1.12.5 Request for a Waiver

The Sponsor requests CBER place Spikevax on surveillance in lieu of routine release to fulfill its responsibilities under 21 CFR 610.2 (a). This request is based on the high degree of characterization attained for mRNA vaccines and the demonstrated continued control of the manufacturing process and facilities. As summarized in EUA 27073 SN 0231 (dated July 30, 2021), (b) (4) of mRNA-1273 LNP ((b) (4) as of June 01, 2021) and mRNA-1273 DP ((b) (4) as of June 01, 2021) have been produced to date with very small reject rates ((b) (4) for mRNA-1273 LNP and (b) (4) for mRNA-1273 DP) supporting the consistency and control of the manufacturing process. In addition, the use of biologically sourced raw materials for mRNA-1273 is limited to (b) (4)
(b) (4)
(b) (4)

The Sponsor has systematically and thoroughly assessed the properties of the mRNA-1273 vaccine with respect to those attributes that affect product quality and potency. These attributes include: the quantity of mRNA delivered; the fidelity of the mRNA sequence, including cap, tail, and open reading frame; the integrity of the mRNA; and various biophysical attributes of the lipid nanoparticles, particularly including the state of mRNA encapsulation and the size distribution of the particles. The Sponsor has directly assessed each of these features for the mRNA-1273 vaccine and controls them as part of the panel of batch analyses as shown in the attached lot release protocol (QC-OTH-0609). The degree of characterization of mRNA-1273 meets or exceeds that for other well-characterized biotech products such as recombinant DNA-derived proteins and monoclonal antibodies.

Continued control of the manufacturing process and facilities has been demonstrated during Phase 3 comparability for mRNA-1273. The quality attributes of the materials are consistent from lot to lot and across manufacturing scales and sites. The product has been characterized to ensure that inherent variability in quality attributes from lot to lot has no adverse impact upon safety or efficacy of the DP. Analytical comparability has been assessed by 1) release, 2) stability, and 3) extended characterization testing. Process comparability has been demonstrated through evaluation of in-process controls and critical process parameters against expected ranges or proven acceptable ranges (PARs). The comparability acceptance criteria were the same as or tighter than the lot release specifications. The assessment covered all the constituent materials,
(b) (4)

Continued capacity expansion and introduction of new materials and equipment will be assessed by Phase 4 comparability demonstration. A Continued Process Verification (CPV) program has

been established to ensure robust control across the lifespan of mRNA-1273 manufacturing post the process and analytical comparability demonstration.

The mRNA-1273 vaccine has demonstrated consistent and robust control through process and product understanding, impurity clearance, and strong analytical capabilities as provided in the CTD sections of 3.2.S.3.2 {CX-024414 LNP}, 3.2.S.3.2 {SM-102 LNP}, 3.2.S.3.2 {mRNA-1273 LNP}, 3.2.P.5.5, 3.2.S.2.6.3 {CX-024414}, 3.2.S.2.6.3 {SM-102 LNP}, 3.2.S.2.6.3 {mRNA-1273 LNP} and 3.2.P.2.3.3 {Comparability}.