



Reason for Submission

- For Release
- For Surveillance
- For Licensing Action*
STN: 125742_0
- Corrected Protocol

Date : 19 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

<u>STN</u>	<u>Lot Number</u>	<u>Lot Type</u>	<u>Electronic Protocol Filename</u>
125742_0	FF2590	FC	20219006.PC1

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:

Protocol updated to correct the serial dilutions for standard endotoxin solution on page 10 of 13.

Signature of Authorized Official
Printed Name and Title of Signatory Title

(b) (6) [Redacted] (b) (6) [Redacted]
19 Aug 2021 16:12:006-0400

REASON: I approve this document.

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(b) (6) [Redacted]

Reason for Submission

- For Release
- For Surveillance
- For Licensing Action*
STN: 125742_0
- Corrected Protocol

cc: STN 125742-0/2229/FC

Lot Number: FF2590
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: 06-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.

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19 Aug 2021 16:12:006-0400

REASON: I approve this document.

Signature: _____
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 Title: (b) (6)
 Electronic Protocol# - 20219006.PC1

Date: _____

cc: STN 125742-0/2229/FC

Lot Number: FF2590

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: 06-Jul-2021

Date of Expiry: 31-Dec-2021

Date of Fill: 06-Jul-2021

Product Information:

COMPONENTS

Component Description	Batch Number	Date of Manuf.	Manufacture Site	Quantity	Target Concentration
BNT162b2 Drug Substance	(b) (4)	(b) (4)	Pfizer Andover	(b) (4)	
BNT162b2 Drug Substance			Pfizer Andover		
LNP Fabrication		(b) (4)	Pharmacia & Upjohn Company LLC		
Bulk Drug Product Formulation		06-Jul-2021	Pharmacia & Upjohn Company LLC		

cc: STN 125742-0/2229/FC

Lot Number: FF2590

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

Lot Number: FF2590

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 amoebocyte 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: FF2590

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			

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Lot Number: FF2590

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)	(b) (4)
R ² for Standard B		
Total RNA (mg/mL)		
Encapsulated RNA (mg/mL)		

Lot Number: FF2590

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	FF2590	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: FF2590

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

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Lot Number: FF2590

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: FF2590

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 amoebocyte lysate; EU=endotoxin unit; CFU=colony forming unit

cc: STN 125742-0/2229/FC

Lot Number: FF2590

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 ameboocyte lysate; EU=endotoxin unit; CFU = colony forming unit

Genealogy Flowchart

(b) (4)



Prepared By:

(b) (6)

(b) (6)

19 Aug 2021 16:14:000-0400

REASON: I approve this document.

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(b) (6)

Approved By:

(b) (6)

(b) (6)

19 Aug 2021 16:12:006-0400

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(b) (6)

SAMPLE INFORMATION

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

(b) (4)

SAMPLE INFORMATION

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



SAMPLE INFORMATION

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

FF2590 Replicates 1-3

(b) (4)



(b) (4)

