

Dated December 08, 2020

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**RESPONSE TO CBER COMMUNICATION REGARDING CLINICAL TOPICS (IR 11)  
RECEIVED ON DECEMBER 08, 2020**

The Sponsor acknowledges CBER's communication regarding Clinical topics (IR 11).

This document provides the Sponsor's responses to CBER's requests (in **Bold**).

**ITEM 7:**

**Please provide a summary table of solicited adverse reactions (local and systemic) with day of onset after Day 7 across study groups for any dose-safety set based on Nov 11th data cut and Nov 25 data cut.**

**Sponsor Response:**

For the request on solicited adverse reactions with day of onset after Day 7, we used data collected on the AE eCRF form as the eDiary was used to capture solicited adverse reactions after each dose. Verbatim terms captured as unsolicited AE were mapped to MedDRA Preferred Terms reflecting the solicited adverse reactions collected by eDiary during the 7 day period after dosing ([Appendix 1](#)). The summary table below are based on data collected on the AE eCRF form using these identified preferred terms with an onset date after Day 7 after each dose.

Based on DS1 which occurred on 11-Nov-2020, solicited local adverse reactions with onset after day 7 after any dose were more common in participants who received mRNA-1273 compared with placebo. The incidence of solicited systemic adverse reactions with onset after Day 7 were comparable between the two groups. The incidence of adverse reactions with onset after Day 7 was generally similar in the younger age group and the older age group.

It is very likely that these reactions are continuations of solicited, particularly local, AR which persist beyond 7 days (Table 14.3.1.6.6, 14.3.1.6.7, 14.3.1.6.8) which were more commonly reported by participants who received mRNA-1273.

Table 1. Summary of Solicited Adverse Reactions with Day of Onset after Day 7 after Any Dose – Safety Set based on (DS1, 11-Nov-2020)

Term	>=18 and <65 Years			>=65 Years			Overall		
	Placebo (N=11415) n (%)	mRNA-1273 (N=11414) n (%)	Total (N=22830) n (%)	Placebo (N=3750) n (%)	mRNA-1273 (N=3770) n (%)	Total (N=7520) n (%)	Placebo (N=15165) n (%)	mRNA-1273 (N=15184) n (%)	Total (N=30350) n (%)
Number of Subjects Reporting Solicited Adverse Reaction [1]	493 (4.3)	513 (4.5)	1006 (4.4)	135 (3.6)	188 (5.0)	323 (4.3)	628 (4.1)	701 (4.6)	1329 (4.4)
Number of Solicited Adverse Reactions [1]	802	783	1585	204	288	492	1006	1071	2077
Pain	23 (0.2)	49 (0.4)	72 (0.3)	10 (0.3)	16 (0.4)	26 (0.3)	33 (0.2)	65 (0.4)	98 (0.3)
Erythema (Redness)	5 (<0.1)	60 (0.5)	65 (0.3)	6 (0.2)	23 (0.6)	29 (0.4)	11 (<0.1)	83 (0.5)	94 (0.3)
Swelling (Hardness)	4 (<0.1)	46 (0.4)	50 (0.2)	2 (<0.1)	8 (0.2)	10 (0.1)	6 (<0.1)	54 (0.4)	60 (0.2)
Lymphadenopathy	0	4 (<0.1)	4 (<0.1)	0	0	0	0	4 (<0.1)	4 (<0.1)
Fever	45 (0.4)	35 (0.3)	80 (0.4)	7 (0.2)	13 (0.3)	20 (0.3)	52 (0.3)	48 (0.3)	100 (0.3)
Headache	268 (2.3)	216 (1.9)	484 (2.1)	58 (1.5)	57 (1.5)	115 (1.5)	326 (2.1)	273 (1.8)	599 (2.0)

Term	>=18 and <65 Years			>=65 Years			Overall		
	Placebo (N=11415)	mRNA-1273 (N=11414)	Total (N=22830)	Placebo (N=3750)	mRNA-1273 (N=3770)	Total (N=7520)	Placebo (N=15165)	mRNA-1273 (N=15184)	Total (N=30350)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Fatigue	142 (1.2)	108 (0.9)	250 (1.1)	30 (0.8)	60 (1.6)	90 (1.2)	172 (1.1)	168 (1.1)	340 (1.1)
Myalgia	72 (0.6)	57 (0.5)	129 (0.6)	21 (0.6)	23 (0.6)	44 (0.6)	93 (0.6)	80 (0.5)	173 (0.6)
Arthralgia	53 (0.5)	63 (0.6)	116 (0.5)	24 (0.6)	28 (0.7)	52 (0.7)	77 (0.5)	91 (0.6)	168 (0.6)

The observations noted above in regard to DS1 are consistent with DS2 which occurred on 25-Nov-2020.

Table 2. Summary of Solicited Adverse Reactions with Day of Onset after Day 7 after Any Dose – Safety Set based on (DS2, 25-Nov-2020)

Term	>=18 and <65 Years			>=65 Years			Overall		
	Placebo (N=11416)	mRNA-1273 (N=11415)	Total (N=22831)	Placebo (N=3750)	mRNA-1273 (N=3770)	Total (N=7520)	Placebo (N=15166)	mRNA-1273 (N=15185)	Total (N=30351)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number of Subjects Reporting Solicited Adverse Reaction [1]	587 (5.1)	600 (5.3)	1187 (5.2)	168 (4.5)	210 (5.6)	378 (5.0)	755 (5.0)	810 (5.3)	1565 (5.2)
Number of Solicited Adverse Reactions [1]	987	927	1914	253	322	575	1240	1249	2489

Term	>=18 and <65 Years			>=65 Years			Overall		
	Placebo (N=11416)	mRNA-1273 (N=11415)	Total (N=22831)	Placebo (N=3750)	mRNA-1273 (N=3770)	Total (N=7520)	Placebo (N=15166)	mRNA-1273 (N=15185)	Total (N=30351)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Pain	25 (0.2)	53 (0.5)	78 (0.3)	12 (0.3)	17 (0.5)	29 (0.4)	37 (0.2)	70 (0.5)	107 (0.4)
Erythema (Redness)	7 (<0.1)	66 (0.6)	73 (0.3)	6 (0.2)	26 (0.7)	32 (0.4)	13 (<0.1)	92 (0.6)	105 (0.3)
Swelling (Hardness)	5 (<0.1)	49 (0.4)	54 (0.2)	3 (<0.1)	11 (0.3)	14 (0.2)	8 (<0.1)	60 (0.4)	68 (0.2)
Lymphadenopathy	1 (<0.1)	7 (<0.1)	8 (<0.1)	1 (<0.1)	0	1 (<0.1)	2 (<0.1)	7 (<0.1)	9 (<0.1)
Fever	53 (0.5)	42 (0.4)	95 (0.4)	11 (0.3)	13 (0.3)	24 (0.3)	64 (0.4)	55 (0.4)	119 (0.4)
Headache	327 (2.9)	250 (2.2)	577 (2.5)	66 (1.8)	65 (1.7)	131 (1.7)	393 (2.6)	315 (2.1)	708 (2.3)
Fatigue	176 (1.5)	124 (1.1)	300 (1.3)	36 (1.0)	62 (1.6)	98 (1.3)	212 (1.4)	186 (1.2)	398 (1.3)
Myalgia	96 (0.8)	76 (0.7)	172 (0.8)	25 (0.7)	26 (0.7)	51 (0.7)	121 (0.8)	102 (0.7)	223 (0.7)

## Appendix 1.

**Appendix Table. Preferred Terms identified for adverse reaction symptoms**

Adverse Event SOC	Adverse Event PT	Solicited Symptom Term
Gastrointestinal disorders	Nausea	Nausea/Vomiting
Gastrointestinal disorders	Vomiting	Nausea/Vomiting
General disorders and administration site conditions	Axillary pain	Pain
General disorders and administration site conditions	Chills	Chills
General disorders and administration site conditions	Fatigue	Fatigue
General disorders and administration site conditions	Injection site erythema	Erythema
General disorders and administration site conditions	Injection site induration	Swelling
General disorders and administration site conditions	Injection site joint pain	Arthralgia
General disorders and administration site conditions	Injection site lymphadenopathy	Underarm Gland Swelling or Tenderness
General disorders and administration site conditions	Injection site pain	Pain
General disorders and administration site conditions	Injection site swelling	Swelling
General disorders and administration site conditions	Pyrexia	Fever
General disorders and administration site conditions	Swelling	Swelling
General disorders and administration site conditions	Vaccination site erythema	Erythema
General disorders and administration site conditions	Vaccination site lymphadenopathy	Underarm Gland Swelling or Tenderness
General disorders and administration site conditions	Vaccination site pain	Pain
General disorders and administration site conditions	Vaccination site swelling	Swelling
Investigations	Body temperature increased	Fever
Musculoskeletal and connective tissue disorders	Arthralgia	Arthralgia
Musculoskeletal and connective tissue disorders	Myalgia	Myalgia
Nervous system disorders	Headache	Headache
Nervous system disorders	Migraine	Headache
Nervous system disorders	Sinus headache	Headache
Nervous system disorders	Tension headache	Headache
Skin and subcutaneous tissue disorders	Erythema	Erythema