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3.2.P.3.4. CONTROL OF CRITICAL STEPS AND INTERMEDIATES –DRUG PRODUCT INTERMEDIATE – STABILITY DATA

Data from stability studies on drug product intermediate (DPI) lots manufactured are presented in this section. An overview of the studies with references to the respective data tables is provided in Table 3.2.P.3.4-1.

Stability testing was performed according to the acceptance criteria in place at the time of testing. The acceptance criteria provided in the tables below represent those in place where the latest time-point tested.

The discussion of the results is provided in [Section 3.2.P.3.4 In-process Monitoring and Control – Drug Product Intermediate 0.5 mg/mL – Stability Summary and Conclusion – Tris/Sucrose](#).

Table 3.2.P.3.4-1. Summary Table of DPI Stability Studies

Lot Number	Formulation	Stability Study Start	Condition	Table Location
FX3647	Tris/Sucrose (Original)	14 Feb 2022	Long Term: -90 to -60 °C	Table 3.2.P.3.4-2
			4.2 1st ind	Table 3.2.P.3.4-8
				Table 3.2.P.3.4-14
				Table 3.2.P.3.4-15
FX8109	Tris/Sucrose (Original)	03 Mar 2022	Long Term: -90 to -60 °C	Table 3.2.P.3.4-3
			4.2 1st ind	Table 3.2.P.3.4-9
FX3649	Tris/Sucrose (Original)	14 Mar 2022	Long Term: -90 to -60 °C	Table 3.2.P.3.4-4
			4.2 1st ind	Table 3.2.P.3.4-10
AC00016	Bivalent [Original and Omicron (BA.4/BA.5)]	Apr 2023	Long Term: -80 to -60 °C	Table 3.2.P.3.4-5
			4.2 1st ind	Table 3.2.P.3.4-11
AC00017	Bivalent [Original and Omicron (BA.4/BA.5)]	Apr 2023	Long Term: -80 to -60 °C	Table 3.2.P.3.4-6
			4.2 1st ind	Table 3.2.P.3.4-12
AC00018	Bivalent [Original and Omicron (BA.4/BA.5)]	Apr 2023	Long Term: -80 to -60 °C	Table 3.2.P.3.4-7
			4.2 1st ind	Table 3.2.P.3.4-13

a. BioNTech Marburg uses -80 to -60 °C as storage and transport condition for drug product intermediate.

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

3.2.P.3.4.1. Long Term Stability Data of DPI at -90 to -60 °C

Data from stability studies on BNT162b2 Tris/Sucrose DPI lots stored at the long term storage condition of -90 to -60 °C are presented in this section. The results are presented in Table 3.2.P.3.4-2 through [Table 3.2.P.3.4-7](#).

Table 3.2.P.3.4-2. Stability Data for Tris/Sucrose DPI Lot FX3647 Stored at -90 to -60 °C (Puurs)

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

Table 3.2.P.3.4-3. Stability Data for Tris/Sucrose DPI Lot FX8109 Stored at 90 to 60 °C (Puurs)

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-4. Stability Data for Tris/Sucrose DPI Lot FX3649 Stored at -90 to -60 °C (Puurs)

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-5. Stability Data for Bivalent [Original and Omicron (BA.4/BA.5) Variant] DPI Lot AC00016 Stored at -80 to -60 °C (BioNTech Marburg)

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-6. Stability Data for Bivalent [Original and Omicron (BA.4/BA.5) Variant] DPI Lot AC00017 Stored at -80 to 60 °C (BioNTech Marburg)

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-7. Stability Data for Bivalent [Original and Omicron (BA.4/BA.5) Variant] DPI Lot AC00018 Stored at -80 to -60 °C (BioNTech Marburg)

Time	4.2 1st ind
Acceptance Criteria^a	4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria^a	4.2 1st ind

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

BNT162b2

3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

3.2.P.3.4.2. Accelerated Stability Data of DPI at 4.2 1st ind

Data from stability studies on BNT162b2 Tris/Sucrose DPI lots stored at the accelerated storage condition of 4.2 1st ind are presented in this section. The results are presented in Table 3.2.P.3.4-8 through [Table 3.2.P.3.4-13](#).

Table 3.2.P.3.4-8. Stability Data for DPI Lot FX3647 Stored at 4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-9. Stability Data for DPI Lot FX8109 Stored at 4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-11. Stability Data for Bivalent [Original and Omicron (BA.4/BA.5) Variant] DPI Lot AC00016 Stored
4.2 1st ind (BioNTech Marburg)

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-12. Stability Data for Bivalent [Original and Omicron (BA.4/BA.5) Variant] DPI Lot AC00017 Stored
4.2 1st ind (BioNTech Marburg)

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-13. Stability Data for Bivalent [Original and Omicron (BA.4/BA.5) Variant] DPI Lot AC00018 Stored
4.2 1st ind (BioNTech Marburg)

Time	4.2 1st ind
Acceptance Criteria^a	4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria^a	4.2 1st ind

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle

3.2.P.3.4.3. Thermal Cycling Stability Data of DPI

Data from stability studies on BNT162b2 Tris/Sucrose DPI lots stored at the two thermal stress conditions are presented in this section.

Results are provided in [Table 3.2.P.3.4-14](#) and [Table 3.2.P.3.4-15](#) respectively.

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-14. Stability Data for DPI Tris/Sucrose Lot FX3647 – Thermal Cycling Study 1 (Puurs)

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

Time	4.2 1st ind
Acceptance Criteria ^a	
4.2 1st ind	

a. Acceptance criteria in place at time of testing.

b. 4.2 1st ind

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle; 4.2 1st ind

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3.2.P.3.4 Control of Critical Steps and Intermediates

Drug Product Intermediate 0.5 mg/mL – Stability Data – Tris/Sucrose

Table 3.2.P.3.4-15. Stability Data for DPI Lot Tris/Sucrose FX3647 - Thermal Cycling Study 2 (Puurs)

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

Time	4.2 1st ind
Acceptance Criteria ^a	4.2 1st ind

a. Acceptance criteria in place at time of testing.

Abbreviations: W = week; M = month; S = to be scheduled; NS = not scheduled at time point; LNP = lipid Nanoparticle; 4.2 1st ind