RESPONSE TO FDA COMMENTS ON INFORMATION REQUEST#39 RECEIVED ON DECEMBER 17, 2021

The Sponsor acknowledges INFORMATION REQUEST#39 dated 17 DECEMBER 2021 in (**BOLD**)

Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: Clinical: Safety Data for Study P301 submitted to module 5 of BLA.

Our review of your August 24, 2021 submission (STN 125752/2) is ongoing. We have the following request for additional information:

ITEM 1:

1. **For cases of dyspnea and syncope that occurred within 7 days after any vaccination dose across study groups, please provide:**

a. (Excel doc) A line listing by participant ID number and study group (different Excel sheets for each group) that provides additional information on each reported case of dyspnea and syncope including but not limited to, day of onset following each dose (dose 1 and dose 2), duration (in days), concomitant medications, concomitant AEs, other underlying conditions.

Sponsor Response:
The corresponding excel spreadsheet is included within this submission.

b. (Excel and Word doc) Two separate summary tables for dyspnea following dose 1 and dose 2 across study groups, that provide the following information based on events that occurred following the most recent dose only

i. Median day of onset and range (days)
ii. Median duration and range (days) of dyspnea and syncope

Sponsor Response:
Table 1-1 Summary of Dyspnoea up to 7 Days After the First Injection, Safety Set

	Placebo (N = 15162)	mRNA-1273 (N = 15184)
Number of Subjects Reporting Dyspnoea, n (%)	5 (<0.1)	5 (<0.1)
Number of Events	5	5
Onset Day		
Median	4.0	4.0
Min, Max	1, 6	1, 6
Duration		
Median	2.0	5.0
Min, Max	1, 13	1, 147

Source: Table 14.3.1.37.3.1

Table 1-2 Summary of Dyspnoea up to 7 Days After the Second Injection, Safety Set

	Placebo (N = 14631)	mRNA-1273 (N = 14731)
Number of Subjects Reporting Dyspnoea, n (%)	7 (<0.1)	9 (<0.1)
Number of Events	7	10
Onset Day		
Median	3.0	1.0
Min, Max	1, 7	1, 4
Duration		
Median	3.0	2.0
Min, Max	1, 29	1, 17

Source: Table 14.3.1.37.3.1

c. (Excel and Word doc) Two separate summary tables for syncope following dose 1 and dose 2 across study groups based on events that occurred following the most recent dose only

i. Median day of onset and range (days)

ii. Median duration and range (days) of dyspnea and syncope

Sponsor Response:

Table 1-3 Summary of Syncope up to 7 Days After the First Injection, Safety Set

	Placebo (N = 15162)	mRNA-1273 (N = 15184)
Number of Subjects Reporting Syncope, n (%)	4 (<0.1)	2 (<0.1)
Number of Events	4	2
Onset Day		
Median	2.5	3.0
Min, Max	1, 4	1, 5
Duration		
Median	1.0	1.0
Min, Max	1, 1	1, 1

Source: Table 14.3.1.37.3.2

Table 1-4 Summary of Syncope up to 7 Days After the Second Injection, Safety Set

	Placebo (N = 14631)	mRNA-1273 (N = 14731)
Number of Subjects Reporting Syncope, n (%)	3 (<0.1)	5 (<0.1)
Number of Events	3	5
Onset Day		
Median	2.0	1.0
Min, Max	1, 2	1, 1

	Placebo (N = 14631)	mRNA-1273 (N = 14731)
Duration		
Median	1.0	1.0
Min, Max	1, 2	1, 1

Source: Table 14.3.1.37.3.2

ITEM 2:

2. **For subjects with deep vein thrombosis in Part A of the study, please provide: a. (Excel doc) A line listing by participant ID number and study group (different Excel sheets for each group) that provides additional information on each reported case of deep vein thrombosis including but not limited to, day of onset following each dose (dose 1 and dose 2), duration (in days), concomitant medications, concomitant AEs, other underlying conditions**

Sponsor Response:

The corresponding excel spreadsheet is included within this submission.

Table 1.5 Summary of Deep Vein Thrombosis up to 28 Days After First Injection, Safety Set

	Placebo (N = 15162)	mRNA-1273 (N = 15184)
Number of Subjects Reporting Deep vein thrombosis, n (%)	2 (<0.1)	0
Number of Events	2	0
Onset Day		
Median	10.0	
Min, Max	9, 11	
Duration		
Median	166.5	
Min, Max	144, 189	

Source: Table 14.3.1.37.4

Table 1-6 Summary of Deep Vein Thrombosis up to 28 Days After Second Injection, Safety Set

	Placebo (N = 14631)	mRNA-1273 (N = 14731)
Number of Subjects Reporting Deep vein thrombosis, n (%)	1 (<0.1)	1 (<0.1)
Number of Events	1	1
Onset Day		
Median	16.0	27.0
Min, Max	16, 16	27, 27

	Placebo (N = 14631)	mRNA-1273 (N = 14731)
Duration		
Median	176.0	186.0
Min, Max	176, 176	186, 186

Source: Table 14.3.1.37.4

ITEM 3:

3. Please complete the following table for pregnancies reported in Part A

Table. Pregnancies Reported in Part A, Safety Set

	mRNA-1273 N=15184 n	**Placebo N=15162 n**
Total number of pregnancies		
Timing of last dose relative to LMP		
Prior to LMP		
Within 30 days after LMP		
>30 days after LMP		
LMP unknown		

Sponsor Response:

Table 3-1 Pregnancies Reported in Part A, Safety Set

	mRNA-1273 N=15184 n	Placebo N=15162 n
Total number of pregnancies	16	11
Timing of last dose relative to LMP		
Prior to LMP	0	0
Within 30 days after LMP	5	8
>30 days after LMP	8	3
LMP unknown	3	0

ITEM 4:

4. Please complete the following table above for Part B, for participants who were in the original placebo group who crossed over to receive mRNA-1273.

Table. Pregnancies Reported in Part B, Safety Set

	Placebo-mRNA-1273 N=
Total number of pregnancies	
Timing of last dose of mRNA-1273 relative toLMP	
Prior to LMP	

Within 30 days after LMP	
>30 days after LMP	
LMP unknown	

Sponsor Response:

Table 4-1 Pregnancies Reported in Part B, Safety Set

	Placebo-mRNA-1273 N=12,648
Total number of pregnancies	19
Timing of last dose of mRNA-1273 relative toLMP	
Prior to LMP	9
Within 30 days after LMP	7
>30 days after LMP	1
LMP unknown	2