moderna

1.0 PURPOSE

This method describes the procedure to assess Drug Substance (DS), [redacted]

2.0 SCOPE

This method applies for the analysis of [redacted] in the cGMP Quality Control Laboratory.

3.0 REFERENCED DOCUMENTS

Document #	Title
FRM-0089	QC Column Tracking Form
FRM-0120	General Quality Control Sample Submission Form
FRM-0180	Quality Control Solution Preparation Form
FRM-0260	HPLC/UHPLC Usage and Maintenance Log
FRM-0727	Analysis of mRNA purity by Size-based RPIP SOP-0996 Assay Performance Worksheet
SOP-0017	Maintaining a RNase Free Work Environment
SOP-0022	Good Documentation Practices
SOP-0033	Out of Specification (OOS)
SOP-0079	Sample Submission and Sample Tracking Procedures in the GMP Quality Control Laboratory
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-0227	[redacted] Operation and Maintenance
SOP-0242	Operation and Maintenance of [redacted] System
SOP-0243	Operation of [redacted]
SOP-0271	Quality Control HPLC/GC Column Monitoring
SOP-0274	Use of Quality Control Laboratory Notebooks
SOP-0403	QC [redacted] Operations Procedure

Document #	Title
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 on this procedure. • Ensuring that all procedures outlined in this document are followed.
Quality Control Personnel	• Following safe operation and maintenance practices outlined within this document. • Executing this procedure as described and following good documentation practices per **SOP-0022**. • Documenting daily operation and maintenance activities in the corresponding instrument logbook using **FRM-0260**. • Documenting and monitoring column use per **SOP-0271** and **FRM-0089**. • Documenting assay information using **FRM-0727** or in a laboratory notebook per **SOP-0274**. • Preparing solutions per **SOP-0081** and documenting preparation using **FRM-0180** or in [redacted] per **SOP-0403**. • Maintaining an RNase free work environment as per **SOP-0017**. • Reporting any instrument malfunction, safety concerns or incidents to Area Managers.

5.0 DEFINITIONS

Term	Definition
[redacted]	
AUC	Area under the curve
cGMP	Current Good Manufacturing Practices
[redacted]	
DP	Drug Product
[redacted]	
HPLC	High Performance Liquid Chromatography
IP	Ion Pair
[redacted]	
LNP	Lipid Nanoparticle
[redacted]	

Term	Definition
mRNA	Messenger ribonucleic acid
PPE	Personal Protective Equipment
RP	Reverse Phase
RT	Retention time
SDS	Safety Data Sheet
[redacted]	[redacted]
UHPLC	Ultra-High-Performance Liquid Chromatography
UV	Ultraviolet
VWD	Variable wavelength detector
Wt	Weight
xg	Times gravity

6.0 EQUIPMENT AND MATERIALS

NOTE: Equivalent equipment, consumables, reagents and materials can be used provided the reagent grade or classification is maintained.

Materials

Materials	Vendor or Supplier	Catalog Number
Sterile [redacted] Microcentrifuge tubes (do not use [redacted] tubes)	[redacted]	[redacted]
Column: [redacted]		
Glass media bottles of various volumes	N/A	N/A
Graduated cylinders of various volumes	N/A	N/A
[redacted]		[redacted]
HPLC [redacted]	[redacted]	
HPLC Caps		
[redacted] pipette tips	[redacted]	
Acetonitrile		
[redacted] (HPLC Grade)		
[redacted]		

Equipment

Equipment	Vendor or Supplier	Catalog Number
UHPLC [redacted]	[redacted]	[redacted]
[redacted]		
[redacted] variable adjustable pipets, capable of measuring [redacted] (recommended: [redacted]		
[redacted] Pipetter		
[redacted]		
Analytical Balance		
Stir Plate		
Calibrated Timer	N/A	N/A

7.0 SAFETY

7.1. Wear the appropriate PPE when working in the cGMP Quality Control laboratory.

7.2. Refer to chemical specific SDS for additional safety information.

8.0 PROCEDURE

8.1. [redacted]

8.1.1. [redacted]

NOTE: Solutions, samples, and standards can be prepared at different volumes and amounts if final concentrations are maintained.

8.1.2. [redacted]

8.1.2.1. [redacted]

8.1.2.2.

8.1.2.3.

8.1.2.4.

8.1.3. [redacted]

8.1.3.1. [redacted]

8.1.3.2. [redacted]

8.1.3.3. [redacted]

8.1.3.4. [redacted]

8.1.3.5. [redacted]

8.1.4. [redacted]

8.1.4.1. [redacted]

8.1.4.2. [redacted]

8.1.4.3. [redacted]

8.1.4.4. [redacted]

8.1.5. [redacted]

8.1.5.1. [redacted]

8.1.5.2. [redacted]

8.1.5.3. [redacted]

8.1.6. [redacted]

8.1.6.1. [redacted]

8.1.6.2.

8.1.6.3.

8.1.7. [redacted]

8.1.7.1. [redacted]

8.1.7.2.

8.1.7.3.

8.1.7.4.

8.2. [redacted]

8.2.1. [redacted]

8.2.2.

8.2.3.

8.3. [redacted]

8.3.1. [redacted]

8.3.2.

8.4. [redacted]

8.4.1. [redacted]

8.4.2.

8.4.3.

8.4.4.

8.5. [redacted]

NOTE: The target final sample concentration is [redacted]

8.5.1. [redacted]

8.5.2.

8.5.3.

8.5.4.

8.5.5.

8.5.6.

8.5.7.

8.5.8.

8.5.9.

8.5.10. [redacted]

8.5.11. [redacted]

8.5.12. [redacted]

8.5.13. [redacted]

8.6. [redacted]

8.6.1. [redacted]

8.6.1.1. [redacted]

8.6.1.2. [redacted]

8.6.1.3. [redacted]

8.6.2. [redacted]

8.6.2.1. [redacted]

8.6.2.2. [redacted]

8.6.3. [redacted]

8.6.3.1. [redacted]

Table 6: Instrument Method Parameters

Parameter	Setting
Instrument:	[redacted]
Column:	[redacted]
Acquisition/Run Time:	[redacted]
Flow Rate:	[redacted]
Detection:	[redacted]
Injection Volume:	[redacted]
Draw Speed:	[redacted]
Dispense Speed:	[redacted]
Column Temperature:	[redacted]
Precolumn Temperature:	[redacted]
Post column Temperature:	[redacted]
Autosampler Temperature:	[redacted]
Needle Wash Settings:	[redacted]

Table 7: [redacted] for SOP-0996

Time (min)	Flow Rate	%MPA	%MPB	Curve
[redacted]				

8.6.4. [redacted]

8.6.4.1. [redacted]

8.6.4.1.1. [redacted]

8.6.4.1.2. [redacted]

Table 8: [redacted]

Time (min)	Flow Rate	%MPA	%MPB	Curve
[redacted]				

8.6.4.2. [redacted]

8.6.4.2.1. [redacted]

8.6.4.2.2. [redacted]

8.6.4.3. [redacted]

8.6.4.4. [redacted]

8.6.4.5. [redacted]

Table 9: Recommended Sample Sequence

Sample	Injections per prep.	Purpose	Instrument Method
[redacted]	[redacted]	[redacted]	
[redacted]			SOP-0996 IM
			SOP-0996 IM
[redacted]			SOP-0996 IM
[redacted]			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM
			SOP-0996 IM

8.6.5. [redacted]

8.6.5.1. [redacted]

8.6.5.2.

8.6.5.3. [redacted]

8.7. [redacted]

8.7.1. [redacted]

8.7.1.1. [redacted]

8.7.1.2. [redacted]

8.7.1.3. [redacted]

8.7.1.4. [redacted]

8.7.2. [redacted]

8.7.2.1. [redacted]

8.7.2.2. [redacted]

8.7.2.3. [redacted]

8.7.3. [redacted]

8.7.3.1. [redacted]

8.7.3.2. [redacted]

8.7.3.3. [redacted]

8.7.3.4. [redacted]

8.8. [redacted]

8.8.1. [redacted]

8.8.1.1. [redacted]

[redacted]

= [redacted] * [redacted]

8.8.1.2. [redacted]

[redacted]

= [redacted] * [redacted]

8.8.1.3. [redacted]

[redacted] = [redacted] * [redacted]

[redacted]

[redacted] = [redacted] * [redacted]

[redacted]

8.8.2. [redacted]

[redacted]

= [redacted]

[redacted]

[redacted]

= [redacted] * [redacted]

8.8.3. [redacted]

[redacted] = [redacted] *

8.8.4. [redacted]

[redacted] = [redacted]

8.9. [redacted]

8.9.1. [redacted]

Table 10: System Suitability Acceptance Criteria

Parameter	Acceptance Criteria
[redacted]	[redacted]

8.10. **Sample Acceptance Criteria**

8.10.1. [redacted]

Table 11: Sample Acceptance Criteria

Parameter	Acceptance Criteria
[redacted]	[redacted]

8.11. [redacted]

8.11.1. [redacted]

8.11.2. [redacted]

8.11.3. [redacted]

8.11.4. [redacted]

8.11.4.1. [redacted]

8.11.4.2. [redacted]

8.11.4.3. [redacted]

8.11.4.4. [redacted]

8.11.4.5. [redacted]

8.11.4.6. [redacted]

8.11.4.7. [redacted]

8.11.4.8. [redacted]

8.11.5. [redacted]

8.11.5.1. [redacted]

8.11.5.2. [redacted]

8.11.6. [redacted]

8.11.7. [redacted]

9.0 ATTACHMENTS

9.1. Attachment 1: Representative Diluent Blank Chromatogram

9.2. Attachment 2: Representative Diluent Blank Chromatogram with background subtraction

9.3. Attachment 3: Representative Sensitivity Solution

9.4. Attachment 4: Representative Reference Standard / DS Sample Chromatogram (full view and zoom)

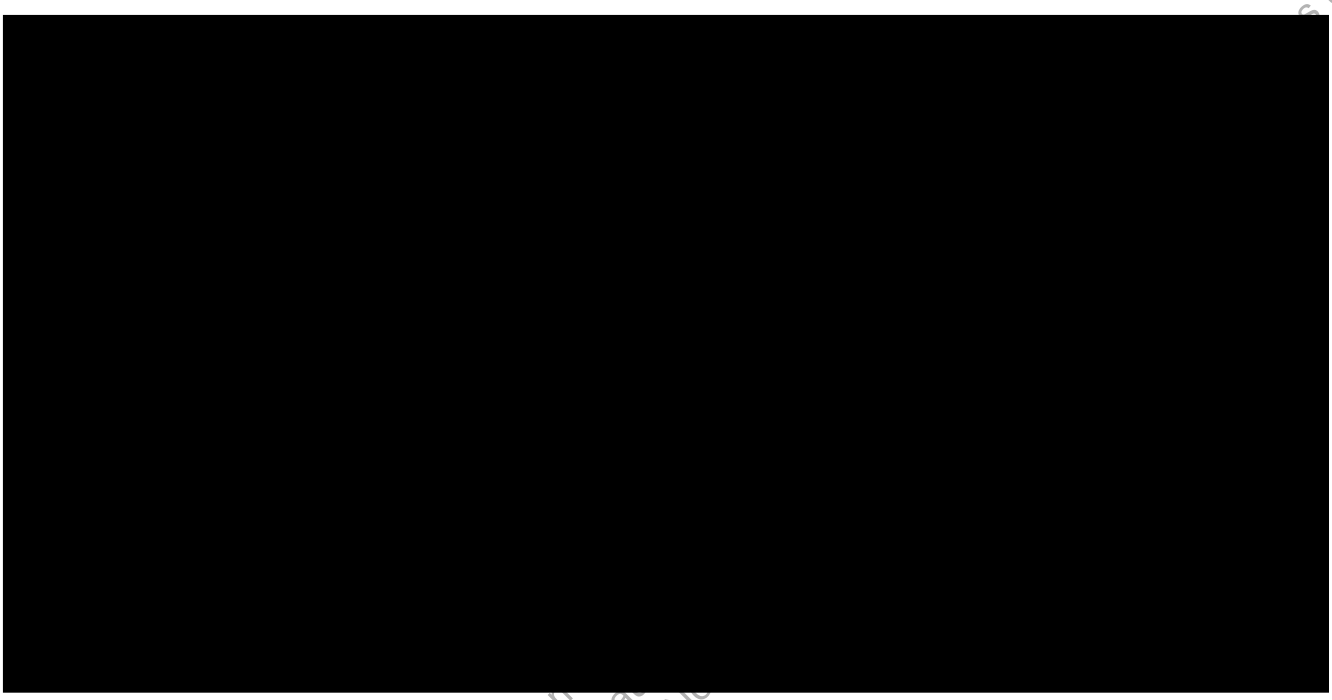
9.5. Attachment 5: Representative DP / LNP Sample Chromatogram (full view and zoom)

10.0 REVISION HISTORY

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

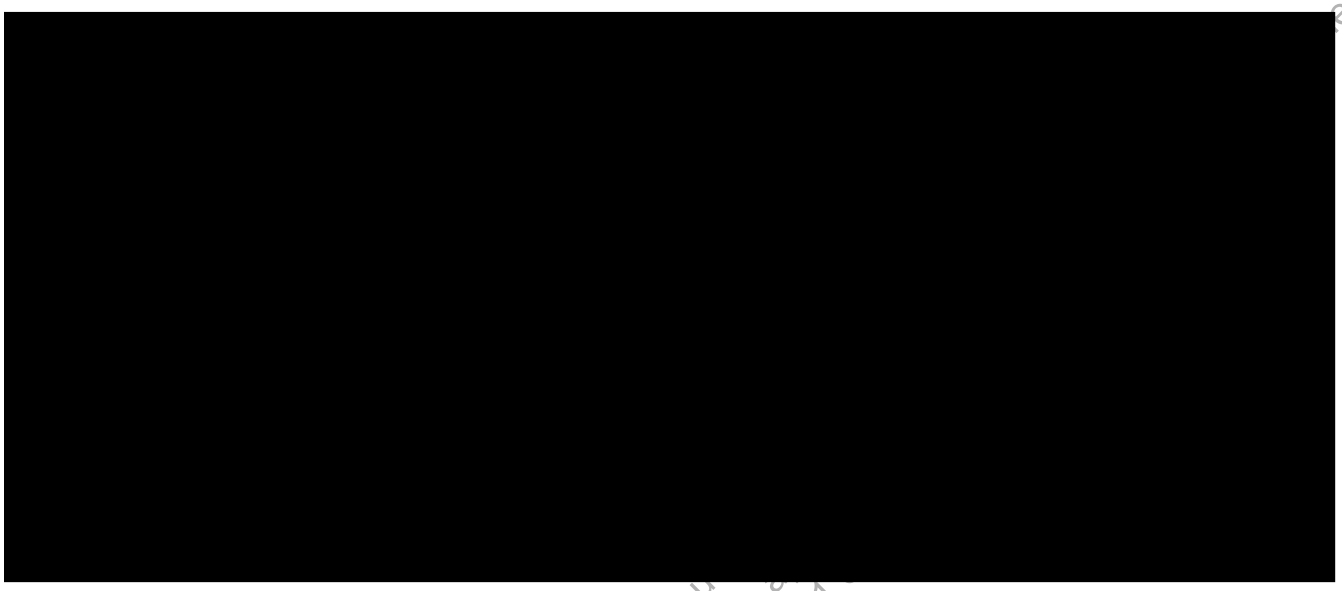
ATTACHMENT 1: Representative Diluent Blank Chromatogram

(Page 1 of 1)



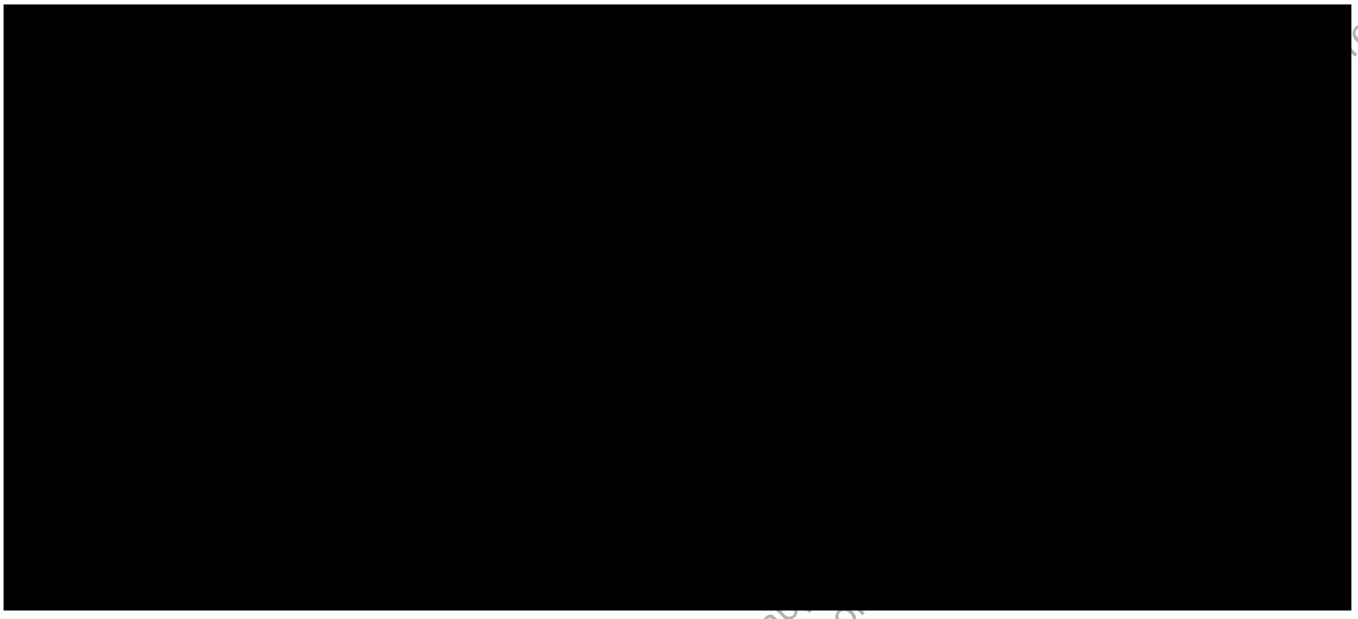
ATTACHMENT 2: Representative Diluent Blank Chromatogram with background subtraction

(Page 1 of 1)



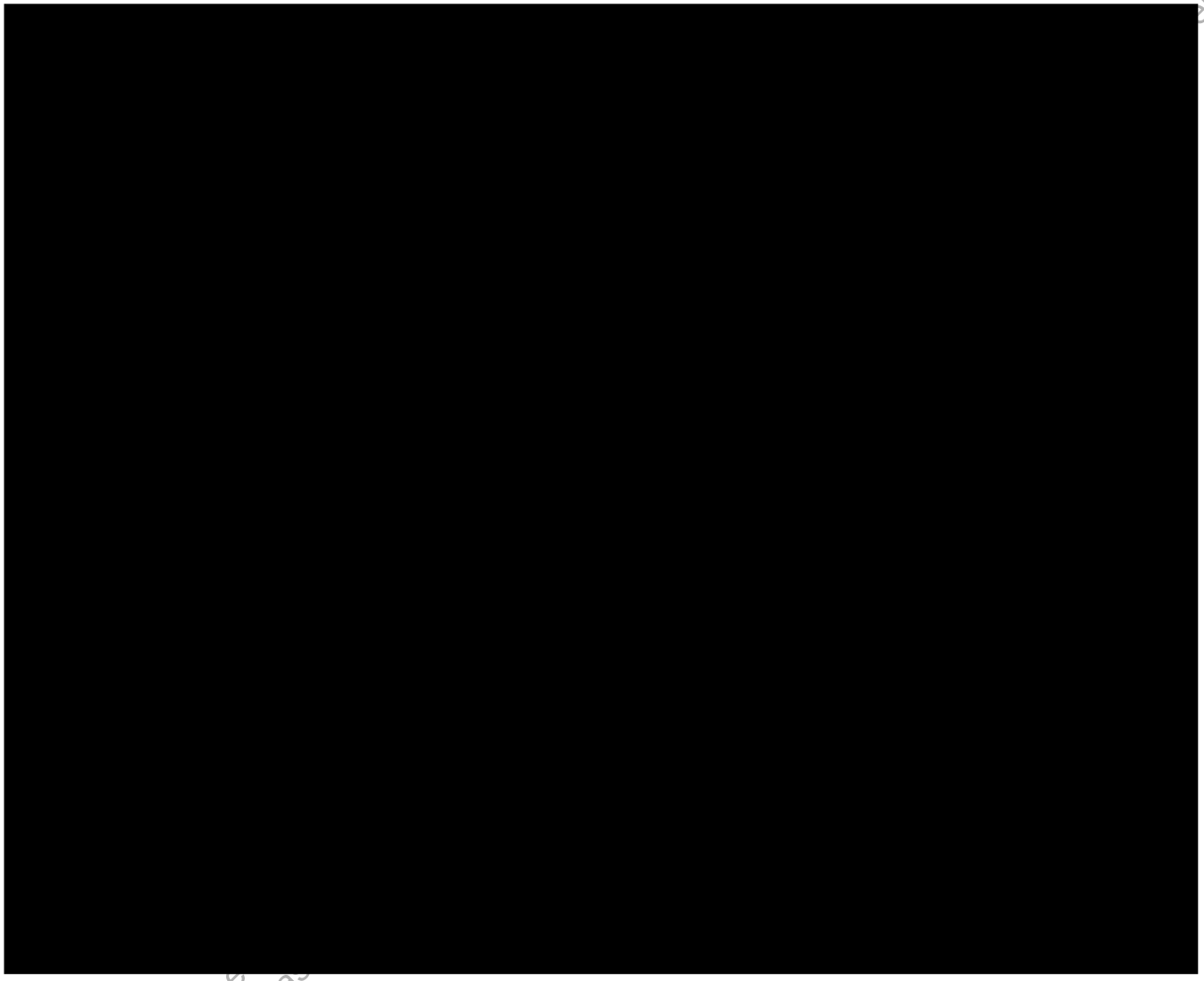
ATTACHMENT 3: Representative Sensitivity Solution

(Page 1 of 1)



ATTACHMENT 4: Representative Reference Standard / DS Sample Chromatogram (full view and zoom)

(Page 1 of 1)



ATTACHMENT 5: Representative DP / LNP Sample Chromatogram (full view and zoom)

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Document Approvals

Approved Date: 09 Oct 2020

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