



(b) (6) **ANALYTICAL METHOD REVIEW MEMO**

To The file: STN 125835/0

From (b) (6)

Through (b) (6)

Applicant Moderna TX, Inc.

Subject Biologics License Application (BLA): Review of bioburden, endotoxin, and sterility analytical methods used for COVID-19 Vaccine, mRNA (mRNA-1283)

Recommendation: Approval

Executive Summary

The bioburden, endotoxin, and sterility analytical methods used for testing and release of mRNA-1283 and the associated analytic method qualifications were reviewed. The assays were adequately described and shown to be suitable for their intended purpose.

Conclusion

The analytical methods and their qualifications reviewed for mRNA-1283 drug substance and drug product were found to be adequate for their intended use.

Documents Reviewed

Information in sections of the original submission that describe control of Drug Substance (DS) and Drug Product (DP) (3.2.S.4 and 3.2.P.5, respectively), including descriptions of DS and DP specifications, analytical procedures of DS and DP and qualifications of these analytical procedures were reviewed. In addition, responses to CBER's Information Requests (IRs) received on November 1, 2024 (Amendment #2) and February 14, 2025 (Amendment #22) were also reviewed as mentioned below.

Background

The mRNA-1283 DP is an RNA-lipid complex dispersion that contains RNA, which encodes the linked N-terminal domain and receptor-binding domain of the spike glycoprotein of the SARS-CoV-2 virus, and four lipids that act as protectants and carriers of the RNA. The DP is a sterile, single-dose, ready-to-use liquid solution at

10 µg/0.2 mL for intramuscular (IM) administration in a 1-mL prefilled syringe (PFS). Each PFS delivers 10 µg of RNA and 200 µg of total lipids as a white to off-white dispersion in preservative-free buffer containing (b) (4) mM Tris and (b) (4) g/L sucrose at pH (b) (4).

This review focuses on qualification of the bioburden, endotoxin, and sterility test performed at the Moderna TX, Inc. in Norwood, MA, USA (b) (4) (DP endotoxin and sterility), and Moderna Biotech Spain, SL, Madrid, Spain (DP endotoxin and sterility) to determine if these methods are suitable for testing of the mRNA-1283 (b) (4) DP under the actual conditions of use at the proposed testing site.

(b) (4)

(b) (4)

2. Endotoxin Method ((b) (4) DP)

Introduction

Endotoxin testing for (b) (4) DP is performed at Moderna TX, Norwood MA, USA (b) (4) and Moderna Biotech Spain, SL, Madrid, Spain (DP). Specification of (b) (4) DP must be met for release of mRNA-1283.

Methods

(b) (4)

The (b) (4) bacterial endotoxin test ((b) (4)-BET) is performed on (b) (4) DP to quantitate bacterial endotoxins by (b) (4)

The methods are described in more detail below together with the tests that were performed, which included a (b) (4) step (described and approved in BLA 125752/0) to demonstrate suitability of the test methods.

(b) (4)

Endotoxin Qualification for (b) (4) DP
(b) (4)

(b) (4)

Conclusion

The method suitability tests were performed and compliant with (b) (4) thus indicating the (b) (4)-BET and (b) (4)-BET test methods are appropriate under the actual conditions of use.

3. Sterility Method (DP)

Introduction

Sterility testing for mRNA-1283 DP is performed at (b) (4) and Moderna Biotech Spain, SL, Madrid, Spain. Acceptance criteria of 'No Growth' must be met for the lot release of mRNA-1283 DP.

Method

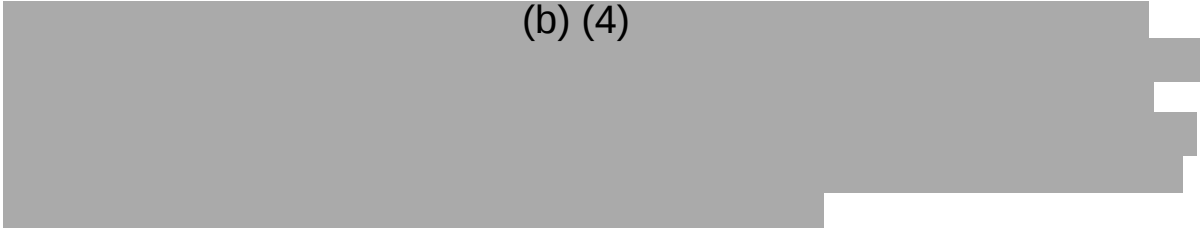
The (b) (4) sterility test is used for (b) (4) solutions in accordance with (b) (4). Test samples are (b) (4)

The method is described in more detail below together with the tests that were performed to determine suitability of the test method.

Sterility Test Qualification for DP

(b) (4)

(b) (4)



Conclusion

The method suitability test was performed and compliant with (b) (4) and testing sites were qualified for their (b) (4) sterility test. Therefore, CBER determined their (b) (4) sterility test method is appropriate under the actual conditions of use at Moderna Biotech S.L. Madrid, Spain and (b) (4) as release and testing sites for sterility testing of mRNA-1283 DP.