

1. RESPONSE TO FDA COMMENTS ON INFORMATION REQUEST#25 DATED NOVEMBER 29, 2021

The Sponsor acknowledges FDA Comments on INFORMATION REQUEST#25 for BLA 125752 dated 29 NOVEMBER 2021 in **(BOLD)**

Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: CMC Information

We are reviewing the CMC information submitted in the BLA STN 125752 regarding the (b) (4) mRNA-1273

LNP DS and mRNA-1273 Drug Product (DP) and have the following questions:

The following comments pertain to the (b) (4) :

ITEM 1:

(b) (4)

Sponsor Response:

Section 3.2.S.4.4 (b) (4) has been updated with the requested information.

ITEM 2:

(b) (4)

a. (b) (4)

b. (b) (4)

c. (b) (4)

Sponsor Response:

Moderna will update the appropriate documents, Section 3.2.S.2.2 (b) (4) and Section 3.2.S.2.5 (b) (4) with a maximum hold time of (b) (4) which is supported by Table 18 of Section 3.2.S.2.5. Moderna shall maintain a normal operating range of (b) (4) as currently utilized in production.

ITEM 3:

(b) (4)

Sponsor Response:

The Table 1s of CTD Sections 3.2.S.2.1 (b) (4) 3.2.S.2.1 {mRNA-1273 LNP} and 3.2.P.3.1 have been revised as summarized in Section 2 of this submission.

The following comment pertains to stability studies:

ITEM 4:

Please provide the most current stability data for (b) (4)

(b) (4) mRNA-1273 DS and DP and for any scale B or clinical and developmental lots.

Sponsor Response:

The most current available stability data have been included in the applicable CTD Section 3.2.S.7.1, 3.2.S.7.3, 3.2.P.8.1, 3.2.P.8.3 as summarized in Section 2 of this submission.

The following clarification pertains to re-processing:

ITEM 5:

The description of the manufacturing processes for the (b) (4)

(b) (4), mRNA-1273 LNP DS, and mRNA-1273 DP indicate that reprocessing is not performed for any process steps. However, process validation protocols were included for a (b) (4) step for (b) (4)

(b) (4) Please clarify if implementation of re-processing to include (b) (4) step will be requested for these process steps.

Sponsor Response:

Implementation of re-processing to include (b) (4) step will be requested for (b) (4) mRNA-1273 LNP manufacture at ModernaTX, Inc. and Lonza, Portsmouth. Moderna intends to execute (b) (4) as a response to events requiring reprocessing: container breach or filter integrity test failure. Moderna does not intend to preemptively execute (b) (4)

Implementation of re-processing to include (b) (4) step will be requested for mRNA-1273 DP manufacture at the Catalent Indiana, LLC, manufacturing site. The summary report is being generated and will be submitted to BLA 125752 in a future amendment.

2. SUMMARY OF CHANGES

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

CTD Section		Changes
(b) (4)		
3.2.S.2.1 {mRNA-1273 LNP}	Manufacturers	<ul style="list-style-type: none"> Table 1 added exclusion of particle size and polydispersity and %RNA Encapsulation from testing at the ModernaTX, Inc. QC Annex in Dedham, MA
(b) (4)		
3.2.S.7.1 {CX-024414}	Stability Summary	<ul style="list-style-type: none"> Minor formatting: Table 11, 3 month column "X" to "x" Table 12, 48 month column "X" to "x" Table 13, 6 month column "X" to "x."
3.2.S.7.3 {CX-024414}	Stability Data	<ul style="list-style-type: none"> Data additions: Lot 4007220002 12 month -20°C data and 6 month 5°C data added Lot 4007220003 12 month -20°C data and 6 month 5°C data added Lot 4007220004 6 month 5°C data added Lot 4007420003 9 month -20°C data and 3 month 5°C data added Lot 4007420004 6 month -20°C data and 3 month 5°C data added Lot 4007420006 3 month 5°C data added Lot 4007420007 3 month 5°C data added Lot 4007420021 3 month 5°C data added Lot 4007421013 6 month -20°C data and 3 month 5°C data added Lot 4007421017 3 month -20°C data and 3 month 5°C data added Lot 4007921001 3 month -20°C data and 3 month 5°C data added
(b) (4)		
3.2.S.7.3 {mRNA-1273 LNP}	Stability Data	<ul style="list-style-type: none"> Data additions: Lot 5006820002 12 month -60°C to -90°C data added Lot 5007521020 6 month -60°C to -90°C data added
3.2.P.3.1	Manufacturers	<ul style="list-style-type: none"> Table 1 added exclusion of particle size and polydispersity and %RNA Encapsulation from testing at the ModernaTX, Inc. QC Annex in Dedham, MA
3.2.P.8.1	Stability Summary	<ul style="list-style-type: none"> Table 2, Table 13 additions: Lot 6008921001 5°C 3 month arm added to protocol Lot 6010121002 5°C 3 month arm added to protocol Lot 6008221002 5°C 3 month arm added to protocol Lot 6008221003 5°C 3 month arm added to protocol Table 16 stability protocols for 6008921001, 6010121002, 6008221002, 6008221003 and to align 5°C protocol presentations
3.2.P.8.3	Stability Data	<ul style="list-style-type: none"> Data additions: Lot 6007320005 9 month -20°C data added Lot 6007320010 3 month -20°C data added Lot 6007520002 6 month 5°C data added Lot 6007520003 6 month 5°C data added Lot 6007920003 6 month 5°C data added Lot 6008520001 'Pending' data status resolved Lot 6009821002 3 month -20°C data added Lot 6010121002 3 month -20°C and 5°C data added Lot 6008221002 3 month -20°C and 5°C data added Lot 6008221003 3 month -20°C and 5°C data added Lot 6008921001 3 month -20°C and 5°C data added Lot 6009921006 3 month -20°C data added