moderna

1.0 PURPOSE

This procedure describes the method for determining free mRNA and the % Encapsulation Efficiency (% EE) in mRNA Lipid Nanoparticles (LNP) and Drug Product (DP) samples by the [redacted]

This method is an [redacted]

2.0 SCOPE

This method applies to testing of formulated mRNA LNP and DP in the Quality Control (QC) laboratory.

3.0 REFERENCED DOCUMENTS

Document #	Title
FRM-0120	General Quality Control Sample Submission Form
FRM-0180	Quality Control Solution Preparation Form
FRM-0735	Assay Performance Worksheet SOP-1000: [redacted]
FRM-0745	[redacted] Working Solution Preparation SOP-1000: [redacted]
SOP-0017	Maintaining a RNase Free Work Environment
SOP-0033	Out of Specification (OOS)
SOP-0081	Preparation of Solutions and Samples in the GMP-Quality Control Laboratory
SOP-0082	Data Review and Reporting in the GMP Quality Control Laboratory
SOP-0144	Operation of the [redacted] Analytical Balance
SOP-0227	[redacted] Operation and Maintenance

Document #	Title
SOP-0254	Operation and Maintenance of [redacted] Reader
SOP-0403	QC [redacted] Procedure
SOP-0409	Quality Control Invalid Assay Procedure
SOP-0820	Reconstitution of Lyophilized Drug Product

4.0 RESPONSIBILITIES

Department/ Functional Area	Responsibility
Department manager or designee	• Ensuring that laboratory personnel are properly trained in this procedure. • Ensuring that all procedures outlined in this document are followed when applicable. • Ensuring that this procedure is revised as necessary.
Laboratory personnel	• Following all procedures as outlined in this document. • Maintaining an RNase free work environment following SOP-0017. • Following proper safety standards in the laboratory.

5.0 DEFINITIONS

Term	Definition
%EE	% Encapsulation Efficiency
Abs	Absorbance
AU	Absorbance Units
CoA	Certificate of Analysis
DP	Drug Product
GMP	Good Manufacturing Practices
LNP	Lipid nanoparticle
mRNA	Messenger ribonucleic acid
RF	Response Factor
RNase	Ribonuclease

6.0 EQUIPMENT AND MATERIALS

Equivalent equipment, materials, reagents and consumables may be used unless otherwise indicated.

Equipment and Materials

Equipment/ Materials	Manufacturer	Part Number/ Model
[redacted]		

Reagents

Reagents	Manufacturer	Part Number	Storage
[redacted]		N/A	N/A
		[redacted]	

Materials/ Consumables

Materials/ Consumables	Manufacturer	Part Number
[redacted]		

Materials/ Consumables	Manufacturer	Part Number
[redacted]		

7.0 SAFETY

7.1. Wear the appropriate personal protective equipment when working in the QC laboratory.

7.2. Adhere to EPA, OSHA, and any other applicable health and safety procedures including Safety Data Sheets (SDS) when working with hazardous materials.

8.0 PROCEDURE

[redacted] per **SOP-0081**.

8.1. **Solution Preparation**

8.1.1. [redacted]

8.1.1.1. [redacted] **SOP-0144**.

8.1.1.2. [redacted]

8.1.1.3. [redacted]

8.1.1.4. [redacted]

8.1.1.5. [redacted]

8.1.1.6. [redacted]

8.1.1.7. [redacted] per **SOP-0403**.

8.1.2. [redacted]

8.1.2.1. [redacted]

8.1.2.2. [redacted] SOP-0254 [redacted]

8.1.2.3. [redacted] "SOP-1000 [redacted]

[redacted]

8.1.2.4. [redacted]

Parameter	Setting
Read Mode	[redacted]
Read Type	
Read at Wavelength	

8.1.2.5. [redacted]

8.1.2.6.

8.1.2.7.

8.1.2.8.

Example preparations provided below.

Total Volume (mL)	Formulation Buffer (mL)	[redacted] Stock Solution (mL)
[redacted]		

[redacted]

8.1.2.9. [redacted]

[redacted]

- [redacted]

8.1.2.10. [redacted] per SOP-0254.

8.2. **System Suitability Testing**

8.2.1.

8.2.2. [redacted]

8.2.3. [redacted] SOP-0254 [redacted]

8.2.4. [redacted]

8.2.4.1. [redacted]

8.2.4.2.

8.2.5. [redacted]

Parameter	Setting
Read Mode	[redacted]
Read Type	
Read at Wavelength	

8.2.6. [redacted]

8.2.7. [redacted]

8.2.8.

8.2.9.

8.2.10.

8.2.11.

8.3. Sample Testing

[redacted]

8.3.1. [redacted]

8.3.2. SOP-0820, [redacted]

8.3.3. [redacted]

8.3.3.1. [redacted]

8.3.4. [redacted]

Parameter	Setting
Read Mode	[redacted]
Read Type	
Read at Wavelength	

8.3.5. [redacted]

8.3.5.1. [redacted]

8.3.5.2.

8.3.5.3.

8.3.6. [redacted]

8.3.6.1. [redacted]

8.3.6.2.

8.3.6.3.

8.3.6.4. [redacted]

Table 1: [redacted]

[redacted] (mg/mL)	[redacted] (µL)	Working solution Volume (mL)	[redacted] (mg)
[redacted]			

Formula 1:

Sample volume (µL) = [redacted]

8.3.6.5. [redacted]

8.3.6.6.

8.3.6.7.

8.3.6.8.

8.3.6.9.

8.3.6.10.

8.3.6.11.

8.3.6.12.

8.3.6.13.

8.3.6.14.

8.3.6.15.

8.3.7. [redacted]

8.3.8. [redacted] SOP-0254.

8.4. **Data Analysis**

8.4.1. [redacted] SOP-1000 [redacted]

8.4.2. [redacted]

8.4.3. [redacted]

8.4.4. [redacted]

8.4.4.1. [redacted]

Table 2: Data Analysis for SOP-1000

Sample	Label	Abs [redacted]	Abs	[redacted]	ΔAbs	Free RNA (mg)	Total mRNA (mg)	%EE
[redacted]								

[redacted]

8.5. Acceptance Criteria

8.5.1. [redacted]

8.5.1.1. [redacted]

Table 3: [redacted]

Parameter	[redacted]
[redacted]	

8.5.2. [redacted]

8.5.2.1. [redacted]

Table 4: [redacted]

Parameter	[redacted]
[redacted]	

8.6. Reporting

8.6.1. [redacted] SOP-0082 [redacted].

8.6.2. [redacted]

8.6.3. [redacted]

8.6.3.1. [redacted]

8.6.3.2. [redacted]

8.6.3.3. [redacted]

8.6.4. [redacted] SOP-0227.

8.6.4.1. [redacted]

8.6.4.2. [redacted]

8.6.5. [redacted]

[redacted] SOP-0033 [redacted]

8.6.6. [redacted]

SOP-0409 [redacted]

8.6.7. [redacted]

9.0 ATTACHMENTS

Attachment I – SOP-1000 Data Analysis spreadsheet (Veeva)

10.0 REVISION HISTORY

Revision #	Effective Date	Change Details	Author
1.0	Refer to Veeva Header for Effective Date	New Document	[redacted]

Document Approvals

Approved Date: 01 Sep 2020

Approval Verdict: Approved	[redacted] Quality Control Approval 26-Aug-2020 19:08:19 GMT+0000
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