

2.3.S.7. STABILITY

2.3.S.7.1. Stability Summary and Conclusions, Omicron (XBB.1.5) Variant

The commercial shelf-life of the BNT162b2 Omicron (XBB.1.5) drug substance is 6 months when stored at the intended storage condition of $-20 \pm 5^{\circ}\text{C}$ in EVA bags. The shelf-life is based on the currently available results of primary stability studies conducted on commercial BNT162b2 Original and Omicron (BA.4/BA.5) 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 (XBB.1.5) drug substance confirmatory batch using process 2 and commercial scale batches manufactured CCI have been enrolled on stability in order to confirm the 6-month shelf-life when stored at the intended storage condition of $-20 \pm 5^{\circ}\text{C}$ in EVA 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 (XBB.1.5) Stability Batch and Studies

A summary of the stability batches, use, and the status of 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
HD1999 (Pfizer Andover, MA, Suite J)	April 2023	Large Scale Confirmatory, Process 2	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
HJ6451 (Pfizer Andover, MA, Suite J)	August 2023	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
HJ6448 (Pfizer Andover, MA, Suite J)	August 2023	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
HJ4185 (Pfizer Andover, MA, Suite J)	August 2023	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
HJ1782	August 2023	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
HJ1783	August 2023	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
HJ1784	September 2023	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
HM4196	October 2023	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
AB00082 (BioNTech Marburg, Line 2)	February 2024	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
AB00083 (BioNTech Marburg, Line 2)	February 2024	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
AB00084 (BioNTech Marburg, Line 2)	March 2024	Process Performance Qualification, CCI Scale, CCI	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete

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

Aliquots of Omicron 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 (XBB.1.5) 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 high performance liquid chromatography; ddPCR = droplet digital polymerase chain reaction

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

Omicron (XBB.1.5) 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 (XBB.1.5) 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 (HD1999) batch, and CCI PPQ batches (HJ4185, HJ6448, HJ6451, HJ1782, HJ1783, HJ1784, HM4196, AB00082, AB00083, and AB00084) stored at the long term condition of -20 ± 5 °C are provided in Section 3.2.S.7.3 Stability Data – [Omicron (XBB.1.5) Variant].

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

Stability data obtained from the commercial scale confirmatory (HD1999) batch, and CCI PPQ batches (HJ4185, HJ6448, HJ6451, HJ1782, HJ1783, HJ1784, HM4196, AB00082, AB00083 and AB00084) stored at the long term condition of -20 ± 5 °C are provided in Section 3.2.S.7.3 Stability Data – [Omicron (XBB.1.5) 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 using both process 2 and CCI :

- 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 initiated for Omicron (BA.4/BA.5) drug substance.
- Long term and accelerated stability studies initiated for Omicron (XBB.1.5) drug substance.
- Long term and accelerated stability studies data for up to 6 months for Omicron (XBB.1.5) drug substance manufactured CCI

No additional photostability studies were performed on CCI DS batches as there is no change in the container closure system. As the container closure remains the same, the conditions affecting the photostability of the product are unchanged. The photostability profile currently determined as supported by the initial studies remains applicable to the drug substance manufactured using CCI

The supporting data and the results of the confirmatory and process performance qualification stability studies for Omicron (XBB.1.5) drug substance manufactured by both process 2 and CCI confirm that the quality attributes remain within acceptable limits throughout a duration of 6 months shelf-life.

The rationale presented provides the justification for the Omicron (XBB.1.5) drug substance shelf-life of 6 months for process 2 and CCI when stored at the recommended temperature of -20 ± 5 °C in EVA 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 Omicron (XBB.1.5) variant 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 EVA 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 EVA Bags**

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

Abbreviations: UV = ultraviolet; RP-HPLC = reverse phase high performance liquid 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 are provided in
Section 3.2.S.7.3.Stability Data [Omicron (XBB.1.5) Variant].