CMC Review Memorandum

Date: August 12, 2021

To: The File

From: Anissa Cheung, DVP, Product Specialist

Through: Jerry Weir, DVP

CC: Ramachandra Naik, DVRPA, Chair;
Michael Smith, DVRPA, RPM;
Laura Gottschalk, DVRPA, RPM;
Kathleen Jones, DMPQ, Lead Inspector

Applicant name: Wyeth BioPharma Division of Wyeth Pharmaceuticals, LLC.

STN: STN 125742/0 Amendment #25
COVID-19 mRNA Vaccine (BNT162/PF-07302048)

Subject: Original BLA submission

Short summary: Applicant's response to observations issued during the FDA Pre-License Inspection

A Pre-License Inspection at Wyeth BioPharma Division of Wyeth Pharmaceuticals, LLC. at Andover, MA for the manufacture of COVID-19 mRNA Drug Substance (DS) was performed between July 19 and July 23, 2021 for COMIRNATY Biological License Application. At the end of the inspection, thirteen inspectional observations were identified. In this submission, the applicant provides response including follow up actions to address these observations and to assure that their product is safe and effective.

My review covers applicant's response on observation 1.

Observation 1

There is insufficient data to support product quality prior to the release of BNT162b2 drug substance (DS) batch (b) (4) manufactured at (b) (4) Pfizer Andover on (b) (4) . (b) (4) was derived from (b) (4) batch (b) (4) and a deviation ((b) (4)) was initiated due to the multiple control limit excursions during the (b) (4) of (b) (4) The (b) (4) were below the control limits and the (b) (4) between (b) (4) and overall (b) (4) (b) (4) both exceeded the control limits. The affected batch (b) (4) was manufactured with a process that deviated from the validated process parameters, and your firm planned to put this batch on stability

to further assess product quality. However, DS batch (b) (4) was not put on stability until July 22, 2021. The affected DS batch was released on (b) (4) and formulated into (b) (4) drug product (DP) lots ((b) (4)) at (b) (4) on (b) (4) . All (b) (4) DP lots were released on (b) (4) .

Applicant's response:
The firm acknowledges that they did not enroll the affected DS lot immediately. In addition, an error was made when they notified FDA in writing on (b) (4) about the deviation associated with DS batch (b) (4) . In that communication, Pfizer stated that the affected DS batch was enrolled on stability, but, in fact, they only commit to enroll the batch on stability no later than September 30, 2021. For the release of the DS batch, Pfizer's Quality Assurance (QA) reviewed all data associated with this affected batch including in process critical quality attributes and DS final release results. All release data were within DS specifications and all critical quality attributes ((b) (4) (b) (4) were within expected historical experience. QA performed a holistic review of all deviations associated to this DS batch, and they concluded that there was no impact to product quality. (b) (4) drug product (DP) lots ((b) (4)) were manufactured at Pfizer (b) (4) from DS batch (b) (4) . Pfizer reviewed the batch release data for these DP batches and all results are within release specifications and within historical experience.

Pfizer proposes the following action to be implemented to prevent the recurrence of delaying the enrollment of DS lots in a stability program:

- Procedure (b) (4) will be revised and made effective to include the requirement that a drug substance batch be enrolled in a stability program within (b) (4) (b) (4) from the date of determination an enrollment is made.
- The procedure will include a requirement for a justification as to why the batch is being enrolled on stability, including whether the stability data is required for drug substance batch release.
- Relevant individuals will be trained per site procedures.

The committed deadline for this action is September 15, 2021.

Reviewer's Comments:
The applicant provides adequate response to address the above observation. (b) (7)(E), (b) (5)