DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

# MEMORANDUM FOR RECORD

**To** STN # 125752/0 January 4, 2022

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Joseph Kulinski, RPM, OVRR
Sudhakar Agnihothram, Chair, BLA Review Committee

**Subject** CBER In-support Sterility and Bacterial Endotoxin Test (BET) Results for COVID-19 mRNA Vaccine, SPIKEVAX

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ModernaTX, Inc. (Moderna) submitted three lots of SPIKEVAX drug product (DP) to CBER for in-support testing: 7006521151 (manufactured at Catalent, Lot 031H21A), 7006521143 (manufactured at Catalent, Lot 064H21A) and 7007621154 (manufactured at Baxter Pharmaceutical Solutions (Baxter, Lot 940875). DBSQC's Laboratory of Microbiology, *In-vivo* Testing and Standards performed sterility and endotoxin testing of these lots submitted in support of STN 125752/0.

1. Sterility (Seth Schulte)

All three DP lots were tested for sterility using CBER's membrane filtration test method (TM: 000388, v10). This compendial sterility test was performed to confirm Moderna's membrane filtration sterility test results of no growth of bacteria and fungi that was recorded as "pass". No microorganism growth was observed in the lots tested by CBER, confirming the test results obtained by Moderna. CBER's in-support sterility test results for all lots met the specification required and confirmed the passing results by Moderna.

2. Bacterial Endotoxin (Hyesuk Kong)

Moderna contracts out its (b) (4) BET to Associates of Cape Cod (ACC), which performs the compendial (b) (4) BET method in accordance with USP <85>. The Standard Operating Procedure (SOP: (b) (4) /mRNA-1273 Release) and complete qualification reports (i.e., 0620-003tesvr, 0620-038tesvr, 0820-039tesvr, 0820074testvr, and 0920-076tesvr) for SPIKEVAX DP endotoxin testing were submitted directly to CBER by ACC under STN 102416/5093 on October 19, 2021; see Moderna's IR response (Amendment 19, item #7) for more information.

All three lots of DP submitted to CBER were tested for bacterial endotoxin using CBER's (b) (4) test method (TM: 000576, v03). The (b) (4) BET performed at CBER included a (b) (4) as per firm's SOP, followed by (b) (4) for a valid test.

There are a number of differences in the tests performed by CBER and ACC. CBER uses the (b) (4) : ACC uses the (b) (4) . The (b) (4) (b) (4)

The results are summarized in Table 1. The three test samples showed slight inhibition in CBER's test as the spike recoveries for the positive product control (PPC) were 70-80%, but the results were valid as the PPC were within the acceptance criterion (b) (4) (b) (4) %. CBER's in-support test results indicate the bacterial endotoxin concentration met the specification of (b) (4) EU/mL for all conformance lots. Therefore, the BET results by CBER confirm the passing results reported by Moderna, as they were both within their proposed specification.

**Table 1: (b) (4) BET Results**

| Moderna Lot Number (Manufacturer Lot) | BET Test Dilution | CBER % Spike Recovery | CBER Results (EU/mL) | Moderna's Results (EU/mL) | Specification (b) (4) EU/mL) met |
|---|---|---|---|---|---|
| 7006521151 (031H21A by Catalent) | 1:1000 | 80 | (b) (4) | (b) (4) | yes (both CBER and Moderna) |
| 7006521143 (064H21A by Catalent) | 1:1000 | 71 | (b) (4) | (b) (4) | yes (both CBER and Moderna) |
| 7007621154 (940875 by Baxter) | 1:1000 | 70 | (b) (4) | (b) (4) | yes (both CBER and Moderna) |

In conclusion, the sterility and bacterial endotoxin results from tests performed by CBER were within their proposed specifications and CBER's results are comparable to the values reported on Moderna's Certificate of Analysis.