



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

| <u>STN</u> | <u>Lot Number</u> | <u>Lot Type</u> | <u>Electronic Protocol</u> <u>Filename</u> |
|------------|-------------------|-----------------|---|
| 125742_0 | FF2590 | FC | 20219006.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) [Redacted] (b) (6) [Redacted]
18 Aug 2021 12:47:028-0400

REASON: I approve this document.

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(b) (6) [Redacted]
[Redacted]

FDA-CBER-2021-583-1350079

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.

(b) (6) (b) (6)
 18 Aug 2021 12:47:028-0400

REASON: I approve this document.

Signature: bcf9b9f3-dcbe-4cfe-a38a-d0dfba6a6f4c
 Title: (b) (6)
 Electronic Protocol# - 20219006.P0

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 | (b) (4) | MEETS TEST |
| Subvisible Particles | Subvisible Particulate Matter | (b) (4) (b) (4) | (b) (4) | (b) (4) |
| pH | (b) (4) | 6.9 - 7.9 | (b) (4) | (b) (4) |
| Osmolality | Osmometry | (b) (4) mOsmol/kg | (b) (4) | (b) (4) |
| LNP Size | Dynamic Light Scattering (DLS) | (b) (4) nm | (b) (4) | (b) (4) |
| LNP Polydispersity | Dynamic Light Scattering (DLS) | (b) (4) | (b) (4) | (b) (4) |
| RNA Encapsulation | Fluorescence assay | (b) (4) % | (b) (4) | (b) (4) |
| RNA content | Fluorescence assay | (b) (4) mg/mL | (b) (4) | (b) (4) |
| ALC-0315 content | HPLC-CAD | (b) (4) mg/mL | (b) (4) | (b) (4) |
| ALC-0159 content | HPLC-CAD | (b) (4) mg/mL | (b) (4) | (b) (4) |
| DSPC content | HPLC-CAD | (b) (4) mg/mL | (b) (4) | (b) (4) |
| Cholesterol content | HPLC-CAD | (b) (4) mg/mL | (b) (4) | (b) (4) |
| Vial content | Container Content | Not less than (b) (4) mL | (b) (4) | (b) (4) |
| Lipid identities | HPLC-CAD | Retention times consistent with references (ALC-0315, ALC-0159, Cholesterol, DSPC) | (b) (4) | 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 | | | |

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)

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) | | |

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)

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) | | |

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)

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

Genealogy Flowchart

(b) (4)



Prepared By:

(b) (6)

(b) (6)

18 Aug 2021 13:32:034-0400

REASON: I approve this document.

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(b) (6)

Approved By:

(b) (6)

(b) (6)

18 Aug 2021 12:47:028-0400

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)

FF2590 Replicates 1-3

(b) (4)



(b) (4)

