moderna

1.0 PURPOSE

The purpose of this document is to describe the process of determining the particle size distribution of mRNA encapsulated lipid nanoparticle (LNP), [redacted], and Drug Product (DP) using Dynamic Light Scattering (DLS).

This method incorporates the utilization of [redacted] filtration of the sample prior to DLS analysis, removing particles [redacted] from the solution, thereby providing a higher quality dataset corresponding to the submicron size range.

2.0 SCOPE

This method applies to cGMP release and stability particle size analysis of final mRNA LNP, [redacted], and DP samples.

3.0 REFERENCED DOCUMENTS

Document #	Title
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-0227	[redacted] Operation and Maintenance
SOP-0333	Operation and Maintenance of [redacted]
SOP-0403	QC [redacted] Operations Procedure
SOP-0409	Quality Control Invalid Assay Procedure
FRM-0120	General Quality Control Sample Submission Form
FRM-0180	Quality Control Solution Preparation Form
FRM-0728	SOP-0998 Assay Performance Worksheet
DPAD-FRM-0010	[redacted] Form

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 procedures outlined in this document, when applicable. • Recording assay performance using FRM-0728. • Maintaining an RNase free work environment per SOP-0017. • Preparing solutions and samples per SOP-0081. • Following proper safety standards in the laboratory.

5.0 DEFINITIONS

Term	Definition
µL	Microliter
[redacted]	
DP	Drug Product
[redacted]	
L	Liter
LNP	Lipid Nanoparticle
mL	Milliliter
mRNA	Messenger Ribonucleic Acid
NaCl	Sodium Chloride
ng	Nanogram
PBS	Phosphate Buffered Saline
S	Seconds
WS	Working Solution

6.0 EQUIPMENT AND MATERIALS

Equivalent equipment, consumables and materials can be used, unless otherwise indicated, and provided they match the reagent grade or specifications.

Equipment

Description	Supplier	Catalog Number
[redacted]	[redacted]	[redacted]

Description	Supplier	Catalog Number
Pipettes, capable of measuring [redacted]	[redacted]	[redacted]
Vortex	[redacted]	[redacted]

Reagents

Use the reagents specified below or equivalent.

Description	Supplier	Catalog or Part Number
[redacted]		

Materials

Description	Supplier	Catalog Number
[redacted]		

Description	Supplier	Catalog Number
[redacted]		

7.0 SAFETY

7.1. Laboratory personnel must wear appropriate PPE when working in the QC Laboratory.

7.2. Removal of the [redacted] main covers by unauthorized personnel, even a supervisor, will invalidate the warranty of the instrument. Failure to follow these guidelines could result in exposure to hazardous voltages and laser radiation.

8.0 PROCEDURE

Reagent and sample preparations may be scaled accordingly, such that the predetermined concentrations are maintained. Prepare and label all solutions per SOP-0081.

8.1. **Sample and Standard Preparation**

8.1.1. [redacted]

8.1.1.1. [redacted] **SOP-0403.**

8.1.1.2. [redacted] **SOP-0403.**

8.1.1.3. [redacted]

[redacted] SOP-0403.

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.

8.1.3.2.

8.1.3.3. [redacted]

8.1.3.4. [redacted]

Amount of sample (µL) = $\frac{final\ sample\ concentration\ (\text{[redacted]}\ mg/mL)}{Initial\ sample\ concentration\ (\frac{mg}{mL})} * \text{[redacted]}\ \mu L$

Amount of [redacted] (µL) = [redacted] µL – Sample (µL)

[redacted]

8.1.3.5. [redacted]

8.1.3.6. [redacted]

8.1.3.7. [redacted]

8.1.3.8. [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]

Amount of sample (µL) = $\frac{\textit{final sample concentration (}\ \textit{mg/mL)}}{\textit{Initial sample concentration }(\frac{mg}{mL})} * \ \mu L$

Amount of [redacted]µL) = [redacted] µL – Amount of Sample (µL)

8.1.4.5. [redacted]

8.1.4.6.

8.1.4.7.

8.1.4.8.

8.2. **Instrument Setup**

8.2.1. [redacted] SOP-0333 [redacted]

8.2.2. [redacted]

8.2.3. [redacted] SOP-0333.

8.2.3.1. [redacted]

8.2.3.2. [redacted] "SOP-0998 [redacted]

8.2.4. [redacted]

8.2.5.

[redacted]

8.2.6. [redacted] SOP-0333.

Table 1: [redacted] **SOP-0998** [redacted]

[redacted] Parameters			
Measurement type: [redacted]			
Parameter	**Property**	**Specification**	**Comment**
Sample	[redacted]	[redacted]	[redacted]
			[redacted]
Measurement	Measurement angle		
	Measurement duration		
	Advanced		
Data Processing	Analysis model:		

Table 2: Instrument Method for SOP-0998 [redacted]

[redacted] Parameters			
Measurement type: [redacted]			
Parameter	**Property**	**Specification**	**Comment**
Sample	[redacted]	[redacted]	[redacted]
Measurement	Measurement angle		
	Measurement duration		
	Advanced		
Data Processing	Analysis model:		

8.3. System Suitability Verification Using [redacted] Standards

[redacted]

8.3.1. [redacted]

8.3.2. [redacted]

8.3.3. [redacted]

8.3.4. [redacted]

8.3.5. [redacted]

8.3.5.1. [redacted]

8.3.6. [redacted]

Table 3: Standard Dispersant Parameters

Solvent	Temperature (°C)	RI	Viscosity (cP)	Dielectric Constant
[redacted]				

[redacted]

8.3.7. [redacted]

8.3.8. [redacted]

8.4. **Testing**

[redacted]

8.4.1. [redacted]

8.4.2. [redacted]

8.4.3. [redacted]

8.4.3.1. [redacted]

8.4.3.2. [redacted]

8.4.4. [redacted]

8.4.5. [redacted]

8.4.5.1. [redacted]

8.4.5.2. [redacted]

8.4.6. [redacted]

8.4.7. [redacted]

8.4.8. [redacted]

8.4.8.1. [redacted]

8.4.8.2. [redacted]

8.4.9. [redacted]

8.4.10.

8.4.11.

8.4.12.

Table 4: Sample Sequence Example

Line #	Sample
1	[redacted]
2	
3	
4	
5	
6	
7	
8	
9	
10	

8.5. **Acceptance Criteria**

8.5.1. System Suitability Criteria

8.5.1.1. Refer to Table 5 for the System Suitability Criteria.

Table 5: System Suitability Acceptance Criteria

Size Standard	Particle Size Z-Average (diameter, nm) Acceptable Range	Polydispersity Index (PdI)
[redacted]	[redacted]	[redacted]

8.5.2. Sample Acceptance Criteria

8.5.2.1. [redacted]

8.5.2.2.

8.5.2.3.

[redacted]

8.6. **Reporting Results**

8.6.1. Follow **SOP-0082** for QC data reporting.

8.6.2. [redacted]

8.6.3.

8.6.3.1. [redacted]

8.6.3.2.

8.6.3.3.

8.6.3.4.

8.6.4. [redacted]

8.6.4.1. [redacted]

8.6.4.2.

8.6.4.3.

8.6.4.4.

8.6.5. [redacted] SOP-0227.

8.6.5.1. [redacted]

8.6.5.2.

8.6.6. [redacted] SOP-0033 [redacted]

8.6.7. [redacted]

SOP-0409 [redacted]

9.0 ATTACHMENTS

9.1. Attachment 1: Example of a [redacted] with Result Quality Acceptable.

9.2. Attachment 2: Example of a [redacted] with Result Quality Unacceptable

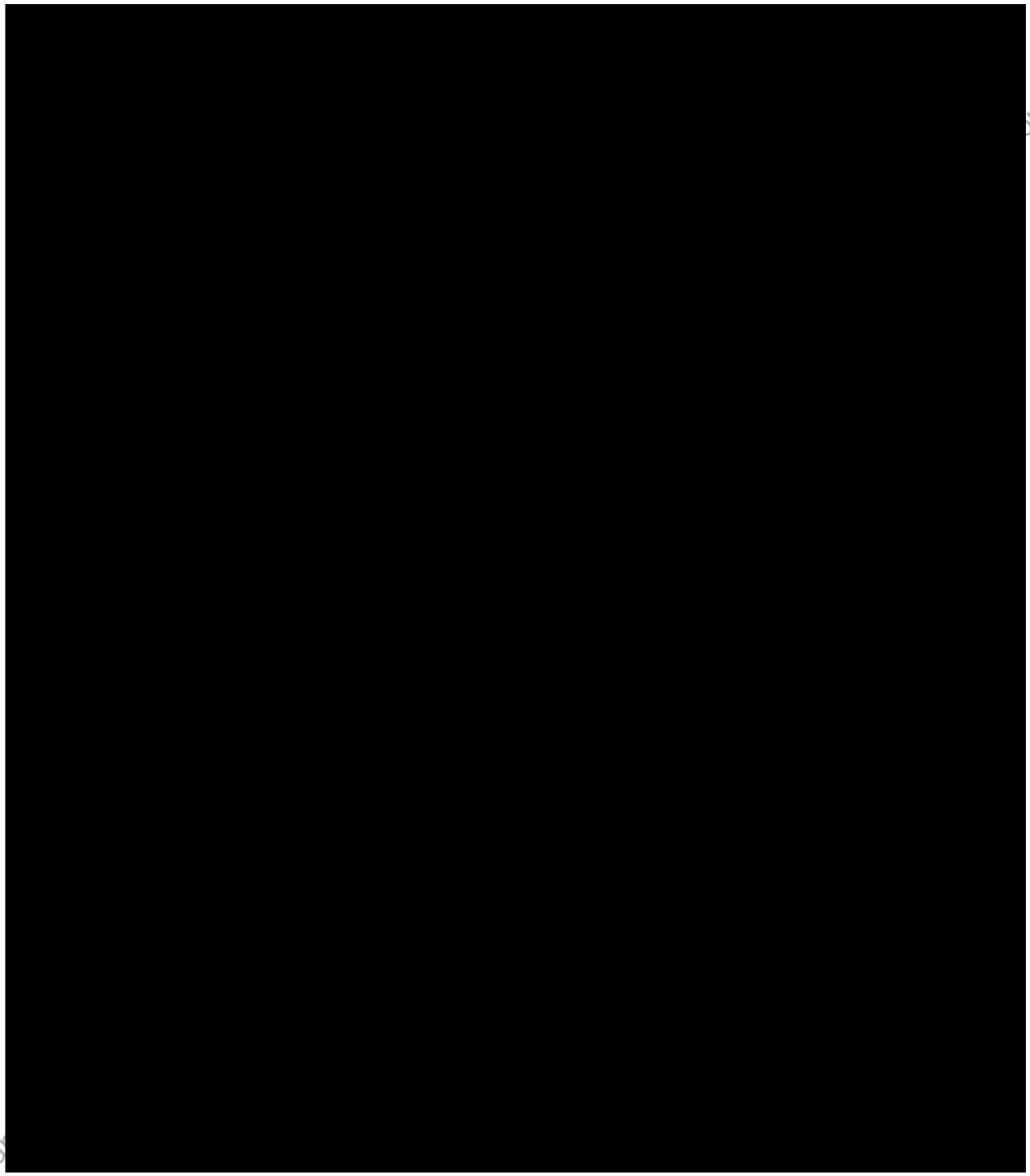
9.3. Attachment 3: Example of a [redacted] with Multimodal Result

9.4. Attachment 4: New SOP Creation with Dispersant Selection

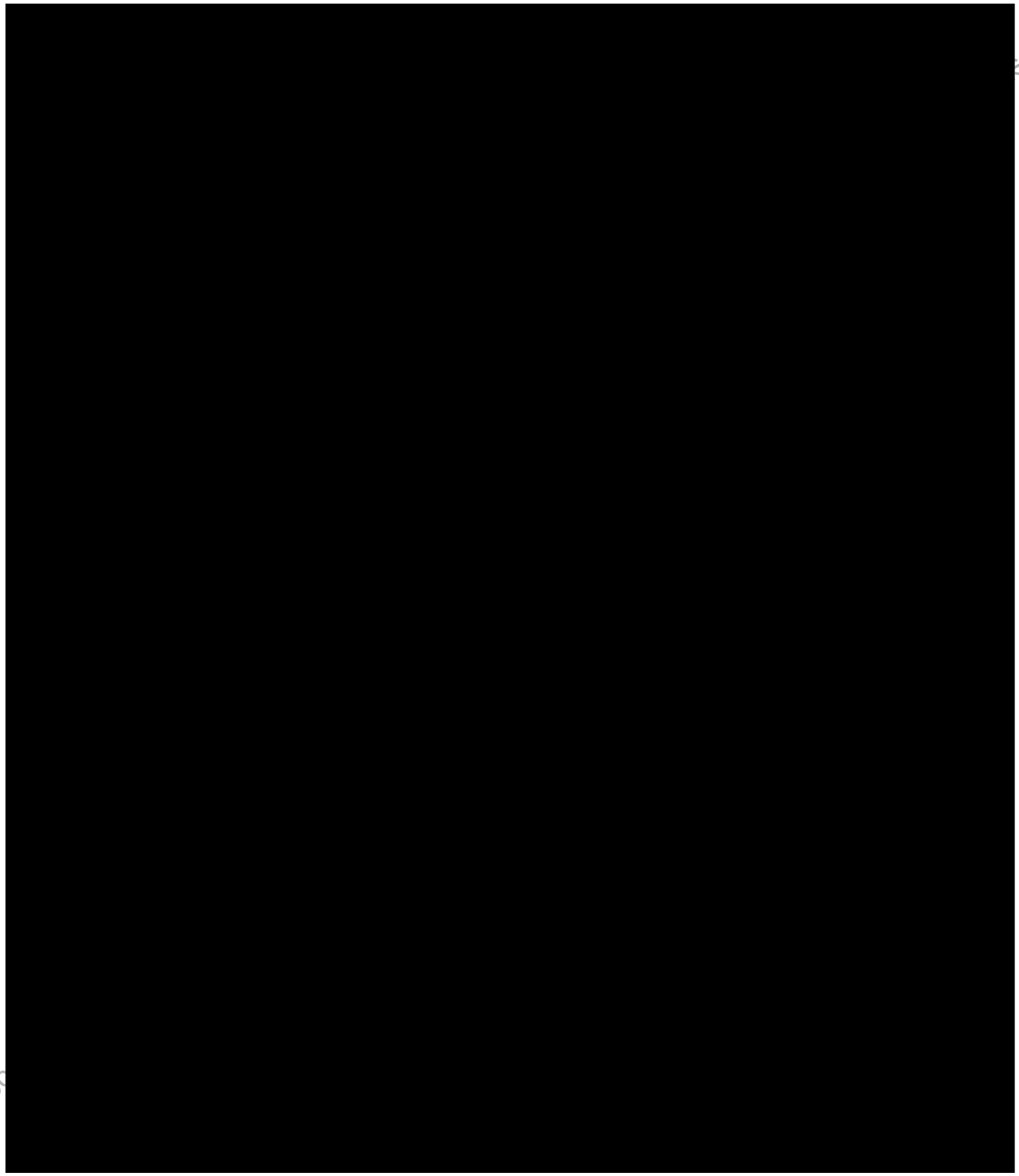
10.0 REVISION HISTORY

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

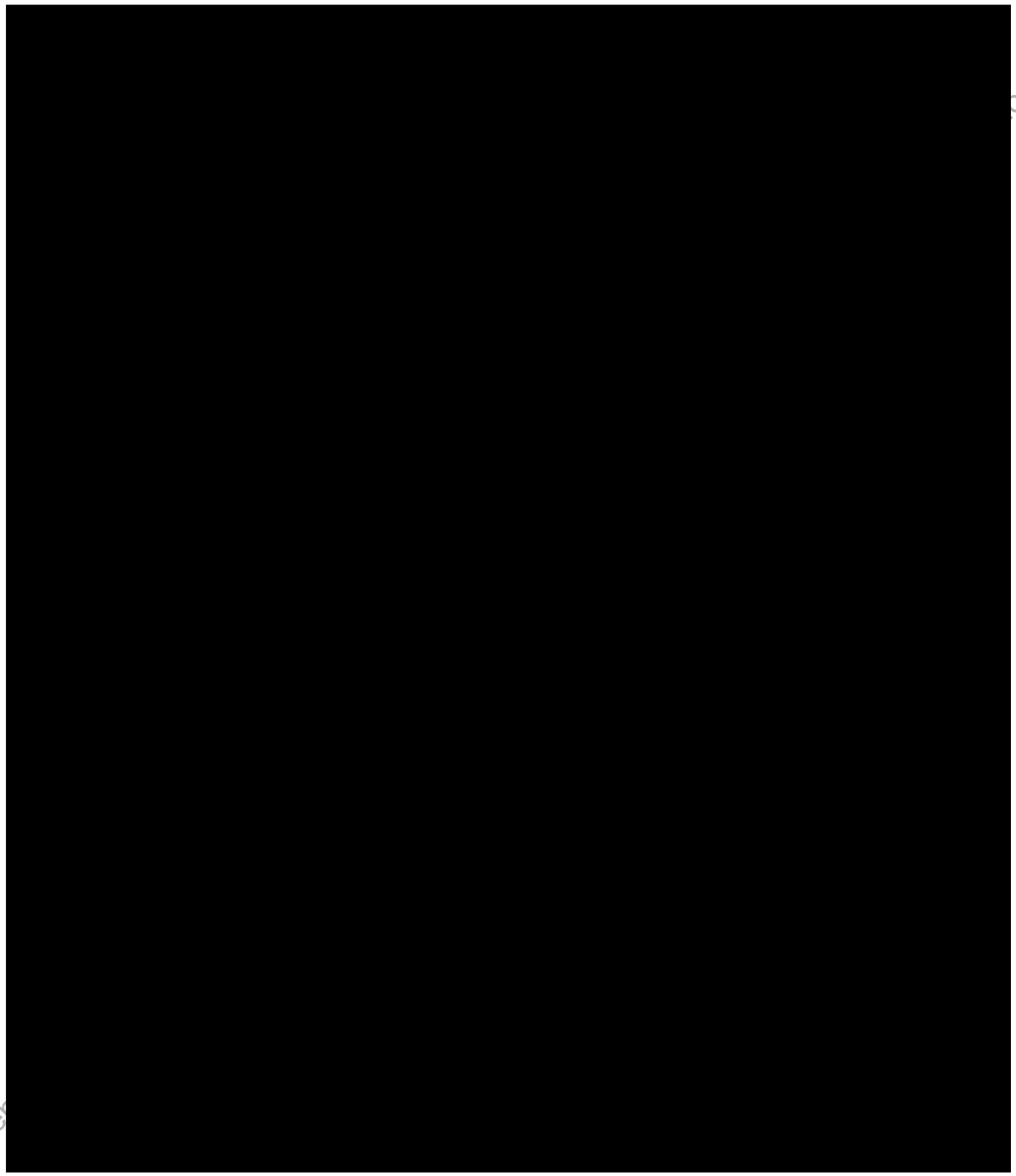
ATTACHMENT 1 - Example of a [redacted] with Result Quality Acceptable
(Page 1 of 2)



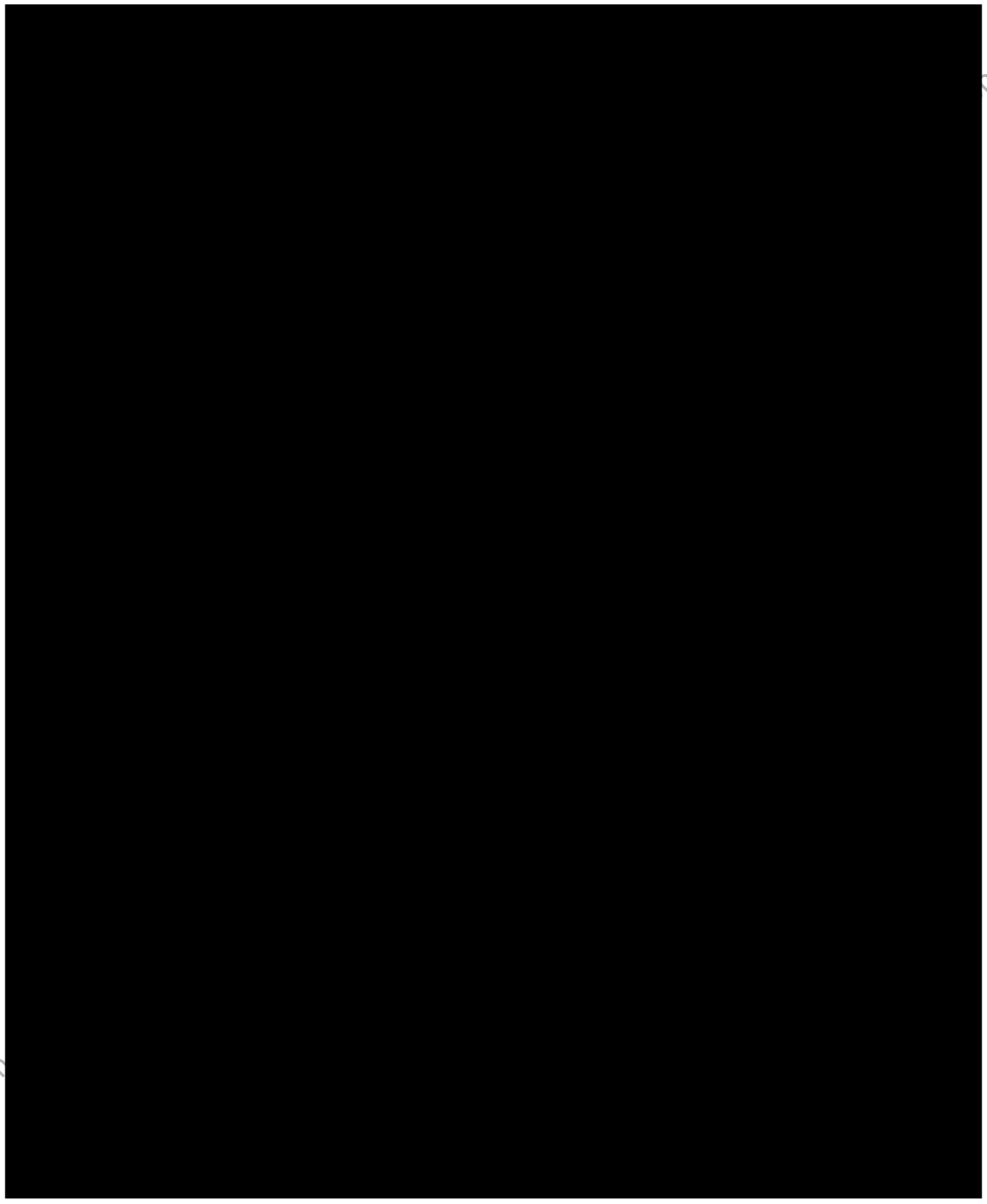
ATTACHMENT 1 - Example of a [redacted] with Result Quality Acceptable
(Page 2 of 2)



ATTACHMENT 2 - Example of a [redacted] with Result Quality Unacceptable
(Page 1 of 2)

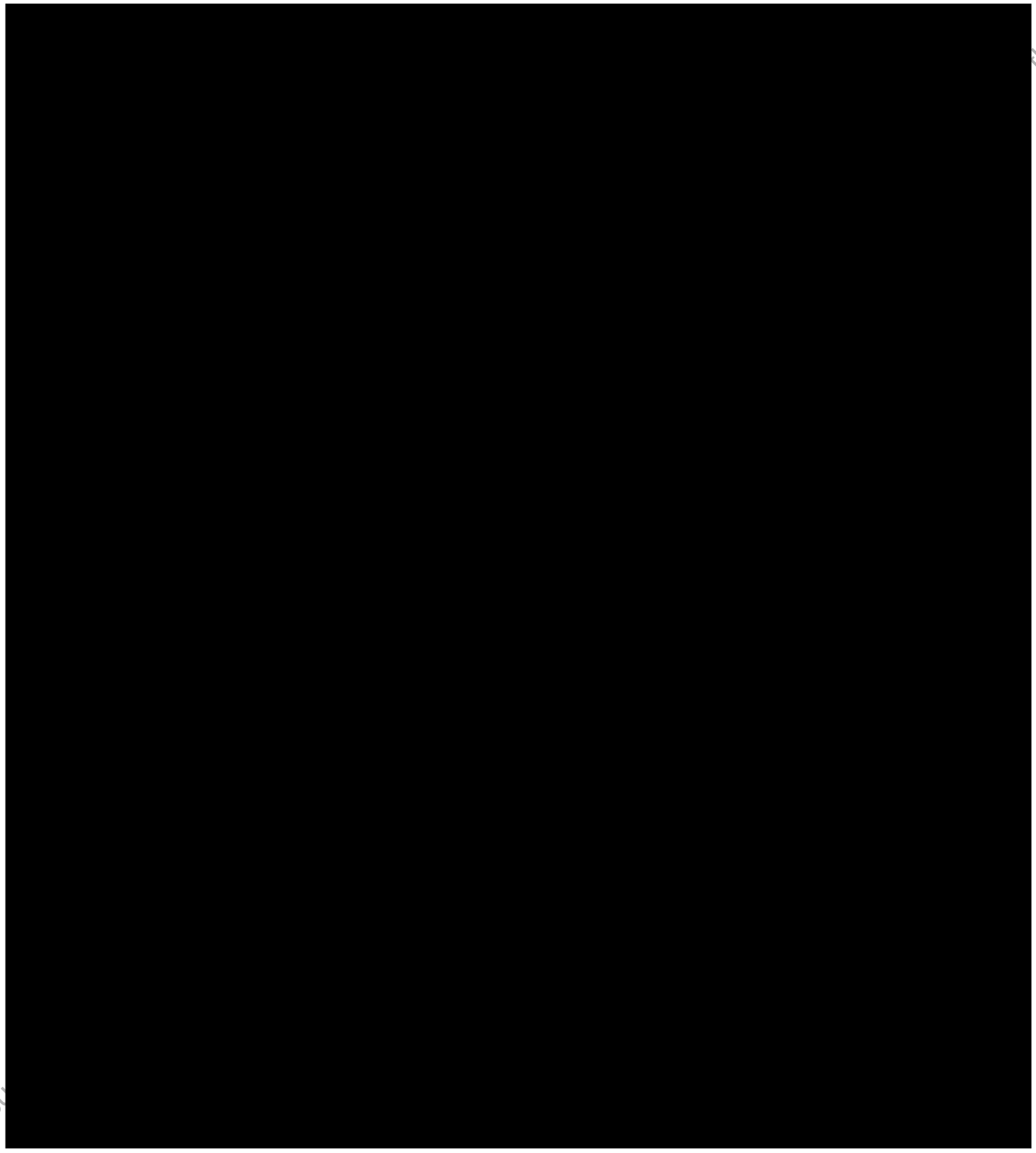


ATTACHMENT 2 - Example of a [redacted] with Result Quality Unacceptable
(Page 2 of 2)



ATTACHMENT 3 - Example of a [redacted] with Multimodal Results

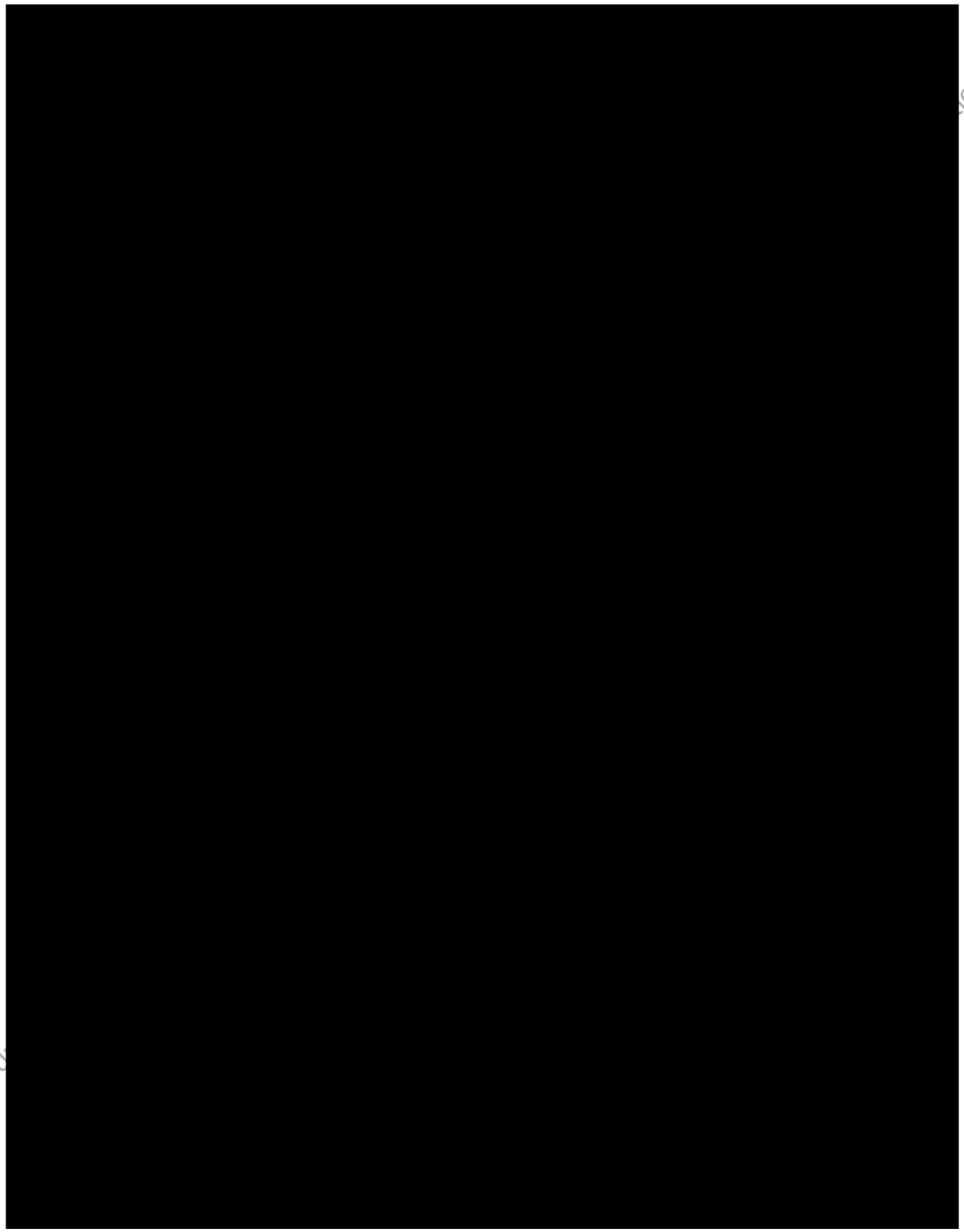
(Page 1 of 1)



ATTACHMENT 4 - New SOP Creation with Dispersant Selection
(Page 1 of 2)

[redacted]

ATTACHMENT 4 - New SOP Creation with Dispersant Selection
(Page 2 of 2)



Document Approvals

Approved Date: 05 Oct 2020

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