U.S. FOOD & DRUG ADMINISTRATION

Information Request

Our Reference: STN: 125752/2

Information Request #23

Date: November 19, 2021

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

From: **Josephine Resnick, Ph.D.**
DVRPA/OVRR/CBER
Email: Josephine.Resnick@fda.hhs.gov

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:

- Regarding the Response to Comments on Clinical:
  - 4a - Moderna proposes to re-submit the following domains with application of the updated lookup table: • CE, • FACE, • FAAE and • AE; and to re-submit the analysis of duration of SAR using CBER's definition of last day-first day+1. As the impact on other SAR analyses is minimum, the Sponsor propose not to re-run other analyses of SAR.
    - **CBER Response:**
      We agree with this proposal.
  - 4b – Moderna accepts CBER's comment and agree to update CE domain adding CENRTPT="Day 7" and CEENTPT="ONGOING" for all last beyond Day 7 events.We have assessed, such update would have no impact on analysis. Thus, the Sponsor would like to propose to implement CBER's suggestion in the future sBLA submission.

- **CBER Response:**
  Ongoing flag should be reported in CE for any future sBLA and any future EUA submissions.

- 4c – Moderna provided a table in which suggestions are offered to flag events that are categorized as reactogenicity, but may be in error or cause confusion. You suggest AESCAT=Missing Reported within 7 days for those events which are a reactogenicity event and have a REMOVEFL=Y in suppae.

  - **CBER Response:**
    We recommend that instead an AESCAT = included with subject diary data. The other subcategories suggested for ongoing reactogenicity events and for the wrong category are acceptable.

  In the situation where there are both subject-reported event and investigator assessments contributing to CE topline records (example 2), regarding EVAL, at TC, CBER suggested to use “INVESTIGATOR”. In order to keep traceability, the Sponsor would like to propose “STUDY SUBJECT/INVESTIGATOR”.

  - **CBER Response:**
    Although “Investigator” is sufficient we agree with your proposal to use “Study Subject/Investigator”.

- 10 - During the teleconference CBER indicated that if the event began on Day 6, within the eDiary assessment period, it should be a SAR that is ongoing and subsequently analyzed in ADAR (not ADAE).

  With regards to the CE-mapping examples, we have the following comments:

  1. Case 2:
     a. CESTDTC can be 2020-11-23.
     b. CEENDTC – unclear if that is the end date as you did not provide information on the event until resolution.
     c. CEENRTPT and CEENTPT may not be null.
  2. Case 4:
     a. It is unclear if the CEENDTC, CEENRTPT and CEENTPT are correct as the event could be ongoing.
  3. Case 5:
     a. It appears that CESTDTC should be 2020-09-30

Please confirm your receipt of this request.

Please contact me if you have questions and include Sudhakar Agnihothram (sudhakar.agnihothram@fda.hhs.gov) and Joseph Kulinski (joseph.kulinski@fda.hhs.gov) on all communications.