



COVID-19 Vaccine (BNT162, PF-07302048)

BB-IND 19736

Request for Assay Qualification Information

July 09, 2020

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1. BACKGROUND

Reference is made to BB-IND 19736 for the COVID-19 Vaccine (BNT162; PF-07302048), which Pfizer and BioNTech are developing for the prevention of COVID-19 in adults ≥ 18 years of age. The IND was effective on April 29, 2020 and Pfizer initiated a Phase 1/2 US clinical study (C4591001) on May 4, 2020.

The purpose of this submission is to provide clinical assays (IgG binding and SARS-CoV-2 neutralizing antibody assays) as requested by CBER on 06 July 2020 in support of the C4591001 Phase 2b/3 study start scheduled for the week of 20 July 2020.

1.1. Pfizer's Response

The immune response to Pfizer/BNT's COVID-19 vaccine candidates has been assessed by measuring serum IgG antibody responses to the RBD or S1 domains of SARS-CoV-2 spike protein in Pfizer's standardized direct Luminex based immunoassay (dLIA) platform and by measuring neutralizing activity in an authentic functional SARS-CoV-2 neutralization assay developed and qualified in the lab of Dr. Pei-Yong Shi at the University of Texas Medical Branch (UTMB) in Galveston, TX (Xie et al, 2020). Pfizer is submitting draft qualification reports and associated test methods for all the above-mentioned assays. Final qualification reports will be sent to CBER once all quality control checks have been completed.

The RBD and S1 IgG dLIA procedures have been developed and qualified in-house. Draft qualification reports for each IgG dLIA (VR-MQR-10211 for S1 IgG dLIA, and VR-MQR-10212 for RBD IgG dLIA) are provided with this submission along with the test method SOPs (VR-TM-10293 and VR-TM-10294). An evaluation of sample (b) (4) linearity, precision and standard curve bias were used to establish an assay range. From these qualification data, a lower limit of quantitation, and descriptive statistics of assay parameters were also determined for both assays. The qualification results from both assays confirmed that these dLIA assays are suitable for their intended use in vaccine assessment trials. At least one of the two assays will be selected for formal assay validation based on which vaccine construct (BNT162b1 or BNT162b2) is selected for efficacy trials. The selected IgG dLIA will be validated as per Pfizer's standard IgG dLIA validation protocol prior to its use for clinical endpoints supporting licensure (eg, lot consistency and immuno-bridging studies).

Functional immune responses to SARS-CoV-2 have been assessed in an authentic SARS CoV-2 neutralization assay that utilizes a green fluorescent reporter SARS-CoV-2 virus (SARS-CoV-2 mNG) developed by Dr. Pei-Yong Shi at the University of Texas Medical Branch (UTMB) in Galveston, TX (Xie et al, 2020). The assay is currently also transferred into BSL-3 laboratories leased by Pfizer at Hackensack Meridian Health in Nutley, New Jersey. The assay has been qualified in the BSL-3 laboratory at UTMB and the draft qualification report (VR-MQR-10214) and the test method (VR-MQR-10214-ATT01 - SHI-SOP-10011) is provided along with this submission. The main assay parameters that were assessed during qualification and other studies were precision (on a comprehensive panel of (b) (4) sera) and performance of the quality control sera over time. As shown in VR-MQR-10214, the assay exhibited good precision for

a cell-based functional assay. Performance of quality control samples run subsequent to qualification was also assessed (results described in [VR-MQR-10214](#)). The qualification results confirmed that the neutralization assay is suitable for its intended use in vaccine assessment trials. We do not plan to utilize the SARS-CoV-2 neutralizing assay for clinical endpoints supporting licensure, and therefore we do not plan to validate this assay. However, prior to Phase 2b/3 clinical testing, the assay performed by Pfizer at Hackensack Meridian Health will be bridged to the assay performed at UTMB using a panel of human (b) (4) and immune sera. When the work has been completed, the bridging report will be sent to CBER.

During the vaccine efficacy trial, diagnosis of SARS-CoV-2 in participants will be determined by testing mid-turbinate swabs using the Xpert® Xpress SARS-CoV-2 test from Cepheid, which has received FDA Emergency Use Authorization. Testing of swab samples will be performed using the GeneXpert Systems at Pfizer's laboratories in Pearl River, NY. Results from performance assessments of assay sensitivity and specificity at Pfizer-Pearl River will be completed as part of an assay method validation. Detection limits and overall assay performance will be summarized in a validation report and will be submitted to the IND prior to the use of this assay for clinical endpoints supporting licensure.

Detection of exposure to SAR-CoV-2 in study participants will be assessed by the Roche Elecsys Anti-SARS-CoV-2 N-Protein Assay. The Roche assay has a reported overall specificity of (b) (4) and a sensitivity of (b) (4) based on days post PCR diagnosis. Testing of serum samples will be performed using Roche Cobas System at Pfizer's laboratories in Pearl River, NY. Roche's EUA information and results from assay performance assessments at Pfizer-Pearl River will be provided to CBER prior to the use of this assay in phase 2b/3.

2. REFERENCES

Xie X, Muruato A, Lokugamage KG, et al. An infectious cDNA clone of SARS-CoV-2. *Cell Host Microbe* 2020;27(5):841-848.e3.