U.S. Food and Drug Administration

Center for Biologics Evaluation and Research
Laboratory Quality System

COMIRNATY (BioNTech Manufacturing GmbH) COVID-19 mRNA Vaccine

Document ID: 125742	Revision Level: 01
Revision Date: August 20, 2021	Effective Date: August 20, 2021
Total Pages: 5 (including this cover page)	

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Product Testing Plans document how CBER currently anticipates regulating licensed products including the circumstances under which CBER testing may be used to evaluate a lot of licensed product. It is the responsibility of each Product Office to develop Product Testing Plans for the licensed products under its purview.

Product Trade Name:	COMIRNATY
License Product Name (Proper Name):	COVID-19 mRNA Vaccine
Product ID (LQDB):	2501
License Number:	2229
STN (RMS-BLA):	125742
Applicant (Supplier):	BioNTech Manufacturing GmbH

Signatures Required to Approve or Update this Product Testing Plan

Product Office Director (or designee):	Marion Gruber, PhD
Product Division Director:	Jerry P. Weir, PhD
Testing Division Director:	Maryna Eichelberger, PhD
Director, DMPQ/OCBQ:	John A. Eltermann, Jr., MS, RPh
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Mode of Product Regulation

Based upon Product Office assessment of the product, including relevant manufacturing, safety, clinical and other considerations, determine which form of CBER review and or release of manufactured product lots is necessary.

Lot Release – Manufacturer may not distribute product until receiving lot-specific release from CBER.

Surveillance – Manufacturer may distribute product without lot-specific release from CBER. Manufacturer is required, according to the terms of the license, to periodically provide CBER with lot-specific testing information and possibly samples.

Exempt – Manufacturer is free to distribute product post-licensure without supplying any additional information or samples to CBER.

Lot Release	
Protocol Review	☐
Protocol Review and Confirmatory CBER Testing	☒
Alternative to Lot Release	
Surveillance	☐
Exempt	☐

Justification for Mode of Regulation:

Briefly, describe how the indicated Mode of Regulation supports CBER's mission to ensure the purity, potency, safety, efficacy, and availability of this biological product including justification for any confirmatory CBER product testing, per 21 CFR 610.2(a). Additionally, for products on Surveillance, summarize the requirements for submission of lot-specific information and sample (if required) as described in the license.

Brief Description: COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) in individuals 16 years of age and older.

COMIRNATY is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of COMIRNATY contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the COMIRNATY also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

COMIRNATY does not contain a preservative. The vial stoppers are not made with natural rubber latex.

Dosage and Administration: COMIRNATY multiple dose vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative (prior to dilution). Each vial must be thawed and diluted prior to administration.

Dilution

- Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP to form COMIRNATY. Do not add more than 1.8 mL of diluent.
- ONLY use 0.9% Sodium Chloride Injection, USP as the diluent. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- After dilution, 1 vial contains 6 doses of 0.3 mL.

COMIRNATY is a suspension for injection. After preparation, a single dose is 0.3 mL. It is administered intramuscularly as a series of 2 doses (0.3 mL each) three weeks apart.

Mode of Lot Release: Protocol review and confirmatory CBER testing

The following discussion forms the rationale for the testing plan for release of this vaccine.

Safety and Purity – The safety and purity of the vaccine will be evaluated from information provided in the lot release protocols for tests performed on the filled vaccine and BNT162b2 drug substance. Refer to the appendices at the end of this document for a description of the items to review on the lot release protocol.

Potency and Identity – The potency and identity of the vaccine will be evaluated from information provided in the lot release protocol for tests performed on the t filled vaccine and BNT162b2 drug substance. Refer to the appendices at the end of this document for a description of the items to review on the lot release protocol.

Anticipated CBER product testing:

List laboratory evaluations to be performed at CBER.

Document ID number	Test Method	Test Specifications	Testing Frequency[1]
(b) (4), (b) (5), (b) (7)(E)			

NOTE: Testing will be added as testing methods are brought on-line.

Lot Testing algorithm(s):

For each Test Method listed above describe how the indicated frequency of testing supports the assurance of product quality.

For each method with testing frequencies other than 100%, describe how lots are pre-selected for testing, i.e. random number table, every n^{th} lot submitted, first X lot(s) submitted per time period, decision tree, etc.

[1] Testing may be performed any time an atypical observation is made during lot release protocol review.

[2] The (b) (5), (b) (7)(E) lots received, then (b) (5), (b) (7)(E)

Conditions anticipated to require temporary over-ride of algorithm:

Specify conditions justifying algorithm over-ride; i.e. Public Health Considerations (e.g. temporary product shortage, sudden increase in demand), Operational Considerations (e.g. temporary unavailability of resources), Lot-specific Compliance Considerations (e.g. questions raised during lot release protocol review).

- Public Health Considerations (e.g., temporary product shortage, sudden increase in demand)
- Operational Considerations (e.g., temporary unavailability of resources
- Lot-specific Compliance Considerations (e.g., questions raised during lot release protocol review)

Specifications for Review of Lot Release Protocols

Note: **The LRS code – Action/Test** indicates under which category this test result will be reviewed. All tests included in this category for the division indicated will be reviewed and found acceptable prior to protocol sign off for this category.

Appendix 1: Specifications for tests on Filled Vaccine

Test	Specifications	LRS code - Action/Test
These tests are reviewed by personnel in Division of Biological Standard and Quality Control (DBSQC)		
Appearance	White to off-white suspension	Appearance/Volume
Appearance (Visible Particulates)	May contain white to off-white opaque amorphous particles	Appearance/Volume
Subvisible Particles	(b) (4)	Appearance/Volume
pH	6.9 - 7.9	Chemical Assay
Osmolality	(b) (4)	Chemical Assay
Lipid nanoparticles (LNP) Size		LNP
LNP Polydispersity		LNP
RNA Encapsulation		RNA content/encapsulation
RNA content		RNA content/encapsulation
ALC-0315 content		Lipid content/identity
ALC-0159 content		Lipid content/identity
DSPC content		Chemical Assay
Cholesterol content		Chemical Assay
Vial content		Appearance/Volume
Lipid identities	Retention times consistent with references (ALC-0315, ALC-0159, Cholesterol, DSPC)	Lipid content/identity
Identity of encoded RNA sequence	(b) (4)	Identity
In Vitro Expression		In vitro expression
RNA Integrity		RNA integrity
Bacterial Endotoxin		Purity-LAL
Sterility	No growth observed	Sterility

Appendix 2: Specifications for tests on BNT162b2 Drug Substance		
Test	**Specifications**	**LRS code - Action/Test**
These tests are reviewed by personnel in DBSQC		
Clarity	(b) (4)	Appearance/Volume
Coloration		Appearance/Volume
pH		Chemical Assay
Content (RNA Concentration)		RNA content/encapsulation
Identity of Encoded RNA Sequence		Identity
RNA Integrity		RNA integrity
5'- Cap		(b) (4)
Poly(A) Tail		
Residual DNA Template		Residual nucleic acid
Residual dsRNA		Residual nucleic acid
Bacterial Endotoxin		Purity-LAL
Bioburden		Sterility

Changes since the last revision

- N/A New document