U.S. FOOD & DRUG ADMINISTRATION

Information Request

Our Reference: STN: 125752/2

Information Request #18

Date: November 10, 2021

To: **Michelle Olsen, Ph.D.**
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From: **Josephine Resnick, Ph.D.**
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Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: Implementation of SOPP 1142

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

Regarding IPRP-HPLC and Nomenclature:

The following comments are related to the reversed-phase ion-pair high performance liquid chromatography (IPRP-HPLC) methods described in SOP 0996 and SOP 1142. Both SOPs are used to test mRNA purity and product-related impurities of CX-024414 mRNA, mRNA-1273 LNP drug substances (DS) and mRNA-1273 LNP drug product (DP). SOP 0996 was used for lot testing and stability studies of clinical lots and all EUA lots, and SOP 1142 will be used post licensure for lot release and stability studies. The following comments pertain to the implementation of SOP 1142.

Different nomenclatures were used for the identification of mRNA purity and product-related impurity peaks in each SOP. In this communication, we will use the following nomenclature for the identification of peaks or peak groups:

- For mRNA purity (RNA purity): main peak (SOPs 0996 and 1142)
- For (b) (4) : (b) (4) (SOP 1142) or (b) (4), SOP 0996)
- For (b) (4) : (b) (4) (b) (4) SOP 0996)

- For (b) (4) , SOP 0996)

SOP-1142:

Regarding SOP 1142, the integration of peaks for the reporting of results for RNA purity and product-related impurities is not clearly described. We have the following comments:

(b) (4)

Method Validation Report QC-MVR-0025 for SOP 1142:

Regarding SOP 1142 validation (QC-MVR-0025), we have the following comments:

(b) (4)

1 page determined to be not releasable: (b)(4)

Bridge Study Report QC-OTH-0801: SOP-0996 and SOP-1142:

Regarding the comparability or results from SOP 0996 and SOP 1142, although the calculations for RNA purity (main peak) and for (b) (4) provide (b) (4) results for SOP 1142 than for SOP 0996, the release and stability acceptance criteria for RNA purity and (b) (4) for mRNA CS-024414 and mRNA-1273 LNP DS and DP were not adjusted. Please provide the following information for the analysis of comparability of the two methods:

(b) (4)

We advise that you provide a response to the above questions in Module 1 of the BLA and update the information in Module 3 after you receive feedback from us.

Please confirm your receipt of this request, and provide your responses as an amendment to STN 125752 at your earliest convenience but no later than November 29, 2021. If there are questions that you will need additional time to respond to, please provide an estimated response date.

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.