

Application Type	BLA, Original Application
STN	125835/0
CBER Received Date	September 30, 2024
PDUFA Goal Date	May 31, 2025
(b) (6)	(b) (6)
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Priority Review	Yes
Reviewer Names	(b) (6)
Review Completion Date/Stamped Date	
Concurrence	(b) (6)
Supervisory Concurrence	(b) (6)
Supervisory Concurrence	(b) (6)
Applicant	ModernaTX, Inc.
Established Name	COVID-19 Vaccine, mRNA
(Proposed) Trade Name	MNEXSPIKE
Dosage Form(s) and Route(s) of Administration	Injectable Suspension, Intramuscular
Dosing Regimen	Single dose of 0.2 mL administered at least 3 months after the last dose of COVID-19 vaccine.
Indication(s) and Intended Population(s)	Active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older who have been previously vaccinated with any COVID-19 vaccine.

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Glossary

Ab[C]	Antibody Concentration
ADHS	Antibody Depleted Human Serum
BLA	Biologics License Application
CI	Confidence Interval
COVID-19	Coronavirus Disease 2019
(b) (4)	(b) (4) Linearity
GM	Geometric Mean
GMC	Geometric Mean Concentration
GCV	Geometric Coefficient of Variation
EUA	Emergency Use Authorization
EXV	Extravariability
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IND	Investigational New Drug
LLOQ	Lower Limit of Quantitation
LOD	Limit of Detection
LOQs	Limits of Quantitation
MF	Master File
MN	Microneutralization
mRNA	Messenger Ribonucleic Acid
nAb	Neutralizing Antibody
RAL	Relative Accuracy and Linearity
RT-PCR	Reverse Transcriptase-Polymerase Chain Reaction
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
STN	Submission Tracking Number
ULOQ	Upper Limit of Quantitation
YOA	Years of Age

ModernaTX, Inc. submitted a Biologics License Application (BLA) to seek licensure of the mRNA-1283 vaccine intended to prevent Coronavirus Disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in individuals 12 years of age (YOA) and older who have been previously vaccinated with any COVID-19 vaccine. The BLA was designated as Priority Review.

The SARS-CoV-2 MN assay is a cell-based assay that was designed to determine the ability of SARS-CoV-2 neutralizing antibodies to inhibit the infection of (b) (4) cells by SARS-CoV-2 reporter virus particles, containing spike mutations of the spike variant of concern, which express (b) (4). The assay was encoded to quantitate pseudovirus neutralizing antibody (nAb) concentrations against three strains of SARS-CoV-2: ancestral SARS-CoV-2 D614G (VSDVAC 62), Omicron BA.4/5 (VSDVAC 137), and Omicron XBB.1.5 (VSDVAC 150).

The design and results of the VSDVAC 150 validation study are summarized as follows:

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The (b) (4) SARS-CoV-2 RT-PCR assay is intended for the qualitative detection of nucleic acid from SARS-CoV-2 in anterior nasal swabs, mid-turbinate nasal swabs, nasopharyngeal and oropharyngeal swabs, and bronchoalveolar lavage fluid. The assay was authorized under Emergency Use Authorization (EUA) and was used to evaluate the primary efficacy endpoint in Study P301.

Method Verification Report 1-P-PR-PRO-9135841VAL investigated assay accuracy as measured in samples derived from nasal swabs and evaluated at (b) (4) central lab. To evaluate accuracy, (b) (4)

The sensitivity and specificity were calculated for the positive samples and negative samples, respectively. All (b) (4) positive samples were detected as positive (sensitivity = (b) (4)) and all (b) (4) negative samples were detected as negative (specificity = (b) (4)).

I consider all validation parameters investigated in both the method validation report and the method verification report to be validated.

2. Clinical and Regulatory Background

ModernaTX, Inc. submitted a BLA to seek licensure of the mRNA-1283 vaccine intended to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 YOA and older who have been previously vaccinated with any COVID-19 vaccine. The BLA was designated as Priority Review.

Compared to mRNA-1273 (trade name: SPIKEVAX), the currently licensed COVID-19 vaccine from ModernaTX, Inc., the Applicant stated that mRNA-1283 has an improved shelf-life at refrigerated temperatures and requires a lower dose to elicit an immune response.

The BLA is primarily supported by immunogenicity, efficacy, and safety data from Phase 3 Clinical Study P301, as well as both immunogenicity and safety data from Phase 3 Clinical Study P301 – Japan. Both Studies were reviewed in a separate review memo under this BLA. This review memo covers the method validation report and method verification report for the SARS-CoV-2 MN assay and (b) (4) SARS-CoV-2 RT-PCR assay, respectively, supporting the BLA.

The SARS-CoV-2 MN assay is a cell-based assay that is designed to determine the ability of SARS-CoV-2 neutralizing antibodies to inhibit the infection of (b) (4) cells by SARS-CoV-2 reporter virus particles, containing spike mutations of the spike variant of concern, which express (b) (4).

The assay was encoded to quantitate pseudovirus nAb concentrations against three strains of SARS-CoV-2: ancestral SARS-CoV-2 D614G (VSDVAC 62), Omicron BA.4/5 (VSDVAC 137), and Omicron XBB.1.5 (VSDVAC 150).

Both VSDVAC 62 and VSDVAC 137 were used to evaluate the primary immunogenicity endpoints in Study P301, while VSDVAC 150 was used to evaluate the primary immunogenicity endpoint in Study P301 – Japan. VSDVAC 150 is the focus of this review memo.

The (b) (4) SARS-CoV-2 RT-PCR assay is intended for the qualitative detection of nucleic acid from SARS-CoV-2 in anterior nasal swabs, mid-turbinate nasal swabs, nasopharyngeal and oropharyngeal swabs, and bronchoalveolar lavage fluid. The assay is authorized under Emergency Use Authorization (EUA) and was used to evaluate the primary efficacy endpoint in Study P301. Method Verification Report 1-P-PR-PRO-9135841VAL is included in this review memo.

3. Sources of Clinical Data and Other Information Considered

3.1 Review Strategy

3.2 BLA Documents That Serve as the Basis for the Statistical Review

The following documents submitted to the BLA are reviewed:

STN 125835/0.0 (submitted on 9/30/2024)

1. Module 5. Clinical Study Reports

- VSDVAC 150 – Validation of a Microneutralization Assay for the Detection of SARS CoV-2 Neutralizing Antibodies (SARS CoV-2-nAb) for Seasonal Variants for the Omicron XBB.1.5 Variant

STN 125835/0.25 (submitted on 3/3/2025)

1. Module 1. Information Amendments
 - Response to Information Request 19
2. Module 5. Clinical Study Reports
 - 1-P-PR-PRO-9135841VAL – The Qualitative Analysis of SARS-CoV-2 Using the (b) (4)

4. Discussion of Individual Studies/Clinical Trials

4.1 Review of Method Validation Report VSDVAC 150

4.1.1 Background

The SARS-CoV-2 MN assay is a cell-based assay that is designed to determine the ability of SARS-CoV-2 neutralizing antibodies to inhibit the infection of (b) (4) cells by SARS-CoV-2 reporter virus particles, containing spike mutations of the spike variant of concern, which express (b) (4).

The assay was encoded to quantitate pseudovirus nAb concentrations against Omicron XBB.1.5 and was used to evaluate the primary immunogenicity endpoint in Study P301 – Japan, which was submitted as part of the BLA to support licensure of mRNA-1283 for individuals 12 YOA and older who have been previously vaccinated with any COVID-19 vaccine.

Method validation report for VSDVAC 150 investigated the following quantitative parameters for the assay: intermediate precision, relative accuracy, LOQs, and (b) (4) linearity.

4.1.2 Sample Antibody Concentration Determination

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4.2 Review of Method Verification Report 1-P-PR-PRO-9135841VAL

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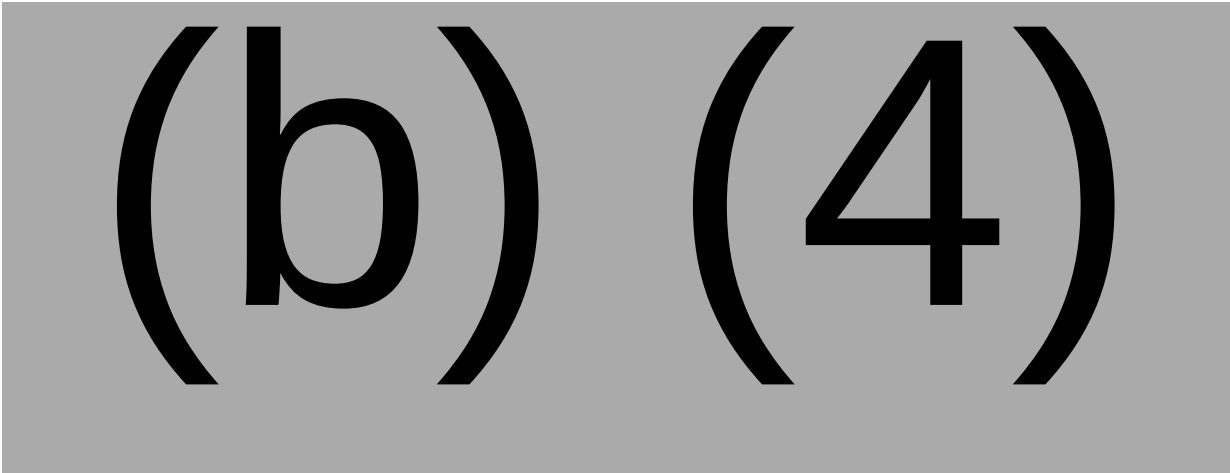


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(b) (4)



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5. Conclusions

I consider all validation parameters investigated in both the method validation report and the method verification report to be validated.