1. RESPONSE TO FDA COMMENTS ON STN 125752: INFORMATION REQUEST #40 DATED DECEMBER 21, 2021

The Sponsor acknowledges FDA COMMENTS ON STN 125752: INFORMATION REQUEST #40 DATED 21 DECEMBER 2021 in (**BOLD**)

Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: CMC Our review of your August 16, 2021 submission (STN 125752/1) is ongoing. We have the following request for additional information:

Information Request

We reviewed the CMC information submitted to BLA 125752 and have the following comments:

ITEM 1:

Regarding the revised proven acceptable ranges (PARs) proposed for total cumulative process duration (CPD) of (b) (4) **and cumulative time out of refrigeration (TOR) of** (b) (4) **please revise all mRNA-1273 Drug Product (DP) eCTD sections of the BLA where appropriate.**

Sponsor Response:

The applicable eCTD sections of the BLA have been revised as indicated in Section 2 of this submission.

ITEM 2:

In section 3.2.P.2.3.1.2.3 Characterization of Cumulative Process Duration, please include:
a. Available information to support the revised PARs for CPD and TOR such as the information provided to support the same changes under EUA 27073; e.g., release testing results, CPDs and TORS for all Catalent DP lots manufactured with exceeded or non-exceeded process durations up to September 2021.

b. Available information on process duration deviations at Baxter and release testing results, CPDs and TORS for all Baxter DP lots manufactured with exceeded or non-exceeded process durations up to September 2021.

Sponsor Response:

Section 3.2.P.2.3.1.2.3 {Process Characterization} has been revised to include available information up to Mid November 2021 to support the revised PARs for CPD and TOR for mRNA-1273 DP lots manufactured at Catalent and Baxter.

ITEM 3:

3. In section 3.2.P.3.3 Description of Manufacturing Process and Process Controls {Baxter}, you indicated that two mRNA-1273 DP multiple dose presentations with fill volumes of 6.3 mL and 8.0 mL are manufactured; however, the information provided for the Baxter manufacturing process in all other sections of the BLA, including the process validation section, is for the 8.0 mL fill volume. Please clarify and, if necessary, revise the appropriate sections of the BLA.

Sponsor Response:

The mRNA-1273 DP 7.5 mL presentation with an 8.0 mL fill volume is the only presentation currently qualified for manufacture at Baxter. The eCTD Section 3.2.P.3.3 {Baxter} has been revised to reference only the mRNA-1273 DP 8.0 mL presentation.

2. SUMMARY OF CHANGES

The summary of revised Module 2 and Module 3 CTD sections that are being submitted with this quality information amendment are described in the following table.

CTD Section		Changes
2.3.P	Quality Overall Summary Drug Product	• Tables 29, 41, 42 and 45 have been revised to change the PAR for TOR from (b) (4)
3.2.P.2.3 {Process Characterization}	Manufacturing Process Development	• Tables 1 and 6 have been revised to change the PAR for TOR from (b) (4) • Section 3.2.P.2.3.1.2.3 has been revised to include supportive data (TOR, CPD, (b) (4) , mRNA-1273 LNP/DP release purity results from Baxter an Catalent lots manufactured through mid-November 2021).
3.2.P.2.3 {Comparability}	Manufacturing Process Development	• Sections 3.2.P.2.3.3.3, 3.2.P.2.3.3.4, 3.2.P.2.3.3.5 and 3.2.P.2.3.3.6 have been revised to change the PAR for TOR from (b) (4) • Tables 10 ,11, 12, 19 footnote b has been revised to change the PAR for TOR from (b) (4) and to reflect the PAR for CPD (TOR and (b) (4) • Tables 22 , 25, 28 and 31 footnote b has been revised to change the PAR for TOR from (b) (4)
3.2.P.3.3 {Baxter}	Description of Manufacturing Process and Process Controls	• Section 3.2.P.3.3.1 revised to remove reference to the (b) (4) presentation with a 6.3 mL fill volume