

RESPONSE TO FDA COMMENTS ON INFORMATION REQUEST#27 DATED  
DECEMBER 06, 2021

The Sponsor acknowledges FDA Comments on INFORMATION REQUEST#27 dated 06 DECEMBER 2021 in **(BOLD)**

**Product: COVID-19 Vaccine, mRNA (SPIKEVAX)**

**Subject: Datasets**

**Our review of your August 24, 2021 submission (STN 125752/2) is ongoing.**

**Please refer to amendment #18 (seq 0020), submitted in response to the teleconference held between Moderna and CBER on October 29, 2021. We have the following comments/responses:**

**ITEM 1:**

**We acknowledge your response to the clinical IR (#24) dated November 30, 2021 regarding the analyses of asymptomatic and SARS-CoV-2 infection, submitted in amendment 28, on December 03, 2021. In your response, corrections were made for 2 subjects for asymptomatic infection and 3 subjects for SARS-CoV-2 infection. However, these corrections do not appear to fully address the issues related to mislabelled samples. Specifically, we note the following 29 discrepancies for asymptomatic infection as presented in Table 6-9 of the P301 CSR:**

**Table 1. Asymptomatic infection starting 14 days post Dose 2**

<b>USUBJID</b>	<b>ADTTEB.PAR AMCD</b>	<b>ADTTEB .CNSR</b>	<b>Date of first positive N- serology or PCR</b>	<b>Date of PDV or unblinding</b>	<b>Infected on or prior to PDV?</b>
<b>mRNA-1273- P301- US303- 2145</b>	<b>TASYCRB1</b>	<b>1</b>	<b>9-Jan-21</b>	<b>9-Jan-21</b>	<b>Yes</b>
<b>mRNA-1273- P301- US303- 2331</b>	<b>TASYCRB1</b>	<b>0</b>	<b>4-Feb-21</b>	<b>29-Jan-21</b>	<b>No</b>
<b>mRNA-1273- P301- US313- 2115</b>	<b>TASYCRB1</b>	<b>0</b>	<b>12-Mar-21</b>	<b>5-Feb-21</b>	<b>No</b>
<b>mRNA-1273- P301- US314- 2275</b>	<b>TASYCRB1</b>	<b>0</b>	<b>8-Mar-21</b>	<b>25-Jan-21</b>	<b>No</b>
<b>mRNA-1273- P301- US319- 2534</b>	<b>TASYCRB1</b>	<b>0</b>	<b>4-Feb-21</b>	<b>21-Dec-20</b>	<b>No</b>
<b>mRNA-1273- P301- US320- 2076</b>	<b>TASYCRB1</b>	<b>0</b>	<b>17-Feb-21</b>	<b>3-Feb-21</b>	<b>No</b>

mRNA-1273- P301-US321- 2148	TASYCRB1	1	4-Mar-21	4-Mar-21	Yes
mRNA-1273- P301-US321- 2191	TASYCRB1	1	5-Mar-21	5-Mar-21	Yes
mRNA-1273- P301-US322- 2380	TASYCRB1	0	2-Feb-21	29-Jan-21	No
mRNA-1273- P301-US322- 2594	TASYCRB1	0	12-Mar-21	17-Dec-20	No
mRNA-1273- P301-US331- 2221	TASYCRB1	0	26-Mar-21	13-Jan-21	No
mRNA-1273- P301-US334- 2338	TASYCRB1	0	25-Jan-21	21-Jan-21	No
mRNA-1273- P301-US339- 2064	TASYCRB1	0	6-Jan-21	31-Dec-20	No
mRNA-1273- P301-US340- 2036	TASYCRB1	1	9-Feb-21	9-Feb-21	Yes
mRNA-1273- P301-US340- 2240	TASYCRB1	0	9-Mar-21	5-Feb-21	No
mRNA-1273- P301-US344-2062	TASYCRB1	0	5-Mar-21	28-Dec-20	No
mRNA-1273- P301-US344-2182	TASYCRB1	0	10-Feb-21	28-Jan-21	No
mRNA-1273- P301-US346-2090	TASYCRB1	0	12-Jan-21	17-Dec-20	No
mRNA-1273- P301-US352-2168	TASYCRB1	0	23-Feb-21	23-Dec-20	No
mRNA-1273- P301-US352-2657	TASYCRB1	0	10-Feb-21	4-Jan-21	No
mRNA-1273- P301-US364-2130	TASYCRB1	0	20-Jan-21	8-Jan-21	No
mRNA-1273- P301-US364-2147	TASYCRB1	0	21-Jan-21	8-Jan-21	No
mRNA-1273- P301-US364-2162	TASYCRB1	0	20-Jan-21	8-Jan-21	No
mRNA-1273- P301-US381-2078	TASYCRB1	0	22-Jan-21	22-Dec-20	No
mRNA-1273- P301-US381-2086	TASYCRB1	0	22-Feb-21	28-Jan-21	No
mRNA-1273- P301-US382-2040	TASYCRB1	0	21-Jan-21	4-Jan-21	No
mRNA-1273- P301-US382-2174	TASYCRB1	0	20-Jan-21	19-Jan-21	No

mRNA-1273- P301-US382-2191	TASYCRB1	0	26-Feb-21	18-Jan-21	No
mRNA-1273- P301-US398-2163	TASYCRB1	0	8-Jan-21	7-Jan-21	No

Similarly, we note the following 39 discrepancies for SARS-CoV-2 infection as presented in Table 6-6 of the P301 CSR:

**Table 2. SARS-CoV-2 infection starting 14 days post Dose 2**

USUBJID	ADTTEB.PAR AMCD	ADTTEB. CNSR	Date of first positive N- serology or PCR	Date of PDV or unblinding	Infected on or prior to PDV?
mRNA-1273- P301- US303-2145	TTINFB1	1	9-Jan-21	9-Jan-21	Yes
mRNA-1273- P301- US303-2331	TTINFB1	0	4-Feb-21	29-Jan-21	No
mRNA-1273- P301- US308-2216	TTINFB1	1	8-Jan-21	9-Feb-21	Yes
mRNA-1273- P301- US313-2115	TTINFB1	0	12-Mar-21	5-Feb-21	No
mRNA-1273- P301- US314-2275	TTINFB1	0	8-Mar-21	25-Jan-21	No
mRNA-1273- P301- US315-2071	TTINFB1	1	27-Jan-21	27-Jan-21	Yes
mRNA-1273- P301- US319-2534	TTINFB1	0	4-Feb-21	21-Dec-20	No
mRNA-1273- P301- US320-2076	TTINFB1	0	17-Feb-21	3-Feb-21	No
mRNA-1273- P301- US321-2148	TTINFB1	1	4-Mar-21	4-Mar-21	Yes
mRNA-1273-P301- US321-2191	TTINFB1	1	5-Mar-21	5-Mar-21	Yes
mRNA-1273- P301- US322-2380	TTINFB1	0	2-Feb-21	29-Jan-21	No
mRNA-1273- P301- US322-2594	TTINFB1	0	12-Mar-21	17-Dec-20	No
mRNA-1273- P301- US328-2090	TTINFB1	0	20-Jan-21	31-Dec-20	No
mRNA-1273- P301- US331- 2221	TTINFB1	0	26-Mar-21	13-Jan-21	No
mRNA-1273- P301- US332- 2226	TTINFB1	1	25-Feb-21	25-Feb-21	Yes

mRNA-1273- P301- US334- 2338	TTINFB1	0	25-Jan-21	21-Jan-21	No
mRNA-1273- P301- US337- 2429	TTINFB1	1	4-Feb-21	4-Feb-21	Yes
mRNA-1273- P301- US339- 2064	TTINFB1	0	6-Jan-21	31-Dec-20	No
mRNA-1273- P301- US340- 2036	TTINFB1	1	9-Feb-21	9-Feb-21	Yes
mRNA-1273- P301- US340- 2240	TTINFB1	0	9-Mar-21	5-Feb-21	No
mRNA-1273- P301- US344- 2062	TTINFB1	0	5-Mar-21	28-Dec-20	No
mRNA-1273- P301- US344- 2107	TTINFB1	1	6-Jan-21	6-Jan-21	Yes
mRNA-1273- P301- US344- 2182	TTINFB1	0	10-Feb-21	28-Jan-21	No
mRNA-1273- P301- US346- 2090	TTINFB1	0	12-Jan-21	17-Dec-20	No
mRNA-1273- P301- US348- 2302	TTINFB1	1	14-Jan-21	14-Jan-21	Yes
mRNA-1273- P301- US352- 2168	TTINFB1	0	23-Feb-21	23-Dec-20	No
mRNA-1273- P301- US352- 2657	TTINFB1	0	10-Feb-21	4-Jan-21	No
mRNA-1273- P301- US354- 2214	TTINFB1	1	22-Jan-21	22-Jan-21	Yes
mRNA-1273- P301- US354- 2215	TTINFB1	1	22-Jan-21	22-Jan-21	Yes
mRNA-1273- P301- US364- 2130	TTINFB1	0	20-Jan-21	8-Jan-21	No
mRNA-1273- P301- US364- 2147	TTINFB1	0	21-Jan-21	8-Jan-21	No
mRNA-1273- P301- US364- 2162	TTINFB1	0	20-Jan-21	8-Jan-21	No
mRNA-1273- P301- US381- 2078	TTINFB1	0	22-Jan-21	22-Dec-20	No
mRNA-1273- P301- US381- 2086	TTINFB1	0	22-Feb-21	28-Jan-21	No
mRNA-1273- P301- US382- 2040	TTINFB1	0	21-Jan-21	4-Jan-21	No
mRNA-1273- P301- US382- 2174	TTINFB1	0	20-Jan-21	19-Jan-21	No
mRNA-1273- P301- US382- 2191	TTINFB1	0	26-Feb-21	18-Jan-21	No

mRNA-1273- P301- US396- 2063	TTINFB1	1	4-Feb-21	4-Mar-21	Yes
mRNA-1273- P301- US398- 2163	TTINFB1	0	8-Jan-21	7-Jan-21	No

**Please comment on whether each subject was correctly censored in your analysis. Please submit the corrected analyses of asymptomatic and SARS-CoV-2 infection, if applicable, starting 14 days after Dose 2 in the PPS, including the sensitivity analysis of asymptomatic infection excluding those with any documented CDC or protocol-defined COVID-19 symptom at any time during the study.**

#### **Sponsor Response:**

The Sponsor appreciate the reviewers' comments. For each of the participants listed in [Table 1](#) and [Table 2](#) of Item 1 of this IR, as well as participants included in Table 1-3 of the SN0024 response to November 12, 2021 IR20 Item 1 (for whom updated analysis of infection and asymptomatic infection were provided in our response to the clinical IR (#24) dated November 30, 2021), the Sponsor has looked into analysis dataset of infection and asymptomatic infection including PDV (ADTTEB), serology results and RT-PCR results that support these two efficacy endpoints (ADIS and ADMB), and is providing comment, reason (or detailed explanation), and action for each of these participants in [Table 1-1](#) below.

The majority of these participants, regarding efficacy endpoints of SARS-CoV-2 infection and asymptomatic infection during blinded phase (including PDV), should be censored on PDV date instead of being considered as event on a date later than PDV date, which was due to a positive RT-PCR and/or serology result (positive bAb against SARS-CoV-2 N protein as measured by Roche Elecsys) on a date later than PDV with visit labeled as 'PDV/OL-D1' (discrepancies), e.g. US3132115. There were several participants who had positive RT-PCR and/or serology result on PDV date but the results were not labeled as 'PDV/OL-D1', instead 'Illness visit' thus these participants were censored on PDV date rather than being considered an event on PDV date, e.g. US3082216.

The Sponsor has incorporated these updates listed in [Table 1-1](#) below and performed the analyses of efficacy against SARS-CoV-2 infection and asymptomatic infection starting 14 days after Dose 2 in the Per-Protocol Set during the blinded follow-up. The results are presented in [Table 1-2](#) and [Table 1-3](#) below; the updated results are consistent with those presented in Table 6-6 (Infections) and Table 6-9 (Asymptomatic infection) in the CSR.

**Table 1-1 List of Participants with Detailed Explanation**

SUBJID	TRT01P	PDVDT	ADTTB.Paramcd="TASYCRB1"		ADTTB.Paramcd="TTINFB1"		Comments	Reason	action
			ADT	CNSR	ADT	CNSR			
US3032145	mRNA-1273	1/9/2021	1/9/2021	1	1/9/2021	1	censored on 09-Jan-2021 (PDV) for all infection and asymptomatic infection for blinded phase; should be event on 09-Jan-2021 (PDV) for all infection and asymptomatic infection	positive serology result on PDV labeled as OL-Day 29, thus was not considered	updated in IR24
US3032331	Placebo	1/29/2021	2/4/2021	0	2/4/2021	0	event on 04-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 29-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 29-Jan-2021; positive serology result on 04-Feb-2021 labeled as PDV/OL-D1	new
US3082216	Placebo	1/6/2021	1/6/2021	1	1/6/2021	1	censored on 06-Jan-2021 (PDV) for all infection and asymptomatic infection for blinded phase; no update	PDV on 06-Jan-2021; positive RT-PCR on 08-Jan-2021 'illness visit'	none
US3132115	Placebo	2/5/2021	3/12/2021	0	3/12/2021	0	event on 12-Mar-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 05-Feb-2021 (PDV) for all infection and asymptomatic infection	PDV on 05-Feb-2021; positive serology result on 12-Mar-2021 labeled as PDV/OL-D1	new

US3142275	Placebo	1/25/2021	3/8/2021	0	3/8/2021	0	event on 08-Mar-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 25-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 25-Jan-2021; positive serology result on 08-Mar-2021 labeled as PDV/OL-D1	new
US3152071	mRNA-1273	1/27/2021	1/27/2021	1	1/27/2021	1	censored on 27-Jan-2021 (PDV) for all infection and asymptomatic infection for blinded phase.	Subject had a positive RT-PCR on 27-Jan-2021 with "Illness Day 1"; participants had negative RT-PCR on 27-Jan-2021 "PDV" and negative RT-PCR on 29-Jan-2021, 02-Feb-2021 and 04-Feb-2021.	IR24
US3192534	mRNA-1273	12/21/2020	2/4/2021	0	2/4/2021	0	event on 04-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 21-Dec-2020 (PDV) for all infection and asymptomatic infection	PDV on 21-Dec-2020; positive RT-PCR result on 04-Feb-2021 labeled as PDV/OL-D1	new
US3202076	Placebo	2/3/2021	2/17/2021	0	2/17/2021	0	event on 17-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 03-Feb-2021 (PDV) for all infection and asymptomatic infection	PDV on 03-Feb-2021; positive serology result on 17-Feb-2021 labeled as PDV/OL-D1	new

US3212148	mRNA-1273	3/4/2021	3/4/2021	1	3/4/2021	1	censored on 04-Mar-2021 (PDV) for all infection and asymptomatic infection for blinded phase; should be event on 04-Mar-2021 (PDV) for all infection and asymptomatic infection	positive serology result on PDV labeled as Day 209, thus were not considered. There was no serology result labeled as OL-Day 1	IR24
US3212191	mRNA-1273	3/5/2021	3/5/2021	1	3/5/2021	1	censored on 05-Mar-2021 (PDV) for all infection and asymptomatic infection for blinded phase; should be event on 05-Mar-2021 (PDV) for all infection and asymptomatic infection	positive serology result on PDV labeled as Day 209, thus were not considered.	new
US3222380	mRNA-1273	1/29/2021	2/2/2021	0	2/2/2021	0	event on 2-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 29-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 29-Jan-2021; positive serology result on 02-Feb-2021 labeled as PDV/OL-D1	new
US3222594	Placebo	12/17/2020	3/12/2021	0	3/12/2021	0	event on 12-Mar-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 17-Dec-2020 (PDV) for all infection and asymptomatic infection	PDV on 17-Dec-2020; positive serology result on 12-Mar-2021 labeled as PDV/OL-D1	new
US3282090	mRNA-1273	12/31/2020	1/20/2021	2	2/18/2021	0	should be censor on 31-Dec-2020 (PDV) for both infection and asymptomatic infection	PDV on 31-Dec-2021; positive RT-PCR and	new



							serology on 18-Feb labeled as PDV/OL-D1		
US3312221	mRNA-1273	1/13/2021	3/26/2021	0	3/26/2021	0	event on 26-Mar-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 13-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 13-Jan-2021; positive RT-PCR result on 26-Mar-2021 labeled as PDV/OL-D1	new
US3322226	Placebo	2/25/2021	2/25/2021	1	2/25/2021	1	Censored on 25-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be event on 25-Feb-2021 (PDV) for all infection and asymptomatic infection	PDV on 25-Feb-2021; positive RT-PCR on 25-Feb-2021 as 'illness visit'	new
US3342338	Placebo	1/21/2021	1/25/2021	0	1/25/2021	0	event on 25-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 21-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 21-Jan-2021; positive serology result on 25-Jan-2021 labeled as PDV/OL-D1	new
US3372429	Placebo		2/4/2021	1	2/4/2021	1	Censored on 4-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be event on 04-Feb-2021 (PDV) for all infection and asymptomatic infection	PDV on 04-Feb-2021; positive RT-PCR on 04-Feb-2021 as 'illness visit'	new

US3382007	Placebo	1/15/2021	3/10/2021	0	3/10/2021	0	event on 10-March-2021 for all infection and asymptomatic infection; should be event on 15-Jan-2021 for all infection and asymptomatic infection	subject's positive serology result on PDV (15-Jan-2021) was labeled as 'OL-D57'; positive serology result on 10-March-2021 was labeled as 'PDV/OL-Day1' and was taken into consideration	IR24
US3392064	Placebo	12/31/2020	1/6/2021	0	1/6/2021	0	event on 06-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 31-Dec-2020 (PDV) for all infection and asymptomatic infection	PDV on 31-Dec-2020; positive RT-PCR result on 06-Jan-2021 labeled as PDV/OL-D1	new
US3402036	Placebo	2/9/2021	2/9/2021	1	2/9/2021	1	censor on 09-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be event on 09-Feb-2021 (PDV) for all infection and asymptomatic infection	PDV on 09-Feb-2021; positive RT-PCR result on 09-Feb-2021 labeled as 'Day 209'	new
US3402153	Placebo	6-Jan-21	13-Jan-21	2			event on 09-Mar-2021 for all infection; cnsr=2 (had other competing event) on 13-Jan-2021 for asymptomatic infection Subject should be censored 6-Jan-2021 for infection and asymptomatic infection for the blinded phase.	Subject had a positive RT-PCR on 09-Mar-2021 labeled as 'PDV/OL-Day 1' thus was considered as event on 09-Mar-2021. Subject had positive serology and RT-PCR result on 13-Jan-2021	updated in IR24, not included in IR27

US3402240	Placebo	1/6/2021	3/9/2021	0	3/9/2021	0	event on 09-Mar-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 06-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 06-Jan-2021; positive RT-PCR result on 09-Mar-2021 labeled as PDV/OL-D1	new
US3442062	mRNA-1273	12/28/2020	3/5/2021	0	3/5/2021	0	event on 05-Mar-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 28-Dec-2020 (PDV) for all infection and asymptomatic infection	PDV on 28-Dec-2020; positive serology result on 05-Mar-2021 labeled as PDV/OL-D1	new
US3442107	Placebo	1/6/2021	1/6/2021	1	1/6/2021	1	Censored on 6-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be event on 06-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 06-Jan-2021; positive RT-PCR on 06-Jan-2021 as 'illness visit'	new
US3442182	Placebo	1/28/2021	2/10/2021	0	2/10/2021	0	event on 10-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 28-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 28-Jan-2021; positive RT-PCR and serology result on 10-Feb-2021 labeled as PDV/OL-D1	new
US3462090	Placebo	12/17/2020	1/12/2021	0	1/12/2021	0	event on 12-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 17-Dec-2020 (PDV) for all infection and asymptomatic infection	PDV on 17-Dec-2020; positive RT-PCR result on 12-Jan-2021 labeled as PDV/OL-D1	new

US3482302	Placebo	1/14/2021	1/14/2021	1	1/14/2021	1	Censored on 14-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be event on 14-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 14-Jan-2021; positive RT-PCR on 14-Jan-2021 as 'illness visit'	new
US3522168	mRNA-1273	12/23/2020	2/23/2021	0	2/23/2021	0	event on 23-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 23-Dec-2020 (PDV) for all infection and asymptomatic infection	PDV on 23-Dec-2020; positive serology result on 23-Feb-2021 labeled as PDV/OL-D1	new
US3522657	mRNA-1273	1/4/2021	2/10/2021	0	2/10/2021	0	event on 10-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 04-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 04-Jan-2021; positive RT-PCR result on 10-Feb-2021 labeled as PDV/OL-D1	new
US3542214	Placebo	1/22/2021	1/22/2021	1	1/22/2021	1	Censored on 22-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be event on 22-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 22-Jan-2021; positive RT-PCR on 22-Jan-2021 as 'illness visit'	new
US3542215	Placebo	1/22/2021	1/22/2021	1	1/22/2021	1	Censored on 22-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be event on 22-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 22-Jan-2021; positive RT-PCR on 22-Jan-2021 as 'illness visit'	new

US3642130	Placebo	1/8/2021	1/20/2021	0	1/20/2021	0	event on 20-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 08-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 08-Jan-2021; positive RT-PCR result on 20-Jan-2021 labeled as PDV/OL-D1	new
US3642147	Placebo	1/8/2021	1/21/2021	0	1/21/2021	0	event on 21-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 08-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 08-Jan-2021; positive serology result on 21-Jan-2021 labeled as PDV/OL-D1	new
US3642162	Placebo	1/8/2021	1/20/2021	0	1/20/2021	0	event on 20-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 08-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 08-Jan-2021; positive RT-PCR result on 20-Jan-2021 labeled as PDV/OL-D1	new
US3812078	mRNA-1273	12/22/2020	1/22/2021	0	1/22/2021	0	event on 22-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 22-Dec-2020 (PDV) for all infection and asymptomatic infection	PDV on 22-Dec-2020; positive serology result on 22-Jan-2021 labeled as PDV/OL-D1	new
US3812086	Placebo	1/6/2021	2/22/2021	0	2/22/2021	0	event on 22-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 06-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 06-Jan-2021; positive serology result on 22-Feb-2021 labeled as PDV/OL-D1	new

US3822040	Placebo	1/4/2021	1/21/2021	0	1/21/2021	0	event on 21-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 04-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 04-Jan-2021; positive serology and RT-PCR result on 21-Feb-2021 labeled as PDV/OL-D1	new
US3822174	Placebo	1/19/2021	1/20/2021	0	1/20/2021	0	event on 20-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 19-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 19-Jan-2021; positive serology and RT-PCR result on 20-Feb-2021 labeled as PDV/OL-D1	new
US3822191	Placebo	1/18/2021	2/26/2021	0	2/26/2021	0	event on 26-Feb-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 18-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 18-Jan-2021; positive RT-PCR result on 26-Feb-2021 labeled as PDV/OL-D1	new
US3962063	mRNA-1273	2/1/2021	2/1/2021	1	2/1/2021	1	PDV on 01-Feb; positive RT-PCR on 04-Feb 'Illness visit'; censored on 01-Feb-2021 for both infection and asymptomatic infection		no action
US3982163	Placebo	1/7/2021	1/8/2021	0	1/8/2021	0	event on 08-Jan-2021 for all infection and asymptomatic infection for blinded phase; should be censor on 07-Jan-2021 (PDV) for all infection and asymptomatic infection	PDV on 07-Jan-2021; positive serology and RT-PCR result on 08-Jan-2021 labeled as PDV/OL-D1	new

**Table 1-2 Updated Analysis of Vaccine Efficacy of mRNA-1273 to Prevent SARS-CoV-2 Infection Regardless of Symptomatology and Severity Starting 14 Days After the Second Injection Including Participant Decision Visit (Per-Protocol Set)**

	<b>Placebo (N=14164)</b>	<b>mRNA-1273 (N=14287)</b>
Number of subjects with SARS-CoV-2 infection regardless of symptomatology and severity, n (%)	1327 (9.4)	275 (1.9)
Vaccine efficacy based on hazard ratio (95% CI) <sup>a</sup>		0.822 (0.797, 0.843)
Person-years <sup>b</sup>	5440.9	5754.2
Incidence rate per 1,000 person-years (95% CI) <sup>c</sup>	243.9 (230.9, 257.4)	47.8 (42.3, 53.8)
Vaccine efficacy based on incidence rate (95% CI) <sup>d</sup>		0.804 (0.777, 0.829)

Abbreviations: CI = confidence intervals.

- <sup>a</sup> Vaccine efficacy (VE), defined as 1 - hazard ratio (mRNA-1273 vs. placebo), and 95% CI are estimated using a stratified Cox proportional hazard model with Efron's method of tie handling and with the treatment group as a covariate, adjusting for stratification factor.
- <sup>b</sup> Person-years is defined as the total years from randomization date to the date of SARS-CoV-2 infection, last date of study participation, or efficacy data cutoff date, whichever is earlier.
- <sup>c</sup> Incidence rate is defined as the number of subjects with an event divided by the number of subjects at risk and adjusted by person-years (total time at risk) in each treatment group. The 95% CI is calculated using the exact method (Poisson distribution) and adjusted by person-years.
- <sup>d</sup> VE is defined as 1 – ratio of incidence rate (mRNA-1273 vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years.

**Table 1-3 Updated Analysis of Vaccine Efficacy of mRNA-1273 to Prevent Asymptomatic SARS-CoV-2 Infection Starting 14 Days After the Second Injection Including the Participant Decision Visit Using the Competing Risk Method (Per-Protocol Set)**

	<b>Placebo (N=14164)</b>	<b>mRNA-1273 (N=14287)</b>
Number of subjects with asymptomatic SARS-CoV-2 infection, n (%)	487 (3.4)	210 (1.5)
Number of subjects with competing event, n (%)	862 (6.1)	61 (0.4)
Vaccine efficacy based on hazard ratio (95% CI) <sup>a</sup>		0.629 (0.564, 0.685)
Person-years <sup>b</sup>	5440.8	5755.2
Incidence rate per 1,000 person-years (95% CI) <sup>c</sup>	89.5 (81.7, 97.8)	36.5 (31.7, 41.8)
Vaccine efficacy based on incidence rate (95% CI) <sup>d</sup>		0.592 (0.520, 0.655)

RT-PCR test and Elecsys anti-SARS-CoV-2 assay results at post-baseline scheduled visits are considered in case definition. Disease cases (COVID-19 or second definition of COVID-19) are considered as competing events for asymptomatic SARS-CoV-2 infection.

- <sup>a</sup> Vaccine efficacy (VE), defined as 1 - hazard ratio (mRNA-1273 vs. placebo), and 95% CI are estimated using Fine and Gray's sub-distribution hazard model with disease cases as competing events and with the treatment group as a covariate, adjusting for stratification factor.
- <sup>b</sup> Person-years is defined as the total years from randomization date to the earliest of the date of symptomatic SARS-CoV-2 infection, the date of asymptomatic SARS-CoV-2 infection, last date of study participation, or efficacy data cutoff date, whichever is earlier.
- <sup>c</sup> Incidence rate is defined as the number of subjects with an event divided by the number of subjects at risk and adjusted by person-years (total time at risk) in each treatment group. The 95% CI is calculated using the exact method (Poisson distribution) and adjusted by person-years.
- <sup>d</sup> VE is defined as 1 – ratio of incidence rate (mRNA-1273 vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years.



As requested, a sensitivity analysis for asymptomatic infection censoring participants who had any documented CDC or protocol-defined COVID-19 symptoms at any time during the study (with censor variable CNSR=2, considered as competing risk) was performed with the above update. For your convenience of review, the results are presented below with the response provided to Information Request 15 (SN0021).

**Table 1-4: Updated Sensitivity analysis of vaccine efficacy (VE) against asymptomatic SARS-CoV-2 infection starting  $\geq 14$  days after dose 2 in the blinded phase, Per-Protocol Set**

	<b>mRNA-1273</b> <b>N=14287</b> <b>n</b> <b>IR/1000 person-</b> <b>years (95% CI)</b>	<b>Placebo</b> <b>N=14164</b> <b>n</b> <b>IR/1000 person-</b> <b>years (95% CI)</b>	<b>VE<sup>a</sup></b> <b>(1- IRR)</b> <b>%</b> <b>(95% CI)</b>	<b>VE<sup>b</sup></b> <b>(1- HR)</b> <b>%</b> <b>(95% CI)</b>
<b>Sensitivity analysis incorporating updates</b>	180 31.3 (26.9, 36.2)	399 73.3 (66.3, 80.9)	57.4 (49.0, 64.4)	61.0 (53.4, 67.3)
<b>Updated analysis (Table 1-3 in this response)</b>	210 36.5 (31.7, 41.8)	487 89.5 (81.7, 97.8)	59.2 (52.0, 65.5)	62.9 (56.4, 68.5)
<b>Sensitivity analysis (Response to Item 1 of IR15 [SN0021])</b>	182 31.6 (27.2, 36.6)	413 75.9 (68.8, 83.6)	58.3 (50.3, 65.2)	61.8 (54.5, 67.9)
<b>Original analysis (P301 CSR Section 6.2.9)</b>	214 37.2 (32.4, 42.5)	498 91.5 (83.7, 99.9)	59.4 (52.2, 65.5)	63.0 (56.6, 68.5)

IR = incidence rate; 1- IRR = 1- incidence rate ratio; 1-HR= 1- hazard ratio

a: VE is defined as  $1 - \text{IRR}$  (mRNA-1273 vs. placebo). The 95% CI of the ratio was calculated using the exact method conditional upon the total number of cases, adjusting for person-years.

b: VE =  $1 - \text{HR}$  and 95% CI were estimated using Fine and Gray's sub-distribution hazard model with COVID-19 disease cases as competing events and with the treatment group as a covariate, adjusting for stratification factor.