U.S. FOOD & DRUG ADMINISTRATION

Information Request

Our Reference: STN: 125752/2

Information Request #37

Date: December 16, 2021

To: **Michelle Olsen, Ph.D.**
ModernaTX, Inc.
Email: Michelle.Olsen@modernatx.com

From: **Joseph Kulinski, Ph.D.**
DVRPA/OVRR/CBER
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Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: Revised Data Sets

Our review of your August 24, 2021 submission (STN 125752/2) is ongoing. We have reviewed your revised data sets submitted December 1, 2021 in amendment 27 and have the following requests for information:

1. Only a few of the terms in AE that are synonymous with solicited adverse reactions that began during the 7 day assessment period and of which you have now subcategorized as “wrong category’ have a flag in suppae “AR remove flag” indicating it is removed from AE and included in CE analysis. Please indicate the additional steps you have taken with these adverse reactions in the datasets, i.e., should they have been flagged and were they summarized with the events in CE and was this summarization included in the ADCE analysis datasets and final report.

2. The number of ongoing events in CE does not match the number of ongoing events in AE (AECAT reactogenicity/AESCAT SAE/Ongoing), i.e. we are finding 5937 events (after removing the “ongoing” immediate events and “ongoing” day 6 events) in CE and 3915 events in AE. We also note that many of the events in CE that appear to be ongoing are not flagged as ongoing so the numerical difference between the 2 datasets could be even more significant. Please explain.

3. We have identified several instances where events that are synonymous with prespecified reactions, but which began on Day 8 or thereafter are being reported in CE. We also noticed that in the initial CE dataset you had 149 events and in the revised CE dataset you had 228 events where this was the situation. If the event began after the assessment period it should be considered unsolicited and be

reported in AE. Please provide a sensitivity analysis of unsolicited events that are synonymous with prespecified reactogenicity events that began on Day 8 or after. If the event occurred on day 7 but was collected on Day 8 (which it appears many of these were) please include this with the summary of the event in CE. This will mean you need to recalculate the duration of the event and update your analysis of duration of SAR using CBER's definition of last day – first day +1.

4. Many of the lymphadenopathy events (equivalent to axillary swelling) beginning within the 7 day assessment period are still in AE (AECAT=adverse event). Please provide additional information on the steps taken in SDTM to remove these events from the ADAE analysis dataset and include them in the ADCE analysis dataset.

Please confirm your receipt of this request and submit your response as an amendment to STN 125752 as soon as possible but no later than December 20, 2021.

Please contact me if you have questions and include Sudhakar Agnihothram (sudhakar.agnihothram@fda.hhs.gov) and Josephine Resnick (josephine.resnick@fda.hhs.gov) on all communications.