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2.3.S.7. STABILITY

This section contains information specific for presentation Tris/sucrose Comirnaty [Original and Omicron (B.1.1.529)], 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

The commercial shelf life of the Omicron (B.1.1.529) drug substance is 6 months when stored at the intended storage condition of $-20 \pm 5^{\circ}\text{C}$ in CCI bags. The initial shelf life is based on the currently available stability data from primary stability studies utilizing material from the commercial wild-type drug substance batches and will leverage the approved shelf-life of the BNT162b2 original vaccine drug substance.

Omicron (B.1.1.529) drug substance stability batches enrolled in stability programs confirm the initial 6 month shelf life when stored at the intended storage condition of $-20 \pm 5^{\circ}\text{C}$ in CCI bags. All testing to date has been performed using analytical methodology and phase appropriate specifications in place at time of testing. 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.7.1.1. Stability Batches and Studies

The stability program is designed to follow ICH guidelines for stability of drug substance (ICH Guideline Q1A: Stability Testing of New Drug Substances and Products; ICH Guideline Q5C: Quality of Biotechnological Products, Stability Testing of Biotechnological/Biological Products).

To date, 4 Omicron (B.1.1.529) drug substance batches have been manufactured at Pfizer Andover and BioNTech Marburg using the CCI scale of the commercial process (process 2). In addition, a clinical trial batch was manufactured at BioNTech Mainz using a combination of process 1 and process 2. These batches have been enrolled on formal stability studies.

A summary of all drug substance batches on stability studies and current available stability data are shown in [Table 2.3.S.7-1](#). Further information on confirmation and extension of the drug substance shelf life is discussed in [Section 3.2.S.7.1 Stability Summary and Conclusions \[Omicron \(B.1.1.529\) Variant\]](#).

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
CQ19-P020.17-DS (BNT Mainz)	December 2021	CTM, Stability	Long Term	-20 ± 5 °C	12 months	On-going
			Accelerated	5 ± 3 °C	6 months	Complete
			Low Temperature	80 to -60 °C	1 week	Complete
22Y539C101 (Pfizer Andover, MA (ACMF))	January 2022	CTM, Large Scale Confirmatory, Stability	Long Term	-20 ± 5 °C	9 months	On-going
			Accelerated	5 ± 3 °C	6 months	Complete
			Low Temperature	80 to -60 °C	1 month	Complete
2241554-MB0002	January 2022	Stability	Long Term	-20 ± 5 °C	9 months	On-going
			Accelerated	5 ± 3 °C	6 months	Complete
			Thermal Stress	25 ± 2 °C / 60 ± 5 % RH	1 month	Complete
2241554-MB0003	January 2022	Stability	Long Term	-20 ± 5 °C	9 months	On-going
			Accelerated	5 ± 3 °C	6 months	Complete
			Thermal Stress	25 ± 2 °C / 60 ± 5 % RH	1 month	Complete
2241554-MB0004	January 2022	Stability	Long Term	-20 ± 5 °C	9 months	On-going
			Accelerated	5 ± 3 °C	6 months	Complete
			Thermal Stress	25 ± 2 °C / 60 ± 5 % RH	1 month	Complete

Abbreviations: CTM= clinical trial material

2.3.S.7.1.2. Study Protocol for Drug Substance Batches at the Long Term Condition (-20 °C)

Aliquots of Omicron (B.1.1.529) drug substance batches have been stored at -20 ± 5 °C. Testing is performed according to the protocol indicated in [Table 2.3.S.7-2](#).

Table 2.3.S.7-2. Stability Protocol Omicron (B.1.1.529) Drug Substance Batches Stored at -20 ± 5 °C (Long Term Storage Condition)

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

- a. Initial data (t0) are from release testing.
b. 1W testing not performed on 22Y539C101.
c. 2 week time point performed on batches 2241554-MB0002, 2241554-MB0003 and 2241554-MB0004 only.
d. 12M testing performed on 22Y539C101
Abbreviations: W = Week, M = Month

2.3.S.7.1.3. 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 condition of Omicron (B.1.1.529) 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 \(B.1.1.529\) Variant\]](#).

2.3.S.7.1.4. Study Protocol for Drug Substance Batches at the Thermal Stress and Low Temperature Support Conditions

To support manufacturing process hold conditions and to study the effects of high and low temporary excursions from the recommended storage conditions, Omicron (B.1.1.529) drug substance aliquots of the batches manufactured by BioNTech Marburg are being stored at 25 ± 2 °C (thermal stress condition). In addition, one batch manufactured by Pfizer is being stored at -90 to -60 °C (low temperature condition) and a clinical batch manufactured by BioNTech Mainz is being stored at -80 ± 10 °C. Testing is being performed according to the protocol indicated in [Section 3.2.S.7.1 Stability Summary and Conclusions \[Omicron \(B.1.1.529\) 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 obtained from 1 commercial scale confirmatory (22Y539C101) and one clinical Omicron (B.1.1.529) drug substance stability batch (CQ19-P020.17-DS) stored at the long term condition of -20 ± 5 °C are presented in [Section 3.2.S.7.3 Stability Data \[Omicron \(B.1.1.529\) Variant\]](#). Up to 9 months of data are available for the confirmatory stability batch 22Y539C101 and 12 months of data are available for the clinical batch CQ19-P020.17-DS. To date, all data remained within the acceptance criteria in place at the time of testing.

Three additional Omicron (B.1.1.529) drug substance batch being manufactured by BioNTech Marburg are being enrolled in a confirmatory stability study (batches 2241554-MB0002, 2241554-MB0003, 2241554-MB0004). Results for up to and including 9 months are available for these batches with all data remaining within the acceptance criteria in place at the time of testing.

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

Stability data from the five BNT162b (B.1.1.529) drug substance batches stored at the accelerated condition of $5 \pm 3^\circ\text{C}$ are presented in [Section 3.2.S.7.3 Stability Data \[Omicron \(B.1.1.529\) Variant\]](#). The data are presented as supporting information for the drug substance shelf life claim. For confirmatory batch 22Y539C101, all results remained within the acceptance criteria in place at the time of testing through at least the 3 month time point. At the 6 month time point, the % intact RNA by Capillary Gel Electrophoresis was out of the CCI specification. Out of specification results can be expected at accelerated conditions and does not impact the overall stability program.

For batch 2241554-MB0002 RNA integrity after 6 months of storage was below the acceptance criterion. All other results for all batches remained within the acceptance criteria in place at the time of testing. At $5 \pm 3^\circ\text{C}$ the maximum intended storage is 1 month. Therefore, not meeting the acceptance criterion for RNA integrity after 6 months at the accelerated condition does not impact product quality.

2.3.S.7.1.5.3. Summary of Stability Data at the Thermal Stress and Low Temperature Conditions

Stability data from two Omicron (B.1.1.529) drug substance stability batches stored at the low temperature support condition of -90 to -60°C or -80 to -60°C are presented in [Section 3.2.S.7.3 Stability Data \[Omicron \(B.1.1.529\) Variant\]](#).

Stability data from three Omicron (B.1.1.529) drug substance stability batches stored at the thermal stress condition of $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{ RH}$ are also presented in [Section 3.2.S.7.3 Stability Data \[Omicron \(B.1.1.529\) Variant\]](#).

For batches 2241554-MB0002, 2241554-MB0003, 2241554-MB0004 after 1 month RNA integrity was below the acceptance criterion. All other results for all three batches remained within the acceptance criteria in place at the time of testing. The drug substance is not intended to be stored at $25^\circ\text{C}/60\% \text{ RH}$. Therefore, not meeting the acceptance criterion for RNA integrity after 1 month at the thermal stress condition does not impact product quality and an investigation was not carried out.

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

The data presented provide rationale and justification for the Omicron (B.1.1.529) drug substance shelf life claim of 6 months when stored at the recommended temperature of $-20 \pm 5^\circ\text{C}$ in CCI bags.

The initial shelf life is based on:

- The results of the stability study conducted on three commercial scale Omicron (B.1.1.529) drug substance batches up to and including the 9-month time point.
- Current 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 results of the stability study conducted on one confirmatory Omicron (B.1.1.529) drug substance batch up to and including the 9month time point.

In addition, the data demonstrate the Omicron (B.1.1.529) drug substance stored in **CCI** bags is stable through:

- 1 month at 5 ± 3 °C.
- 1 month at -90 to -60 °C

The data of the currently on-going stability studies will be provided in the future and will be used to confirm the initial shelf life of the drug substance, supported by ongoing stability studies on the original vaccine.

2.3.S.7.2. Post-approval Stability Protocol and Stability Commitment

Upon completion of the ICH stability protocols, post-approval, a minimum of one batch of BNT162b2 Omicron (B.1.1.529) 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 **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 (Months) ^a
Appearance (Clarity)	0, 6, 12, 18, 24
Appearance (Coloration)	
pH	
UV Spectroscopy (Content (RNA Concentration))	
Capillary Gel Electrophoresis (RNA Integrity)	
5'-CAP (RP-HPLC)	
Poly (A) Tail (ddPCR)	0, End of shelf life
Bioburden	
Endotoxin	

a. Additional test intervals may be included for the purpose of extending expiry.

2.3.S.7.3. Stability Data

Stability data for long term conditions, accelerated condition, thermal stress and photostability studies are provided in Section 3.2.S.7.3.Stability Data [Omicron (B.1.1.529) Variant].