

RESPONSE TO FDA COMMENTS ON CLINICAL RECEIVED ON 23 SEPTEMBER 2021

The Sponsor acknowledges FDA comments on CLINICAL topics (in **Bold**)

**Assays (Antibody Quantification)**

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

**ITEM 1:**

**Regarding the document titled Summary of Biomarker Assays Used in mRNA-1273 Program, based on the information summarized in Table 1, for Phase 3 study 301, the quantification of neutralizing antibodies (nAb) and binding antibodies (bAb) were each performed in two laboratories using different assays (nAb: Live Virus MN at Battelle or Pseudovirus VNA at Duke; bAb: Anti-S-2P IgG ELISA at PPD or Anti-S IgG Multiplex MSD at VRC VIP). Please describe which clinical samples were tested in each laboratory, the rationale for the segregation of the samples among the laboratories and the impact on the overall analysis of results.**

**Sponsor Response**

In P301, to characterize immune response to mRNA-1273, a Random Subcohort for Immunogenicity was selected that included a total of 1591 participants based on treatment group (Placebo, mRNA-1273), baseline SARS-CoV-2 status, stratification factor for randomization, and minority status. All available clinical samples for these participants in this pre-selected random subcohort were sent to each of the testing laboratories, e.g. Duke, VRC VIP, and Battelle. Please note that the testing results of the Live Virus MN by Battelle were not yet available at the time of the BLA submission. At the time of collection, immunology assessment samples were processed and divided into 1mL aliquots. Available aliquots for each subject within the immunogenicity subcohort were then shipped to each lab and tested. Hence, all available samples within the immune subcohort were tested in each assay with no segregation of samples.

<b>Assay</b>	<b>Lab</b>	<b>samples</b>	<b>Notes</b>
Live Virus MN	Battelle	all available samples	not included in BLA submission
Pseudovirus VNA	Duke University	all available samples	
Anti-S-2P IgG ELISA	PPD vaccine	all available samples	
Anti-S IgG Multiplex MSD	VRC/VIP	all available samples	