the experience from commercial production.

3. In document INX100433827: COVID-19 Vaccine Drug Substance Process Validation Final Report, a deviation (PR ID 5222684) described that for PPQ batches 20Y513C301 – 20Y513C601, (b) (4) was set (b) (4). However, in

Table 4-5 Results for Additional Process Inputs, (b) (4) (4) rate for all the impacted batches was recorded as (b) (4) Please explain this discrepancy.

4. Regarding the process validation and/or evaluation for the (b) (4) (b) (4) in Pfizer Kalamazoo and Pfizer Puurs, please describe any process controls and performance verification implemented at the DS (b) (4) during PPQ execution and provide available data to support the use of both (b) (4) (b) (4) . Please also confirm that the (b) (4) (b) (4) for all evaluated PPQ lots was within the target (b) (4)

5. Please update the Table 3.2.A.3.1.1-1 Nomenclature of ALC-0315 in Section 3.2.A.3.1.1 Nomenclature [ALC-0315] to include the product number/code for the lipid ALC-0315 manufactured in (b) (4)

6. Regarding your response (in STN 125742/0.16 dated July 23, 2021) to our IR query 3 dated July 9, 2021, about the validation of the CGE Integrity method, we do not agree that a conclusion of a quantification limit of (b) (4) (b) (4) . The results as shown in Table 3 may infer a quantification limit for (b) (4) (b) (4) (b) (4) We acknowledge that the assay is not for the assessment of impurity and the actual quantification limit for impurity was not determined.

Please provide your response in an Amendment to STN 125742/0 by Friday, August 6, 2021. If you have any questions about this communication, please feel free to contact us.

Regards,

Mike

- Please confirm receipt of this e-mail.

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