1. RESPONSE TO FDA COMMENTS ON INFORMATION REQUEST #38 RECEIVED ON DECEMBER 16, 2021

The Sponsor acknowledges INFORMATION REQUEST#38 dated 16 DECEMBER 2021 in (**BOLD**)

Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: CMC Information

Our review of your August 16, 2021 submission (STN 125752/1) is ongoing and we have the following requests for information regarding CMC information:

CX-024414 mRNA:

ITEM 1:

Please clarify which container closure system is used to store the linearized pDNA template lots manufactured at Aldevron and the containers used to store samples from the (b) (4) lots of pDNA template placed in the Aldevron long-term stability studies at -20°C ± 5°C.

Sponsor Response:

Linearized pDNA template lots manufactured at Aldevron are stored in (b) (4) (b) (4) The containers used to store samples from the (b) (4) lots of pDNA template placed in the Aldevron long-term stability studies at -20°C ± 5°C are (b) (4).

ITEM 2:

We reviewed the updated long-term stability data submitted in Amendment 29 on December 6, 2021 in response to our Information Request (IR) #25 dated November 29, 2021. Based on the available stability results for CX-024414 mRNA stored at -20°C ± 5°C, please (b) (4) the proposed shelf-life for this intermediate (b) (4) and update BLA section 3.2.S.7 *Stability {CX-024414 mRNA}* accordingly. The shelf life may be extended to (b) (4) (b) (4) post approval when supportive data become available.

Sponsor Response:

Based on the available stability results for CX-024414 mRNA stored at -20°C ± 5°C, the shelf-life has been (b) (4). Revised CTD Section 3.2.S.7.1 {CX-024414} is provided.

ITEM 3:

In Tables 1 and 2 of section 3.2.S.7.3 *Stability Data {CX-024414}*, the links to the stability reports correspond to CX-024414 mRNA Certificates of Analysis rather than to the stability reports referenced in this section. Please correct as appropriate.

Sponsor Response:

The links in Tables 1 and 2 of Section 3.2.S.7.3 Stability Data {CX-024414}, have been revised to correspond to appropriate CX-024414 stability reports. The latest stability data was provided as part of the responses to CMC information request (IR#25) in BLA 125752 SN 0029 dated December 03, 2021.

(b) (4)

ITEM 4:

Regarding the updated long-term stability data submitted in Amendment 29, in section 3.2.S.7.3 *Stability Data* {(b) (4) } Table 2 (b) (4) *Registration Stability Data,* we note that lot (b) (4) manufactured in process (b) (4) was added. However, no stability data or supportive CMC information were provided regarding the use of (b) (4) Please clarify whether (b) (4) will be used for commercial manufacture.

Sponsor Response:

(b) (4) is intended for commercial manufacture. The Sponsor acknowledges no stability data for lot (b) (4) was provided with Amendment 29 in Section 3.2.S.7.3 (b) (4) this lot was set down on stability October 20, 2021 and stability testing is ongoing and data is being reviewed. The approved stability data for lot (b) (4) will be provided in an informational amendment to BLA 125752 when available. Comparability data for manufacture on Process (b) (4) (b) (4) was added to Table 3 of Section 3.2.S.2.6.3.3.2 (b) (4) Comparability} as part of BLA 125752 SN 0014 dated October 15, 2021 demonstrating pre- and post-change results were comparable.

mRNA-1273 LNP DS:

ITEM 5:

Based on the available stability results submitted in Amendment 29 for mRNA-1273 LNP DS lots stored at -60°C to -90°C, please (b) (4) the proposed shelf life for the commercial mRNA-1273 LNP DS lots from (b) (4) and update BLA section 3.2.S.7 *Stability {mRNA-1273 LNP} accordingly*. The shelf life may be extended to (b) (4) post approval when supportive data become available.

Sponsor Response:

Based on the available stability results stored at -60°C to -90°C, the shelf-life has been (b) (4) from (b) (4) . Revised CTD Section 3.2.S.7.1 {mRNA-1273 LNP} has been provided.

(b) (4)

ITEM 6:

With regard to your response to item 5 in IR #25 dated November 29, 2021, you indicated that implementation of a (b) (4) step will be requested as an amendment to the BLA. We request that the implementation of this change be submitted as a prior approval supplement, post regulatory action on the BLA.

Sponsor Response:

(b) (4) qualification protocols have been submitted as part of the initial BLA submission in informational amendments as indicated in the following table and would be included as part of initial BLA approval.

(b) (4)

According to CBER guidance for industry: Chemistry, Manufacturing and Controls Changes to an Approved Application: Certain Biological Products June 2021, (b) (4)

Therefore, the Sponsor proposes that data generated as part of approved protocols could be provided as a CBE-30 informational amendment to BLA 125752.

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.S {CX-024414}	Quality Overall Summary Drug Substance	• Section 2.3.S.7.1 (page 43) revised initial shelf life from (b) (4)
2.3.S. {mRNA-1273 LNP}	Quality Overall Summary Drug Substance	• Section 2.3.S.7.1 (page 67) revised initial shelf life from (b) (4)
3.2.S.7.1 {CX-024414}	Stability Summary and Conclusions	• Page 2 Revised initial shelf life from (b) (4)
3.2.S.7.1 {mRNA-1273 LNP}	Stability Summary and Conclusions	• Page 2 Revised initial shelf life from