Reason for Submission
☐ For Release
☐ For Surveillance
☒ For Licensing Action*
STN: 125742_0
☐ Corrected Protocol

Date : 18 Aug 21

Subject: Electronic Protocol Signature Page

License No.: 2229
Company Name: Pharmacia & Upjohn Company LLC for BioNTech Manufacturing GmbH

Pharmacia & Upjohn Company LLC for BioNTech Manufacturing GmbH hereby submits the following lot as an electronic submission by Electronic Submissions Gateway (ESG). All test conducted on this lot are reported and pass specifications as required.

COVID-19 Vaccine, mRNA

STN	Lot Number	Lot Type	Electronic Protocol Filename
125742_0	FF2588	FC	20219004.P0

Sample Status
☐ Sample Not Required
☐ Sample Submitted with Protocol
☒ Sample Previous Submitted: 16-Aug-2021

Virus Verification

Software Name: Symantec Web Security Service	
Company Name: Symantec	Version: 7.2.1
Date of Definitions: 18-Aug-2021	Date of Scan: 18-Aug-2021

I certify that the submission is virus-free.
The approximate file size of this submission is approximately 1.25MB.

Comments:
N/A

Signature of Authorized Official
Printed Name and Title of Signatory Title
(b) (6)
(b) (6)
18 Aug 2021 12:50:010-0400
REASON: I approve this document.
bcf9b9f3-dcbe-4cfe-a38a-d0dfba6a6f4c
(b) (6)

Reason for Submission
☐ For Release
☐ For Surveillance
☒ For Licensing Action*
STN: 125742_0
☐ Corrected Protocol

cc: STN 125742-0/2229/FC

Lot Number: FF2588
License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

Manufacturer Name: Pharmacia & Upjohn Company LLC for BioNTech Manufacturing GmbH

Manufacturer Address: 7000 Portage Rd., Kalamazoo, MI 49001 USA

Trade name: COMIRNATY

Date of Manufacturing: 04-Jul-2021 Expiration Date: 31-Dec-2021

Fill Information

Container Type:	Vial	**Volume per container:**	0.45mL
Approved Storage Period:	6 months	**Storage Temperature:**	-90°C to -60°C
Number of containers manufactured:	(b) (4)	**Number of Doses per container:**	6
Number of containers for release:	(b) (4)		
Volume of single human dose:	30 µg/Dose	**Start Date of period of Validity:**	Date of Manufacture

All tests conducted on this lot are reported and pass specifications as required.

(b) (6) (b) (6)
18 Aug 2021 12:50:010-0400
REASON: I approve this document.

Signature: bcf9b9f3-dcbe-4cfe-a38a-d0dfba6a6f4c Date:
Title: (b) (6)
Electronic Protocol # - 20219004.P0

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

Manufacturing Site: Pharmacia & Upjohn Company LLC, 7000 Portage Rd., Kalamazoo, MI 49001 USA

Date of Manufacture: 04-Jul-2021 **Date of Expiry:** 31-Dec-2021

Date of Fill: 05-Jul-2021

Product Information:

COMPONENTS

Component Description	Batch Number	Date of Manuf.	Manufacture Site	Quantity	Target
BNT162b2 Drug Substance	(b) (4)	(b) (4)	Pfizer (b) (4)	(b) (4)	
BNT162b2 Drug Substance			Pfizer (b) (4)		
LNP Fabrication		(b) (4)	Pharmacia & Upjohn Compan LLC		
Bulk Drug Product Formulation		04-Jul-2021	Pharmacia & Upjohn Compan LLC		

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

Table 1. Filled Vaccine Quality Control Tests

Test	Test Method	Specification	Date of Test	Result
Appearance	Appearance (Visual)	White to off-white suspension	(b) (4)	MEETS TEST
Appearance (Visible Particulates)	Appearance (Particles	May contain white to off-white opaque amorphous particles		MEETS TEST
Subvisible Particles	Subvisible Particulate Matter	(b) (4) (b) (4)		(b) (4)
pH	(b) (4)	6.9 - 7.9		
Osmolality	Osmometry	(b) (4) mOsmol/kg		
LNP Size	Dynamic Light Scattering (DLS)	(b) (4) nm		
LNP Polydispersity	Dynamic Light Scattering (DLS)	(b) (4)		
RNA Encapsulation	Fluorescence assay	(b) (4) %		
RNA content	Fluorescence assay	(b) (4) mg/mL		
ALC-0315 content	HPLC-CAD	(b) (4) mg/mL		
ALC-0159 content	HPLC-CAD	(b) (4) mg/mL		
DSPC content	HPLC-CAD	(b) (4) mg/mL		
Cholesterol content	HPLC-CAD	(b) (4) mg/mL		
Vial content	Container Content	Not less than (b) (4) mL		
Lipid identities	HPLC-CAD	Retention times consistent with references (ALC-0315, ALC-0159, Cholesterol, DSPC)		Positive

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

Table 1 (Continued) Filled Vaccine Quality Control Tests

Test	Test Method	Specification	Date of Test	Result
Identity of encoded RNA sequence	RT-PCR	Identity confirmed	(b) (4)	Positive
In Vitro Expression	Cell-based Flow Cytometry	(b) (4) % Cells Positive	(b) (4)	(b) (4)
RNA Integrity	Capillary Gel Electrophoresis	(b) (4) % intact RNA	(b) (4)	
Bacterial Endotoxin	Endotoxin (LAL)	(b) (4) EU/mL	(b) (4)	

Abbreviations: LNP = Lipid nanoparticles; CAD = charged aerosol detector; RT-PCR = reverse transcription polymerase chain reaction; LAL = Limulus amebocyte lysate; EU = endotoxin unit

Filled Vaccine Quality Control Tests (cont.)

Sterility

Method: (b) (4) **Type:** Final Container

Container: Sterility-(b) (4)

Date On Test	Medium/Temperature	Date Off Test	Specification	Test Result
(b) (4)	(b) (4)		No growth observed	No growth observed
			No growth observed	No growth observed

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

Filled Vaccine Quality Control Tests (Continued)

Lipid Identity

Specification (b) (4) **Limit** **Result** **Pass**

Lipid	Standard Retention Times (RT)	Sample Retention Time	(b) (4)
ALC-0315 content	(b) (4)		
ALC-0159 content			
DSPC content			
Cholesterol content			

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

Filled Vaccine Quality Control Tests (Continued)

RNA encapsulation and content test

Test date ___(b) (4) ___

Test method _____**TM8940A**____

Specification: RNA Encapsulation (b) (4) **Result** __(b) (4) _____

Specification: Content RNA Content (b) (4) mg/mL Result ___(b) (4) ___

Sample/Control	Acceptance Criteria	Result
R^2 for Standard A	(b) (4)	
R^2 for Standard B		
Total RNA (mg/mL)		(b) (4)
Encapsulated RNA (mg/mL)		

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

Filled Vaccine Quality Control Tests (Continued)

Identity of encoded RNA sequence test

Test method __RT-PCR_____

Test date __(b) (4) _____

Specification **Identity confirmed** **Result** __Positive_____

Sample/Control	Lot number	Replicate	Ct value	Acceptance criteria	Pass/Fail
DP Sample	FF2588	1	(b) (4)		Pass
		2			
		3			
Positive PCR Control	(b) (4)	1			Pass
		2			
		3			
Positive (b) (4) Control	PF-07302048-DP-RM	1			Pass
		2			
		3			
Negative PCR Control	NA	1			Pass
		2			
		3			
Negative (b) (4) Control	NA	1			Pass
		2			
		3			

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

Filled Vaccine Quality Control Tests (Continued)

In Vitro Expression Assay

Test date (b) (4)

Test method **LAB-38621**

Specification (b) (4) **cells positive**

	Acceptance Criteria	Result
(b) (4) Lot number		(b) (4)
Positive Control lot number		
% cell viability	(b) (4)	
Average Number of Cells Counted for Sample		
Test Result (% positive cells)		

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

Filled Vaccine Quality Control Tests (Continued)

Limulus Amebocyte Lysate Test

(b) (4)

Calculations or additional comments

N/A

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

BNT162b2 Drug Substance

Lot Number: (b) (4)

Date of Manufacture: (b) (4) **Date of Expiry:** (b) (4)

Storage Temperature: -25˚C to -15˚C **Approved Storage Period:** (b) (4) months

Consumed Quantity: (b) (4)

Table 1. Drug Substance Quality Control Tests

Test	Test Method	Specification	Date of Test	Result
Clarity	Appearance (Clarity)	(b) (4)		
Coloration	Appearance (Coloration)			
pH	(b) (4)			
Content (RNA Concentration)	UV Spectroscopy			
Identity of Encoded RNA Sequence	RT-PCR			
RNA Integrity	Capillary Gel Electrophoresis			
5'- Cap	RP-HPLC			
Poly(A) Tail	ddPCR			
Residual DNA Template	qPCR			
Residual dsRNA	Immunoblot			
Bacterial Endotoxin	Endotoxin (LAL)			
Bioburden	Bioburden			

Abbreviations: NTU = Nephelometric Turbidity Units; B = brown; RT-PCR = reverse transcription polymerase chain reaction; ddPCR = droplet digital PCR; qPCR = quantitative PCR; dsRNA = double stranded RNA; LAL = Limulus amebocyte lysate; EU = endotoxin unit; CFU = colony forming unit

cc: STN 125742-0/2229/FC

Lot Number: FF2588

License Name of Product: COVID-19 mRNA Vaccine (nucleoside modified)

BNT162b2 Drug Substance

Lot Number: (b) (4)

Date of Manufacture: (b) (4) **Date of Expiry:** (b) (4)

Storage Temperature: -25˚C to -15˚C **Approved Storage Period:** (b) (4) months

Consumed Quantity: (b) (4)

Table 1. Drug Substance Quality Control Tests

Test	Test Method	Specification	Date of Test	Result
Clarity	Appearance (Clarity)	(b) (4)		
Coloration	Appearance (Coloration)			
pH	(b) (4)			
Content (RNA Concentration)	UV Spectroscopy			
Identity of Encoded RNA Sequence	RT-PCR			
RNA Integrity	Capillary Gel Electrophoresis			
5'- Cap	RP-HPLC			
Poly(A) Tail	ddPCR			
Residual DNA Template	qPCR			
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Bacterial Endotoxin	Endotoxin (LAL)			
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Abbreviations: NTU = Nephelometric Turbidity Units; B = brown; RT-PCR = reverse transcription polymerase chain reaction; ddPCR = droplet digital PCR; qPCR = quantitative PCR; dsRNA = double stranded RNA; LAL = Limulus amebocyte lysate; EU = endotoxin unit; CFU = colony forming unit

Prepared By:

(b) (6)

(b) (6)

18 Aug 2021 13:34:023-0400

REASON: I approve this document.

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(b) (6)

Approved By:

(b) (6)

(b) (6)

18 Aug 2021 12:50:010-0400

REASON: I approve this document.

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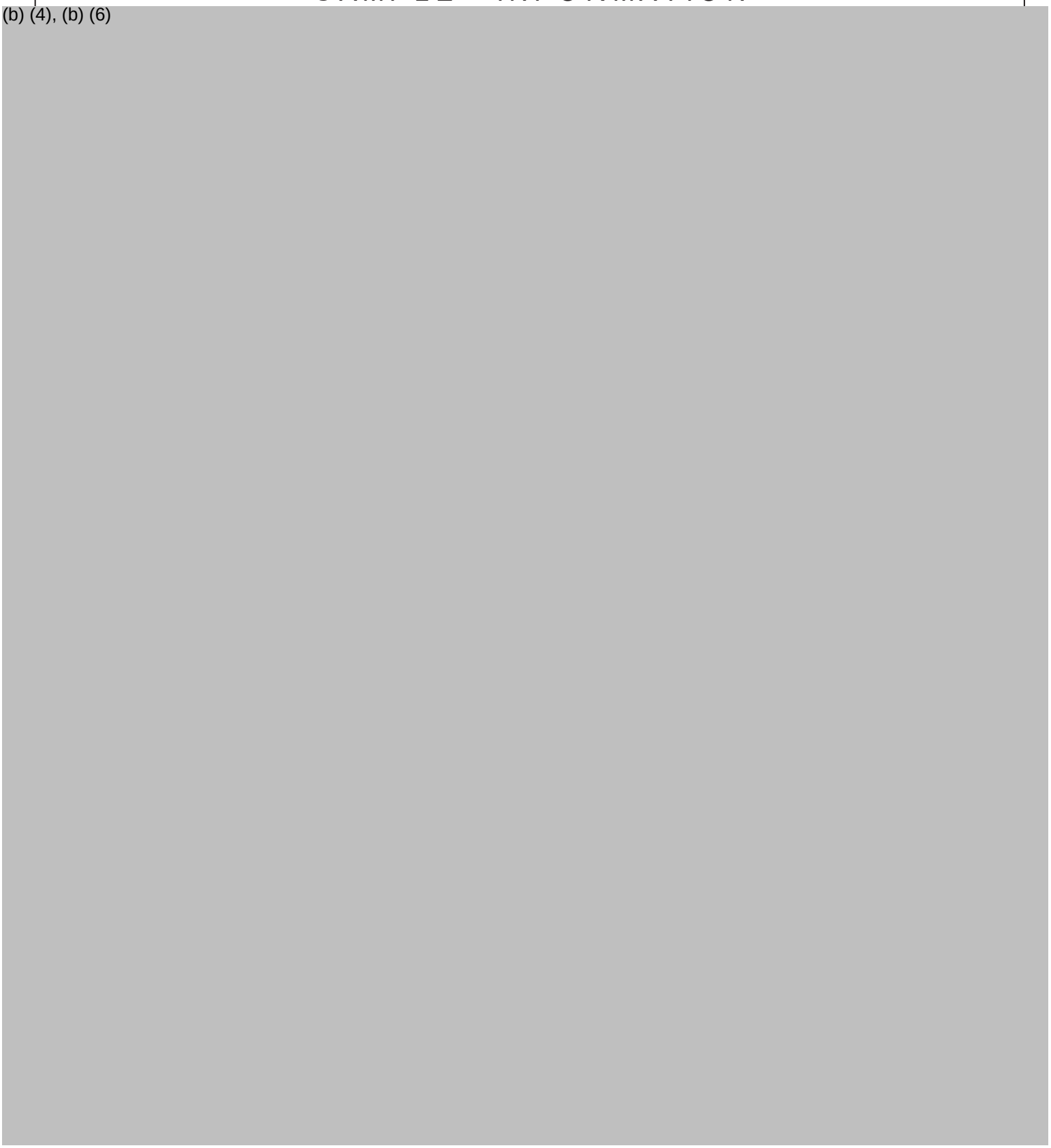
(b) (6)

SAMPLE INFORMATION

(b) (4), (b) (6)

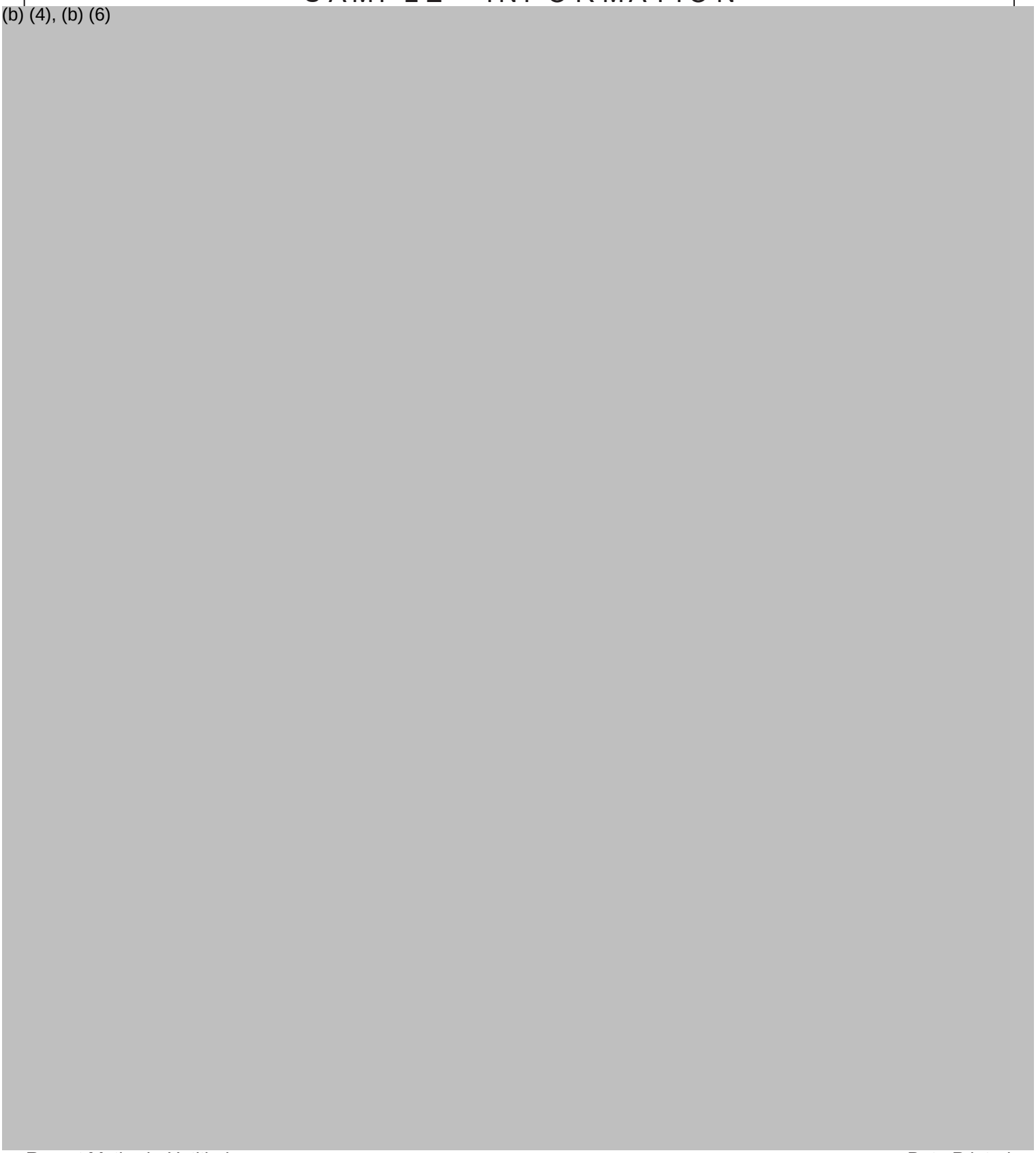


SAMPLE INFORMATION

(b) (4), (b) (6)

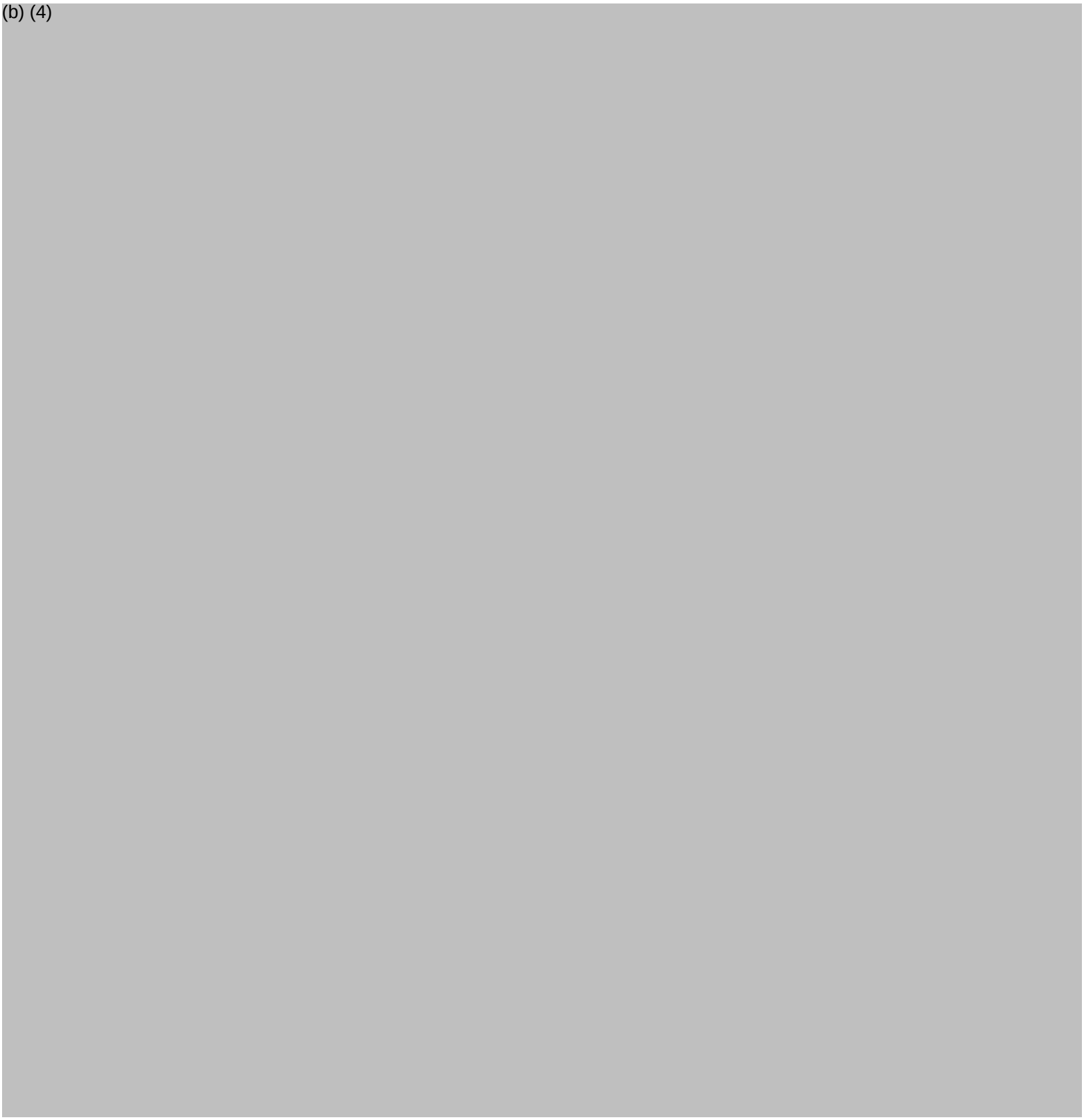
SAMPLE INFORMATION

(b) (4), (b) (6)



FF2588 Replicates 1-3

(b) (4)



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