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### **3.2.P.8.1 Stability Summary and Conclusion**

#### **3.2.P.8.1.1 Stability Summary**

The mRNA-1273 Drug Product (DP) registration stability program was executed according to ICH Q1A (R2), *Stability Testing of new Drug Substances and Products*, and ICH Q5C, *Stability Testing of Biotechnological/Biological Products*. mRNA-1273 DP material stored in the commercial container closure system, defined in [Section 3.2.P.7](#), will be assigned an initial shelf life of 6 months when stored at the recommended long-term storage condition of -15°C to -25°C (-20°C).

The shelf life is justified from the composite of data generated from three PPQ lots ([Section 3.2.P.8.1.3.2](#)), three clinical lots ([Section 3.2.P.8.1.3.2](#)), and two development lots ([Section 3.2.P.8.1.3.1](#)) manufactured at ModernaTX, Inc. (Norwood, MA). Stability and characterization studies designed to evaluate product stability under freeze/thaw conditions are discussed in [Section 3.2.P.8.1.3.4](#). All lots of mRNA-1273 Drug Product manufactured at ModernaTX, Inc. used the manufacturing process described in [Section 3.2.P.2.3](#) for PPQ, clinical lots and development lots. All lots of mRNA-1273 Drug Product manufactured at Catalent Pharma Solutions used the manufacturing process described in [Section 3.2.P.3.3](#). Stability samples were stored in a container made of the same materials (10R clear Type 1 borosilicate glass vial with rubber serum stopper and an aluminum seal with flip-off cap) as the commercial closure system.

For SM-102 containing mRNA-based vaccines, the mRNA purity, as assessed by reverse-phase high-performance liquid chromatography (RP-HPLC); % RNA encapsulation, as assessed by fluorescence; particle size and polydispersity, as assessed by dynamic light scattering (DLS); and lipid impurities, as assessed by ultra-high-performance liquid chromatography with charged aerosol detection (UPLC-CAD) have been demonstrated to be stability-indicating (refer to [Section 3.2.P.5.2](#) for analytical procedures).

An overview of the mRNA-1273 Drug Product stability program is provided in [Table 1](#). The data from these studies are presented in [Section 3.2.P.8.3](#).

**Table 1: GMP mRNA-1273 Drug Product Stability Testing Overview**

Lot Number	Usage	Concentration Fill Volume	mRNA-1273 LNP Lot Number	Date of Manufacture	Site of Manufacture	Stability Storage Condition
6007520001	Clinical Supplies and Stability	0.20 mg/mL 5.0 mL	5006820002	28 May 2020	ModernaTX, Inc.	<ul style="list-style-type: none"><li>• -60°C to -90°C</li><li>• -20°C ± 5°C (Intended Long-term)</li><li>• 2°C to 8°C (Intended Short-term)</li><li>• 25°C ± 2°C</li></ul>
6007520002				02 Jun 2020		
6007520003				04 Jun 2020		
6007520004	Moderna PPQ		5006820003	25 Jun 2020		<ul style="list-style-type: none"><li>• -60°C to -90°C</li><li>• -60°C to -90°C followed by storage at 2°C to 8°C (Intended Short-term)</li></ul>
6007520005			5006820003	30 Jun 2020		
6007520006			5006820003 and 5006820004	08 Jul 2020		
6007520007	Clinical Supplies and Stability		5006820003 and 5006820005	09 Jul 2020		<ul style="list-style-type: none"><li>• -20°C ± 5°C (Intended Long-term)</li><li>• -20°C ± 5°C followed by storage at 2°C to 8°C (Intended Short-term)</li></ul>
6007320001	Catalent PPQ	0.20 mg/mL 6.3 mL	5006820003 and 5006820004	30 Jul 2020	Catalent Pharma Solutions	<ul style="list-style-type: none"><li>• -20°C ± 5°C (Intended Long-term)</li><li>• -20°C ± 5°C followed by storage at 2°C to 8°C (Intended Short-term)</li><li>• 25°C ± 2°C</li></ul>
6007320002			5006820006	06 Aug 2020		
6007320003			5006820007	11 Aug 2020		

Abbreviations: PPQ = process performance qualification

Material for the development of mRNA-1273 Lipid Nanoparticle (LNP) (Lot AMPDP-200022) was prepared using a manufacturing process which is representative of the ModernaTX, Inc. GMP mRNA-1273 LNP process as described in [Section 3.2.S.2.2 {mRNA-1273 LNP}](#). Two separate lots of mRNA-1273 Drug Product were prepared with Lot AMPDP-200022 using 20 mM Tris and 87 mg/mL sucrose, pH 7.5 as the formulation buffer, as specified in [Section 3.2.P.3.3](#). One development lot was prepared with a total RNA content of (b) (4) mRNA (b) (4). The other development lot was prepared with a total RNA content of (b) (4) mRNA (b) (4). At the time of manufacture of the development lots, the final total mRNA content for the GMP mRNA-1273 Drug Product had not been finalized. Therefore, these two different total RNA contents were filled in order to appropriately bracket any proposed total RNA content (final total RNA content was established as (b) (4) mRNA). Therefore, the stability of mRNA-1273 Drug Product at dosage strength of 0.10 mg/mL (b) (4) and 0.5 mg/mL (b) (4) is a suitable bracket to establish the initial long-term (storage between -60°C to -90°C) and short-term (storage between 2°C to 8°C) use periods for mRNA-1273 Drug Product at the intended clinical dose concentration of 0.20 mg/mL mRNA.

An overview of development mRNA-1273 Drug Product stability studies is provided in [Table 2](#).

**Table 2: Development mRNA-1273 Drug Product Stability Testing Overview**

Lot Number	Usage	Concentration Fill Volume	mRNA-1273 LNP Lot Number	Date of Manufacture	Stability Storage Condition
(b) (4)	Initial Use Period	0.10 mg/mL 0.6 mL	AMPDP-200022	01 Apr 2020	<ul style="list-style-type: none"> <li>-60°C to -90°C (Intended Long-term)</li> <li>-20°C ± 5°C</li> <li>2°C to 8°C (Intended Short-term)</li> </ul>
	Initial Use Period	0.5 mg/mL 0.6 mL	AMPDP-200022	01 Apr 2020	<ul style="list-style-type: none"> <li>-60°C to -90°C (Intended Long-term)</li> <li>-20°C ± 5°C</li> <li>2°C to 8°C (Intended Short-term)</li> </ul>

### 3.2.P.8.1.2 Stability Study Protocols

#### 3.2.P.8.1.2.1 Study Protocols to Support the Initial Use Period for mRNA-1273 Drug Product

Development mRNA-1273 Drug Product stability samples used to establish initial use period are tested according to the protocol described in Table 3. Samples stored at the intended condition are evaluated against the acceptance criteria provided in the stability tables. Samples stored at accelerated storage conditions used the acceptance criteria at the intended condition as a reference point to characterize stability trends at the accelerated conditions.

**Table 3: Development mRNA-1273 Drug Product Stability Protocols for 0.10 mg/mL mRNA and 0.5 mg/mL mRNA**

Condition	Time Interval (Months)												
	0	1	2	3	4	5	6	9	12	18	24	36	48
-60°C to -90°C	ABCD	A	N/A	AB	N/A	N/A	A	A	AB	A	AB	AB	AB
-20°C ± 5°C		N/A	A	AB	N/A	N/A	AB	AB	AB	N/A	AB	N/A	AB
2°C to 8°C		A	AB	AB	A	A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

A = Appearance, %purity, particle size, polydispersity, %RNA encapsulation

B = RNA content, lipid content, lipid impurities, lipid identity, pH, cell-free translation

C = Bacterial endotoxin, bioburden, particulate matter

D = Osmolality, identity

N/A = Not required per the stability protocol

#### 3.2.P.8.1.2.2 Real-Time Stability Study Protocols for GMP mRNA-1273 Drug Product Lots Manufactured at ModernaTX, Inc. (Norwood, MA)

GMP mRNA-1273 Drug Product stability samples (Lot 6007520001, Lot 6007520002, Lot 6007520003 and PPQ Lot 6007520004) are tested according to the protocols described in Table 4. Samples stored at the intended condition are evaluated against the acceptance criteria in the stability tables. Samples stored at accelerated storage conditions used the acceptance criteria at the intended condition as a reference point to characterize stability trends at the accelerated conditions.

**Table 4: GMP mRNA-1273 Drug Product Stability Protocol for Lots Manufactured at ModernaTX, Inc. (Norwood, MA)**

Condition	Months (unless noted)												
	0	24 hr	72 hr	1	2	2.5	3	4	6	9	12	18	24
-60°C to -90°C	ABCDE	N/A	N/A	ABC	AB	N/A	ABC	N/A	ABC	ABC	ABCD	ABC	ABCD
-20°C ± 5°C		N/A	N/A	ABC	AB	N/A	ABC	N/A	ABC	ABC	ABC	N/A	N/A
2°C to 8°C		N/A	N/A	ABC	B	B	ABC	B	ABCD	N/A	N/A	N/A	N/A
23°C to 27°C		ABC	ABC	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

A = %RNA encapsulation

B = Appearance, %purity, particle size, polydispersity

C = In-vitro Translation, pH, total RNA content, lipid content and lipid impurities

D = Bacterial endotoxins, particulate matter, sterility

E = Identity, lipid identity, osmolality, container content

N/A = not required per stability protocol

GMP mRNA-1273 Drug Product stability samples from PPQ Lot 6007520005 and PPQ Lot 6007520006 are tested according to the protocols described in Table 5. This protocol has been established to monitor stability for samples stored between -60°C to -90°C followed by storage at 2°C to 8°C at specified intervals for up to three (3) months. Samples stored at the intended condition are evaluated against the acceptance criteria provided in the stability tables. Samples stored at accelerated storage conditions used the acceptance criteria at the intended condition as a reference point to characterize stability trends at the accelerated conditions.

**Table 5: GMP mRNA-1273 Drug Product Matrix Stability Protocol for PPQ Lot 6007520005 and PPQ Lot 6007520006**

Condition	Months						
	0	1	2	2.5	3	6	9
-60°C to -90°C (upright)	ABCDE	ABC <sup>(1)</sup>	ABC	N/A	ABC <sup>(2)</sup>	ABC	ABCD <sup>(3)</sup>
-60°C to -90°C followed by 2°C to 8°C (inverted)	N/A	B	B	B	ABCD	N/A	N/A

A = Appearance (after thaw from -60°C to -90°C), %RNA encapsulation

B = Appearance (after 2°C to 8°C storage), %purity, particle size, polydispersity

C = In-vitro Translation, pH, total RNA content, lipid content and lipid impurities

D = Bacterial endotoxins, particulate matter, sterility

E = Identity, lipid identity, osmolality, container content

N/A = not required per stability protocol

- 1) After thaw from -60°C to -90°C at T = 1 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 1 month, at T = 2 month, at T = 2.5 month and T = 3 month.
- 2) After thaw from -60°C to -90°C at T = 3 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 1 month, at T = 2 month, at T = 2.5 month and T = 3 month.
- 3) After thaw from -60°C to -90°C at T = 9 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 1 month, at T = 2 month, at T = 2.5 month and T = 3 month.

GMP mRNA-1273 Drug Product stability samples from Lot 6007520007 are tested according to the protocols described in Table 6. This protocol has been established to monitor stability for samples stored between -15°C to -25°C followed by storage at 2°C to 8°C at specified intervals for up to eight (8) weeks. Samples stored at the intended condition are evaluated

against the acceptance criteria provided in the stability tables. Samples stored at accelerated storage conditions used the acceptance criteria at the intended condition as a reference point to characterize stability trends at the accelerated conditions.

**Table 6: GMP mRNA-1273 Drug Product Matrix Stability Protocol for Lot 6007520007**

Condition	Months (unless noted)											
	0	2 wks	4 wks	1	6 wks	8 wks	3	6	9	12	15	18
-20°C ± 5°C (upright)	ABCDE	N/A	N/A	N/A <sup>(1)</sup>	N/A	N/A	B <sup>(2)</sup>	ABCD	B <sup>(3)</sup>	ABCDE	ABCD	ABCDE
-20°C ± 5°C followed by 2°C to 8°C (inverted)		BC	BC	N/A	BC	ABCDE	N/A	N/A	N/A	N/A	N/A	N/A

A = Appearance, %RNA encapsulation

B = %Purity

C = Particle size, polydispersity, appearance

D = In-vitro Translation, pH, total RNA content, lipid content and lipid impurities

E = Bacterial endotoxins, particulate matter, sterility

F = Identity, container content, lipid identity, osmolality

N/A = not required per stability protocol

- 1) After thaw from -20°C ± 5°C at T = 1 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 2 weeks, at T = 4 weeks, at T = 6 weeks and T = 8 weeks.
- 2) After thaw from -20°C ± 5°C at T = 3 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 2 weeks, at T = 4 weeks, at T = 6 weeks and T = 8 weeks.
- 3) After thaw from -20°C ± 5°C at T = 9 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 2 weeks, at T = 4 weeks, at T = 6 weeks and T = 8 weeks.

### 3.2.P.8.1.2.3 Real-Time Stability Study Protocols for GMP mRNA-1273 Drug Product Lots Manufactured at Catalent Pharma Solutions (Bloomington, IN)

GMP mRNA-1273 Drug Product stability samples from PPQ Lot 6007320001 manufactured at Catalent Pharma Solutions are tested according to the protocols described in [Table 7](#). GMP mRNA-1273 Drug Product stability samples from PPQ Lot 6007320002 and PPQ Lot 6007320003 manufactured at Catalent Pharma Solutions are tested according to the protocols described in [Table 8](#). Samples stored at the intended condition are evaluated against the acceptance criteria provided in the stability tables. Samples stored at accelerated storage conditions used the acceptance criteria at the intended condition as a reference point to characterize stability trends at the accelerated conditions. This protocol has been established to monitor stability for samples stored between -15°C to -25°C followed by storage at 2°C to 8°C at specified intervals for up to eight (8) weeks.

**Table 7: GMP mRNA-1273 Drug Product Stability Protocol for PPQ Lot 6007320001  
Manufactured at Catalent Pharma Solutions (Bloomington, IN)**

Condition	Months (unless noted)													
	0	24 hr	72 hr	2 wks	4 wks	1	6 wks	8 wks	3	6	9	12	18	24
-20°C ± 5°C	ABCDE	N/A	N/A	N/A	N/A	ABC <sup>(1)</sup>	N/A	N/A	ABC <sup>(2)</sup>	ABC	ABC	ABCD	ABC	ABCD <sup>(3)</sup>
-20°C ± 5°C followed by 2°C to 8°C (inverted)		N/A	N/A	B	B	N/A	B	ABCD	N/A	N/A	N/A	N/A	N/A	N/A
23°C to 27°C		B	B	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

A = Appearance

B = %Purity, particle size, polydispersity

C = In-vitro Translation (Potency), %RNA encapsulation, pH, total RNA content, lipid content and lipid impurities

D = Bacterial endotoxins, particulate matter, container content integrity test

E = Identity, lipid identity, osmolality, sterility

N/A = not required per stability protocol

- 1) After thaw from -20°C ± 5°C at T = 1 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 2 weeks, at T = 4 weeks, at T = 6 weeks and T = 8 weeks.
- 2) After thaw from -20°C ± 5°C at T = 3 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 2 weeks, at T = 4 weeks, at T = 6 weeks and T = 8 weeks.
- 3) After thaw from -20°C ± 5°C at T = 24 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 2 weeks, at T = 4 weeks, at T = 6 weeks and T = 8 weeks.

**Table 8: GMP mRNA-1273 Drug Product Stability Protocol for PPQ Lot 6007320002  
and PPQ Lot 6007320003 Manufactured at Catalent Pharma Solutions  
(Bloomington, IN)**

Condition	Months (unless noted)													
	0	24 hr	72 hr	2 wks	4 wks	1	6 wks	8 wks	3	6	9	12	18	24
-20°C ± 5°C	ABCDE	N/A	N/A	N/A	N/A	ABC <sup>(1)</sup>	N/A	N/A	ABC <sup>(2)</sup>	ABC	ABC	ABCD	ABC	ABCD
-20°C ± 5°C followed by 2°C to 8°C (inverted)		N/A	N/A	B	B	N/A	B	ABCD	N/A	N/A	N/A	N/A	N/A	N/A
23°C to 27°C		B	B	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

A = Appearance

B = %Purity, particle size, polydispersity

C = In-vitro Translation (Potency), %RNA encapsulation, pH, total RNA content, lipid content and lipid impurities

D = Bacterial endotoxins, particulate matter, container content integrity test

E = Identity, lipid identity, osmolality, sterility

N/A = not required per stability protocol

- 1) After thaw from -20°C ± 5°C at T = 1 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 2 weeks, at T = 4 weeks, at T = 6 weeks and T = 8 weeks.
- 2) After thaw from -20°C ± 5°C at T = 3 month, stability testing at 2°C to 8°C (inverted) is conducted at T = 2 weeks, at T = 4 weeks, at T = 6 weeks and T = 8 weeks.



### 3.2.P.8.1.2.4 Freeze/Thaw Stability Study Protocol for mRNA-1273 Drug Product

Stability studies in support of mRNA-1273 Drug Product freeze-thaw cycling were performed using representative mRNA-1273 Drug Product. Two separate lots of mRNA-1273 Drug Product were formulated from Lot AMPDP-200022. One development lot was prepared with a total RNA content of (b) (4) mRNA (DHM-47522). The other development lot was prepared with a total RNA content of (b) (4) mRNA (DHM-47518). Similarly, as the studies to establish the initial use period, mRNA-1273 Drug Product lots at dosage strength of 0.10 mg/mL mRNA (DHM-47522) and 0.5 mg/mL mRNA (DHM-47518) were utilized to bracket for freeze-thaw cycling studies. (b) (4)

The freeze-thaw cycling was repeated up to five times. Samples were tested for appearance, %purity, %RNA encapsulation, particle size and polydispersity after samples were subjected to one freeze-thaw cycle (b) (4), three freeze-thaw cycles (b) (4) and five freeze-thaw cycles (b) (4).

### 3.2.P.8.1.2.5 Bracketing Clinical In-use Stability Study Protocol for mRNA-1273 Drug Product

Clinical in-use stability studies were performed to mimic handling of mRNA-1273 Drug Product at the clinical sites, using representative materials, representative test articles and the appropriate dose preparation procedure for clinical use. Two lots of mRNA-1273 Drug Product (representative multi-dose vials with 6.5 mL fill volume) were used for the study as described in Table 9 and manufactured under cGMP conditions, were used for bracketing the intended clinical dose concentrations to demonstrate compatibility of administration materials (b) (4) with mRNA-1273 Drug Product. Similarly, as the studies to establish the initial use period, mRNA-1273 Drug Product lots at dosage strength of 0.10 mg/mL mRNA (Lot 6006820001) and 0.5 mg/mL mRNA (Lot 6006920001) were utilized to bracket the clinical in-use studies. mRNA-1273 Drug Product was not diluted for this study.

**Table 9: Preparation Configurations for the Clinical In-use Stability Studies**

Lot No.	Dose, µg	Dose Concentration (mg/mL)	Dose volume (mL)
6006820001	(b) (4)	0.10	0.5
6006920001	(b) (4)	0.5	0.5

### 3.2.P.8.1.2.6 Clinical In-use Stability Study Protocol to Support Emergency Use Authorization/Commercial Image for mRNA-1273 Drug Product

Clinical in-use stability studies were performed to mimic the handling of the commercial image of mRNA-1273 Drug Product at the clinical sites, using representative materials, representative test articles and the appropriate dose preparation procedure for clinical use. GMP Lot 6007520007 was used for the study as described in [Table 10](#) and manufactured under cGMP conditions. These clinical in-use studies were conducted using the intended commercial dose concentration to demonstrate compatibility of administration materials (polypropylene and polycarbonate syringes and stainless-steel needles) with mRNA-1273 Drug Product. mRNA-1273 Drug Product was not diluted for this study.

**Table 10: Preparation Configuration for the Clinical In-use Stability Studies to Support Emergency Use Authorization/Commercial Image**

Lot No.	Dose, µg	Dose Concentration (mg/mL)	Dose volume (mL)
6007520007	(b) (4)	0.20 (neat)	0.5

### 3.2.P.8.1.3 Stability Study Results

#### 3.2.P.8.1.3.1 Stability Study Results to Support the Initial Use Period for mRNA-1273 Drug Product

Stability testing results for development mRNA-1273 Drug Product Lot (b) (4) (0.10 mg/mL) are provided in [Table 1](#), [Section 3.2.P.8.3](#), [Table 2](#), [Section 3.2.P.8.3](#) and [Table 3](#), [Section 3.2.P.8.3](#).

(b) (4)



(b) (4)



Stability testing results for development mRNA-1273 Drug Product Lot (b) (4) (0.5 mg/mL) are provided in [Table 4, Section 3.2.P.8.3](#), [Table 5, Section 3.2.P.8.3](#) and [Table 6, Section 3.2.P.8.3](#).

(b) (4)



### **3.2.P.8.1.3.2 Stability Study Results for GMP mRNA-1273 Drug Product manufactured at ModernaTX, Inc.**

Stability data for GMP mRNA-1273 Drug Product is presented in the following section. Stability testing for Lot 6007520001, Lot 6007520002 and Lot 6007520003 has been conducted at T = 2 month. There is no stability data available for PPQ Lot 6007520004, PPQ Lot 6007520005, PPQ Lot 6007520006 and Lot 6007520007.

Stability testing results for GMP mRNA-1273 Drug Product Lot 6007520001 (0.20 mg/mL) are provided in [Table 7, Section 3.2.P.8.3](#), [Table 8, Section 3.2.P.8.3](#), [Table 9, Section 3.2.P.8.3](#) and [Table 10, Section 3.2.P.8.3](#).

(b) (4)



Stability testing results for GMP mRNA-1273 Drug Product Lot 6007520002 (0.20 mg/mL) are provided in [Table 11, Section 3.2.P.8.3](#), [Table 12, Section 3.2.P.8.3](#), [Table 13, Section 3.2.P.8.3](#) and [Table 14, Section 3.2.P.8.3](#).

(b) (4)



(b) (4)



No stability data is available for GMP mRNA-1273 Drug Product, PPQ Lot 6007520004, PPQ Lot 6007520005, PPQ Lot 6007520006, or Lot 6007520007. Stability results for these GMP lots will be submitted as data becomes available.

**3.2.P.8.1.3.3 Stability Study Results for GMP mRNA-1273 Drug Product manufactured at Catalent Pharma (Bloomington, IN)**

No stability data is available for GMP mRNA-1273 Drug Product, PPQ Lot 6007320001, PPQ Lot 6007320002 and PPQ Lot 6007320003. Stability results for these GMP PPQ lots manufactured at Catalent Pharma will be submitted as data becomes available.

### 3.2.P.8.1.3.4 Freeze/Thaw Stability Study Results

Freeze-thaw stability studies were performed using representative mRNA-1273 Drug Product lots at 0.10 mg/mL mRNA (Lot DHM-47522) and 0.5 mg/mL mRNA (Lot DHM-47518). mRNA-1273 Drug Product samples were subjected to a series of five freezing and thawing cycles and assessed for appearance, % RNA encapsulation, mRNA purity by RP-HPLC, mean particle size and polydispersity index.

For Lot DHM-47522 (0.10 mg/mL mRNA), for five cycles of storage between -60°C to -90°C and thaws at room temperature, (b) (4)

These data are presented in [Table 19, Section 3.2.P.8.3](#).

For Lot DHM-47522 (0.10 mg/mL mRNA), for five cycles of storage between -60°C to -90°C and thaws between 2°C to 8°C, (b) (4)

These data are presented in [Table 20, Section 3.2.P.8.3](#).

For Lot DHM-47518 (0.5 mg/mL mRNA), for five cycles of storage between -60°C to -90°C and thaws at room temperature, (b) (4)

These data are presented in [Table 21, Section 3.2.P.8.3](#).

For Lot DHM-47518 (0.5 mg/mL mRNA), for five cycles of storage between -60°C to -90°C and thaws between 2°C to 8°C, (b) (4)

These data are presented in [Table 22, Section 3.2.P.8.3](#).

These studies support five freeze/thaw cycles for bracketing dosage strengths of 0.10 mg/mL to 0.5 mg/mL mRNA for mRNA-1273 Drug Product.

### 3.2.P.8.1.3.5 Clinical In-Use Stability Study Results

#### 3.2.P.8.1.3.5.1 Bracketing Clinical In-Use Stability Study Results

Bracketing clinical in-use stability studies for mRNA-1273 Drug Product were conducted using Lot 6006820001 and Lot 6006920001 and materials of contact planned for clinical dosing (b) (4) to determine

material compatibility and in-use stability. mRNA-1273 Drug Product under evaluation is a multi-dose vial. The study was designed to enable direct removal of product solution from vial and holding in syringes. The product solution was held in the vial at room temperature for either 1 hour or 7 hours after thaw. Dosing syringes were prepared from the vial after 1 hour and then again after 7 hours upon completion of a 1 hour thaw at room temperature. The syringes were then held for 0, 8, and 24 hours at room temperature and refrigerated conditions, and assayed for RNA content by AEX-HPLC, % purity by RP-HPLC, lipid content by UPLC-CAD, % RNA encapsulation, and mean particle size and polydispersity by DLS. Attributes of mRNA-1273 Drug Product stayed within specification when held in a vial for 6 hours at room temperature, followed by storage in a syringe for 8 hours, at either 0.5 mg/mL or 0.10 mg/mL. Clinical in-use stability was demonstrated for bracketing dosage strengths of 0.10 mg/mL to 0.5 mg/mL mRNA for up to 6 hours in the vial followed by 8 hours in the syringe at either ambient temperature or at storage between 2°C to 8°C. These data are provided in [Table 23, Section 3.2.P.8.3](#) to [Table 28, Section 3.2.P.8.3](#).

### **3.2.P.8.1.3.5.2 Clinical In-Use Stability Study Results to Support Emergency Use Authorization/Commercial Image**

Clinical in-use stability studies for mRNA-1273 Drug Product were conducted using Lot 6007520007 and materials of contact planned for clinical dosing (b) (4)

(b) (4) to determine material compatibility and in-use stability. mRNA-1273 Drug Product under evaluation is a multi-dose vial. The study was designed to enable direct removal of product solution from vial and holding in syringes. The product solution was held in the vial at room temperature for either 1 hour or 7 hours after thaw. Dosing syringes were prepared from the vial after 1 hour and then again after 7 hours upon completion of a 1-hour thaw at room temperature. The syringes were then held for 0, 4, 8, and 12 hours at room temperature and refrigerated conditions, and assayed for % purity by RP-HPLC, % RNA encapsulation, in-vitro translation (potency), and mean particle size and polydispersity by DLS. Attributes of mRNA-1273 Drug Product stayed within acceptance criteria when held in a vial for up to 7 hours at room temperature after first puncture, followed by storage in a syringe for up to 12 hours. Clinical in-use stability was demonstrated for dosage strengths of 0.20 mg/mL for 6 hours after first puncture in the vial followed by 8 hours in the syringe at either ambient temperature or at storage between 2°C to 8°C. These data are provided in [Table 29, Section 3.2.P.8.3](#) to [Table 31, Section 3.2.P.8.3](#).



### 3.2.P.8.1.4 Conclusions and Use Period Claim

Based on the two months of stability data for GMP mRNA-1273 Drug Product lots (Lot 6007520001, Lot 6007520002 and Lot 6007520003) and three (3) month of bracketing dosage stability data for development mRNA-1273 Drug Product, Lot (b) (4) (0.10 mg/mL) and (b) (4) (0.5 mg/mL), a use period of six (6) months at a long-term storage condition of either between -60°C to -90°C or -15°C to -25°C is proposed for mRNA-1273 Drug Product.

Based on the 76 days of stability data for GMP mRNA-1273 Drug Product lots (Lot 6007520001, Lot 6007520002 and Lot 6007520003) and three (3) months of bracketing dosage stability data for development mRNA-1273 Drug Product, Lot (b) (4) (0.10 mg/mL) and (b) (4) (0.5 mg/mL), a use period of (b) (4) at the short-term storage condition between 2°C to 8°C after thawing from a frozen condition between -60°C to -90°C is proposed for mRNA-1273 Drug Product.

Based on the clinical in-use dosage stability data for GMP Lot 6007520007 (0.20 mg/mL), mRNA-1273 Drug Product was demonstrated stable when held for 6 hours after first puncture in the dosing vial followed by 8 hours in the dosing syringe, at either ambient temperature or at 2°C to 8°C.

#### **Extension of Use Period**

If no long-term GMP stability data is available, the use period will be determined using the appropriate supporting non-GMP stability data and per the discretion of the Quality Unit. If  $\leq 6$  months long-term GMP stability data is available, use period is determined using real-time data times 2 or up to 12 months at the discretion of the Quality Unit after taking into consideration any other relevant development stability data. If  $\geq 6$  months long-term GMP stability data is available, use period extensions will be made per the discretion of the Quality Unit. Expiry cannot exceed the length of the stability study.