

**RESPONSE TO CBER COMMUNICATION REGARDING CLINICAL TOPICS
(IR#8) RECEIVED ON DECEMBER 06, 2020**

The Sponsor acknowledges CBER's communication regarding Clinical topics (IR#8).

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

Item 1:

We acknowledge that given time restraints, it would not be possible to provide narratives for all SAEs from the Phase 3 study. As part of our review, we will need to independently assess causality for all SAEs, which is also difficult to do without narratives. Please provide a summary table including all SAEs from the study, with information of the time of the dose and time to onset for the cases and why the investigator and/or Moderna concluded the event was unrelated (eg, biological implausibility, alternative diagnosis) as well as other elements or comments regarding the case which may help in our assessment of these events. Please respond with a proposal for this summary table within 24 hours.

Sponsor Response:

An Excel summary table is included in this sequence for your review.

Item 2:

Based on our review of Phase 2 Study (mRNA-1273-P201) Primary Analysis (Extraction Date: 06Nov2020), we note the following:

- A. 1 SAE (PT: Pneumonia) in the 50ug group and none in the 100 ug [Source 14.3.1.13.2]**
- B. 1 participant in the 50ug group who was SARS-CoV-2 RT-PCR positive between the Day 29 and Day 57 visit. No participants in the 100ug group were tested positive through Day 57. [Source Table 14.2.3.1]**

Please confirm the above information; clarify if these participants (one with SAE, one with +RT-PCR) are the same participant or two separate participants; and provide case narratives or any additional information pertaining to these events.

Please also comment if any new data subsequent to the Nov 6th data extraction (post-Day 57) are available for review with regard to Phase 2 SAE data and SARS-CoV-2 test results.

Sponsor Response:

These two events described above, involve two separate participants, US2081123 and US2041047. The SAE of pneumonia occurred on Study Day 33 in a 65 year-old male with osteoarthritis of the lower back, spinal stenosis, erectile dysfunction, depression and attention deficit/hyperactivity disorder who received mRNA-1273 and received the first dose on 30 June 2020. On 25 Jul 2020, the subject was seen in the office by the primary investigator for symptoms of headache, cough, body aches all over, weakness and fever and tested via nasal swab for SARS-CoV-2, later reported as negative and second nasal swab on 29 July was also negative for SARS-CoV-2. The participant was hospitalized from 1 to 5 Aug 2020 with community acquired pneumonia, with bilateral infiltrates on chest x ray, leukocytosis and hypotension and treated with azithromycin and ceftriaxone and then discharged with levofloxacin. The AE of double pneumonia (community acquired) was considered resolved on 26 August. The investigator discontinued the second dose of investigational product as a result of the participants acute illness. The Medwatch report (MOD-2020-000192) is provided with this response.

The second event 33 year old white male with a past-medical history significant for alopecia, back pain, GERD and seasonal allergies. Concomitant medications are finasteride, tramadol, famotidine and cetirizine. The participant received dose 1 of mRNA-1273 50 mcg on 02 June 2020 and dose 2 on 30 June. As specified in the protocol schedule of assessments, nasopharyngeal (NP) swabs were collected and were negative for SARS-CoV-2 by RT-PCR at Day 1 (V1; 02 June) and at Day 29 (V4; 30 June). At Day 57 (V7; 04 August), scheduled NP swab was positive for SARS- CoV-2 despite the participant having no symptoms suggestive of COVID-19. Unscheduled visits occurred on 13 August and 09 September at which time the participant remained asymptomatic with normal vital signs and physical examination. Nasopharyngeal swabs from these unscheduled visits were negative for SARS-CoV-2. In summary, the participant is a 33 yearold white male who has remained asymptomatic for COVID-19 despite having a pre-scheduled NP swab positive for SARS-CoV-2 at study Day 57.

Since the database lock for the primary analysis through study Day 57, two additional SAE have been reported. US2021031, a 72 year old male who received two doses mRNA-1273 100 µg reported an SAE of arrhythmia after being struck by lightning. US2071083 is an 87 year-old female with a history of bradycardia who received two doses of mRNA-1273 50 µg who reported an SAE of bradycardia, chronic one month and 12 days after the last dose of IP. The Medwatch reports associated with these two SAE are provided with this response (MOD-2020-000782 and MOD-2020-000810).

In terms of SARS-CoV-2 positive results, since study start there have been fifteen (15) cases identified to date (see Table below). As a reminder, SARS-CoV-2 testing was performed in study P201 at three (3) protocol-specified time points, Day 1, Day 29 and Day 57 and at unscheduled visits based on self-reporting of symptoms.

SARS-CoV-2 testing results in P201 as of 7 December 2020.

Protocol-specified testing - cases	Placebo	mRNA-1273 50µg	mRNA-1273 100µg
Day 1	0	0	0
Day 29	1 (2021137)	0	0
Day 57	2 (2031081;2031102)	1 (2041047)	0
	Placebo	mRNA-1273 50µg	mRNA-1273 100µg
Symptomatic testing -day of test (subject ID)	Day 36 (2021094) Day 49 (2051072-local lab) Day 71 (2021155) Day 92 (2051035) Day 100 (2021082) Day 115 (2081046) Day 128 (2021175) Day 130 (2071041) Day 144 (2071092) Day 154 (2041022)	Day 10 (2071106-local lab)	0