2.3.S.7. STABILITY

2.3.S.7.1. Stability Summary and Conclusions, Omicron (LP.8.1) Variant

The commercial shelf-life of the BNT162b2 Omicron (LP.8.1) drug substance is 6 months when stored at the intended storage condition of -20 ± 5°C in CCI bags. The shelf-life is based on the currently available results of primary stability studies conducted on commercial BNT162b2 Original, Omicron (BA.4/BA.5), and Omicron (XBB.1.5), Omicron (JN.1) and Omicron (KP.2) drug substance batches and will correspond to the approved shelf-life of the Original vaccine drug substance (see 3.2.S.7.1 Stability Summary and Conclusions).

An Omicron (LP.8.1) drug substance confirmatory batch is enrolled on stability in order to confirm the 6-month shelf-life when stored at the intended storage condition of -20 ± 5°C in CCI bags. The analytical procedures used in the stability programs were developed to monitor the composition, strength, purity, safety and general quality attributes of drug substance.

2.3.S.7.2. Omicron (LP.8.1) Stability Batch and Studies

The Omicron (LP.8.1) drug substance confirmatory batch is enrolled in the stability program and monitored in accordance with the approved protocols. A summary of the stability batch, use, and the stability studies are presented in Table 2.3.S.7-1.

Table 2.3.S.7-1. Summary of On-going Stability Studies

Batch Number	Date of Manufacture	Batch Use	Study Type	Storage Condition	Available Data	Study Status
MH3322 (Pfizer Grange Castle)	Mar 2025	CCI Confirmatory, Stability	Long Term	-20 ± 5 °C	Release	On-going
			Accelerated	5 ± 3 °C		On-going

2.3.S.7.2.1. Study Protocol for Drug Substance Batches at the Long Term Condition (-20 °C)

Aliquots of the Omicron (LP.8.1) drug substance confirmatory batches have been stored at -20 ± 5 °C. Testing is performed according to the protocol indicated in Table 2.3.S.7-2 and Table 2.3.S.7-3.

Table 2.3.S.7-2. Stability Protocol Omicron (LP.8.1) Drug Substance Batch Stored at -20 ± 5 °C (Long Term Storage Condition)

Analytical Procedure	Test Intervals [a]
Appearance (Clarity)	0, 1M, 2M, 3M, 6M
Appearance (Coloration)	0, 1M, 2M, 3M, 6M
pH (Potentiometry)	0, 1M, 2M, 3M, 6M
Content (RNA Concentration) (UV Spectroscopy)	0, 1M, 2M, 3M, 6M
RNA Integrity (Capillary Gel Electrophoresis)	0, 1M, 2M, 3M, 6M
5'-Cap (RP-HPLC)	0, 1M, 2M, 3M, 6M
Poly (A) Tail (ddPCR)	0, 1M, 2M, 3M, 6M
Endotoxin (LAL)	0, 6M
Bioburden	0, 6M

a. Initial data (t0) are from release testing.
Abbreviations: M = Month; UV = Ultraviolet, RP-HPLC = Reverse Phase Liquid High Performance Chromatography; ddPCR = Droplet Digital Polymerase Chain Reaction; LAL = Limulus Amebocyte Lysate

2.3.S.7.2.2. Study Protocol for Drug Substance Batches at the Accelerated Condition

To support manufacturing process, hold conditions and to study the effects of temporary excursions above the recommended storage conditions of Omicron (LP.8.1) drug substance aliquots have been stored at +5 ± 3 °C. Protocols are detailed in Section 3.2.S.7.1 Stability Summary and Conclusions [Omicron (LP.8.1) Variant].

2.3.S.7.2.3. Summary of Stability Data

2.3.S.7.2.3.1. Summary of Stability Data at the Long Term Storage Condition

Stability data obtained from the commercial scale confirmatory (MH3322) batch stored at the long term condition of -20 ± 5 °C will be updated when available in Section 3.2.S.7.3 Stability Data – [Omicron (LP.8.1) Variant].

2.3.S.7.2.3.2. Summary of Stability Data at the Accelerated Condition

Stability data obtained from the commercial scale confirmatory (MH3322) batch stored at the accelerated condition of 5 ± 3 °C will be updated when available in Section 3.2.S.7.3 Stability Data – [Omicron (LP.8.1) Variant].

2.3.S.7.2.3.3. Conclusions for Shelf Life and Storage

The shelf-life is based on currently available results from primary stability studies conducted on the commercial drug substance batches of the Original vaccine and the approved shelf-life of the Original vaccine drug substance (3.2.S.7.1 Stability Summary and Conclusions).

The following drug substance stability data are considered supporting information for establishing the drug substance stability profile:

- Long-term, accelerated, thermal stress, low temperature and photostability data from BNT162b2 Original studies designed to follow ICH guidelines for stability of drug substance.

- Long term and accelerated stability studies completed for Omicron (BA.4/BA.5) drug substance.
- Long term and accelerated stability studies completed for Omicron (XBB.1.5) drug substance.
- Long term and accelerated stability studies completed for Omicron (JN.1) drug substance.
- Long term and accelerated stability studies completed for Omicron (KP.2) drug substance.
- Long term and accelerated stability studies initiated for Omicron (LP.8.1) drug substance.

The confirmatory stability studies for Omicron (LP.8.1) drug substance are currently on-going. Data from these studies will be provided in the future and will be used to confirm the shelf-life of the drug substance.

The rationale presented provides the justification for the Omicron (LP.8.1) drug substance shelf-life of 6 months when stored at the recommended temperature of -20 ± 5 °C in CCI bags.

2.3.S.7.3. Post-approval Stability Protocol and Stability Commitment

Upon completion of the ICH stability protocols, post-approval, a minimum of one batch of BNT162b2 drug substance manufactured will be enrolled in the commercial stability program at the long term storage conditions of -20 ± 5 °C each year that drug substance is manufactured. The protocol for storage at -20 ± 5 °C in CCI bags is provided in Table 2.3.S.7-3.

Table 2.3.S.7-3. Post-Approval Commercial Stability Protocol for BNT162b2 Drug Substance Stored at -20 ± 5°C in CCI Bags

Analytical Procedure	Test Intervals
Appearance (Clarity)	0M, 1M, 2M, 3M, 6M
Appearance (Coloration)	
pH	
UV Spectroscopy (Content (RNA Concentration))	
Capillary Gel Electrophoresis (RNA Integrity)	
5'-Cap (RP-HPLC)	
Poly (A) Tail (ddPCR)	
Bioburden	0M, 6M
Endotoxin (LAL)	

Abbreviations: M = Month, UV= Ultraviolet, RP-HPLC = Reverse Phase Liquid High Performance Chromatography; ddPCR = Droplet Digital Polymerase Chain Reaction; LAL = Limulus Amebocyte Lysate

2.3.S.7.4. Stability Data

Stability data for long term conditions and accelerated conditions will be provided when available in Section 3.2.S.7.3.Stability Data [Omicron (LP.8.1) Variant].