

3.2.S.4.2. OVERVIEW

This section contains information specific for presentation Tris/sucrose Comirnaty [Original and Omicron (B.1.1.529)], which is discontinued. For information purposes, non-compendial analytical method information supportive of the stability data is maintained, along with the corresponding analytical validation information.

Analytical procedures for Omicron (B.1.1.529) variant drug substance (DS) release and stability testing are listed in Table 3.2.S.4.2-1. Several of the analytical procedures are identical to the corresponding commercial BNT162b2 original vaccine procedures, while others have been updated for analysis of the Omicron (B.1.1.529) variant. The change to the Omicron (B.1.1.529) variant vaccine is solely driven by the variant-based sequence change. A change in this variant mRNA sequence is limited to the sequence encoding the S glycoprotein, and does not significantly change the size of the mRNA. The drug substance concentration, formulation process, and process controls remain unchanged. A change in nucleotide sequence for the Omicron (B.1.1.529) variant vaccine will not impact quality attribute criticality designation, and only the identity quality attribute will be impacted by the change in sequence. For identity testing, Omicron variant-specific reagents are utilized and the analytical procedure for assessment of identity is described in Section 3.2.S.4.2 Analytical Procedures Reverse Transcription-Polymerase Chain Reaction (RT-PCR) [Omicron (B.1.1.529) Variant]. The Section 3.2.S.4.2 Analytical procedures – Quantitative Polymerase Chain Reaction (qPCR) [Omicron (B.1.1.529) Variant] description is updated to allow for an additional calculation which accounts for a base pair size difference between original and variant.

Table 3.2.S.4.2-1. Analytical Procedures for Omicron (B.1.1.529) Drug Substance

Analytical Procedure	Quality Attribute	Original Vaccine Analytical Procedure Updated for Omicron (B.1.1.529) Variant (Yes/No)
Appearance ^a	Clarity and Color	No
Potentiometry ^a	pH	No
UV Spectroscopy	Content (RNA Concentration)	No
RT-PCR	Identity of encoded RNA sequence	Yes
RP-HPLC	5'-Cap	No
ddPCR	Poly (A) Tail	No
IP-RP-HPLC	Poly (A) Tail Length	No
qPCR	Residual DNA Template	Yes
Immunoblot	Residual dsRNA	No
Capillary Gel Electrophoresis	RNA Integrity	No
Endotoxin (LAL) ^a	Bacterial Endotoxin	No
Bioburden ^a	Bioburden	No

a. Compendial method used in stability

Abbreviations: ddPCR = digital droplet polymerase chain reaction, dsRNA = double stranded RNA, LAL = limulus amoebocyte lysate, qPCR = quantitative polymerase chain reaction, RP-HPLC = reversed phase-high performance liquid chromatography, RT-PCR = reverse transcription-polymerase chain reaction