

2.3.S.7. STABILITY

This section contains information specific for presentation Comirnaty [Original and Omicron (BA.4/BA.5)], which is discontinued. For information purposes, data/information supportive of the platform development approach for other presentations is maintained.

2.3.S.7.1. Stability Summary and Conclusions, Omicron (BA.4/BA.5)

The commercial shelf life of the BNT162b2 Omicron (BA.4/BA.5) (herin referred to as Omicron) drug substance is 6 months when stored at the intended storage condition of $-20 \pm 5^{\circ}\text{C}$ in **CCI** bags. The shelf-life is based on the currently available results of primary stability studies conducted on commercial BNT162b2 Original drug substance batches and will correspond to the approved shelf-life of the original vaccine drug substance (see Section [3.2.S.7.1 Stability Summary and Conclusions](#)).

Omicron drug substance confirmatory and process performance qualification (PPQ) batches are enrolled on stability in order to confirm the initial 6-month shelf-life when stored at the intended storage condition of $-20 \pm 5^{\circ}\text{C}$ 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.

Two ICH Omicron drug substance process 2a batches were enrolled on stability to confirm the initial 6 month shelflife when stored at the intended storage condition of $-20 \pm 5^{\circ}\text{C}$ in **CCI** bags.

2.3.S.7.1.1. Omicron (BA.4/BA.5) Stability Batch and Studies

The Omicron drug substance confirmatory batches are enrolled in the stability program and monitored in accordance with the approved protocols. A summary of the stability batches, 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
GH5745 (Pfizer Andover, MA (Suite J))	July 2022	Clinical, Large Scale Confirmatory, Stability, Process 2, Stability	Long Term	-20 ± 5 °C	18 months	On-going
			Accelerated	5 ± 3 °C	6 months	Complete
GP6836 ^a (Pfizer Grange Castle, Dublin)	December 2022	Process 2, Stability	Long Term	-20 ± 5 °C	12 ^b months	Complete
			Accelerated	5 ± 3 °C	6 months	Complete
AB00029 (BioNTech Marburg, DS Line 2)	December 2022	Process Performance Qualification, Process 2, Stability	Long Term	-20 ± 5 °C	12 months	On-going
			Accelerated	5 ± 3 °C	6 months	Complete
			Thermal Stress	25 ± 2 °C/ 60 ± 5 % RH	1 month	Complete
AB00031 (BioNTech Marburg, DS Line 2)	December 2022	Process Performance Qualification, Process 2, Stability	Long Term	-20 ± 5 °C	12 months	On-going
			Accelerated	5 ± 3 °C	6 months	Complete
			Thermal Stress	25 ± 2 °C/ 60 ± 5 % RH	1 month	Complete
AB00034 (BioNTech Marburg, DS Line 2)	January 2023	Process Performance Qualification, Process 2, Stability	Long Term	-20 ± 5 °C	12 months	On-going
			Accelerated	5 ± 3 °C	6 months	Complete
			Thermal Stress	25 ± 2 °C/ 60 ± 5 % RH	1 month	Complete
HD9156 (Pfizer Andover, MA Suite J)	May 2023	ICH CC1 Scale, Process 2a, Stability	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete
HE2721 (Pfizer Andover, MA Suite J)	May 2023	ICH CC1 Scale, Process 2a, Stability	Long Term	-20 ± 5 °C	6 months	Complete
			Accelerated	5 ± 3 °C	3 months	Complete

a. Batch GP6836 has been included to support a maximum cumulative hold at commercial scale at Pfizer, Grange Castle.

b. Batch GP6836 was terminated after the 12 month timepoint in error.

2.3.S.7.1.2. 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 (BA.4/BA.5) Process 2 Drug Substance Batches GH5745 and GP6836^b Stored at -20 ± 5 °C (Long Term Storage Condition)

Analytical Procedure	Test Intervals ^a
Appearance (Clarity)	0, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
Appearance (Coloration)	0, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
Potentiometry	0, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
Content (RNA Concentration) (UV Spectroscopy)	0, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
RNA Integrity (Capillary Gel Electrophoresis)	0, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
5'-Cap (RP-HPLC) ^b	0, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
Poly (A) Tail (ddPCR) ^b	0, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
Endotoxin (LAL)	0, 6M, 24M
Bioburden	0, 6M, 24M

a. Initial data (t0) are from release testing.

b. Batch GP6836 tested to 12 months. 18 month and 24 month timepoints cancelled.

Abbreviations: W = Week; M = Month; UV = ultraviolet; RP-HPLC = reverse phase high performance liquid chromatography; ddPCR = droplet digital polymerase chain reaction; LAL = Limulus amoebocyte lysate

Table 2.3.S.7-3. Stability Protocol for Omicron (BA.4/BA.5) Process 2 Drug Substance Batches AB00029, AB00031, AB00034 Stored at -20 ± 5 °C (Long Term Storage Condition)

Analytical Procedure	Test Intervals ^a
Appearance (Clarity)	0, 1W, 2W, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
Appearance (Coloration)	0, 1W, 2W, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
pH (Potentiometry)	0, 1W, 2W, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
Content (RNA Concentration) (UV Spectroscopy)	0, 1W, 2W, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
RNA Integrity (Capillary Gel Electrophoresis)	0, 1W, 2W, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
5'-Cap (RP-HPLC)	0, 1W, 2W, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
Poly (A) Tail (ddPCR)	0, 1W, 2W, 1M, 2M, 3M, 6M, 9M, 12M, 18M, 24M
Endotoxin (LAL)	0, 6M, 24M
Bioburden	0, 6M, 24M

a. Initial data (t0) are from release testing.

Abbreviations: W = Week; M = Month; UV = ultraviolet; RP-HPLC = reverse phase high performance liquid chromatography; ddPCR = droplet digital polymerase chain reaction; LAL = Limulus amoebocyte lysate

Table 2.3.S.7-4. Stability Protocol for Omicron (BA.4/BA.5) Process 2a Drug Substance Batches 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
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 (t=0) are from release testing.

Abbreviations: M = Month; UV = ultraviolet; RP-HPLC = reverse phase high performance liquid chromatography; ddPCR = droplet digital polymerase chain reaction; LAL = Limulus amoebocyte lysate

2.3.S.7.1.3. Study Protocol for Drug Substance Batches at the Accelerated Condition

Omicron (BA.4/BA.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 (BA.4/BA.5) Variant].

2.3.S.7.1.4. Study Protocol for Drug Substance Batches at the Thermal Stress Condition

Omicron (BA.4/BA.5) drug substance aliquots have been stored at 25 ± 2 °C/ 60 ± 5 % RH. Testing is performed according to the protocol indicated in Section 3.2.S.7.1 Stability Summary and Conclusions [Omicron (BA.4/BA.5) Variant].

2.3.S.7.1.5. Summary of Stability Data

2.3.S.7.1.5.1. Summary of Stability Data at the Long Term Storage Condition

Stability data up to 6 months are available from the ICH batches (HD9156 and HE2721) manufactured using process 2a. Stability data up to 18 month is available from the clinical scale confirmatory (GH5745) batch stored at the long term condition of -20 ± 5 °C and up to 12 months are available for confirmatory (GP6836) batch stored at the long term condition of -20 ± 5 °C. Stability data up to 12 months for 3 PPQ batches (AB00029, AB00031 and AB00034) stored at the long term condition of -20 ± 5 °C.

2.3.S.7.1.5.2. Summary of Stability Data at the Accelerated Condition

Stability data up to 3 months are available from the ICH batches (HD9156 and HE2721) manufactured using process 2a and process 2 stability data up to 6 month are available from the clinical confirmatory batches GH5745 and GP6836 and for 3 PPQ batches (AB00029, AB00031 and AB00034) stored at the accelerated condition of 5 ± 3 °C. is the results are presented in [Section 3.2.S.7.3 Stability Data – \[Omicron \(BA.4/BA.5\) Variant\]](#).

2.3.S.7.1.5.3. Summary of Stability Data at the Thermal Stress Condition

Stability data up to 1 month for three process performance qualification batches stored at the thermal stress condition of 25 ± 2 °C/ 60 ± 5 % RH are presented in [Section 3.2.S.7.3 Stability Data – \[Omicron \(BA.4/BA.5\) Variant\]](#). The results for all 3 batches showed OOS for RNA integrity at the 1 month pull point. This does not impact the product quality as it is outside the approved storage duration at this condition.

2.3.S.7.1.5.4. Conclusions for Shelf Life and Storage

The initial 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 ([Section 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 2a:

- 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 data from Omicron (BA.4/BA.5) studies continue to support the 6 month shelf for process 2a
- Long term and accelerated stability data for up to 9 months for Omicron (BA.4/BA.5) using process 2 and process 2a.

The supporting data and the results of the confirmatory stability studies for Omicron (BA.4/BA.5) drug substance manufactured by both process 2 and process 2a confirm that the quality attributes remain within acceptable limits throughout a duration of 6 months.

No photostability study was performed on the new 2a process because there was no change in the container closure system. Since the container closure remains the same, the conditions affecting the photostability of the product are unchanged. Therefore, the photostability profile determined during the initial studies for the process 2 remains applicable to the product manufactured under the new 2a process.

The rationale presented provides the justification for the Omicron (BA.4/BA.5) drug substance shelf-life of 6 months for process 2 and process 2a when stored at the recommended temperature of -20 ± 5 °C in **CCI** bags.

2.3.S.7.3. Stability Data

Stability data for long term conditions and accelerated conditions will be provided in [Section 3.2.S.7.3. Stability Data \[Omicron \(BA.4/BA.5\) Variant\]](#).