Application Information	
BLA/NDA or Efficacy Supplement STN#	125742/45
Proprietary Name: ***NOTE**: If a primary and alternate are proposed, specify both names, identifying which is primary and which is alternate*	COMIRNATY
Established/Proper Name:	COVID-19 Vaccine, mRNA
Dosage Form/Strength, if applicable:	Suspension for injection. After preparation, a single dose is 0.3 mL (30 mcg).
Applicant:	BioNTech Manufacturing GmbH
License No.:	2229 (active)
If foreign applicant, is a U.S. Agent identified?	Yes
Date of Application:	December 16, 2021
Date of Receipt:	December 16, 2021
Date clock started after Refusal to Accept for Filing (UN):	N/A
PDUFA Goal Date:	June 17, 2022
Date of Filing Meeting:	January 31, 2022
Filing Date:	February 14, 2022
Proposed indication(s)/Proposed change(s):	**Initial licensed indication:** 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. **Proposed indication:** 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 **12** years of age and older.
Submission Type: *Refer to the CDER web site for more information on 505(b)(2) assessments.*	*Indicate by using **Bold** the type of submission*: BLA NDA **Efficacy Supplement**
Review Classification:	*Indicate by using **Bold** the type of review classification*
	Standard
	Priority
	Resubmission after withdrawal

Application Information	
	Resubmission after refuse to file
Part 3 Combination Product? ***Note 1:*** *Verify whether the applicant accurately designated the product as a combination product or not. If designated as a combination product, verify whether the type selected (e.g., CPN, CP1, CP2, etc.) is accurate. If RPM disagrees with the applicant's designation or the type of combination, consult with the file Chair and appropriate management and notify the applicant immediately of CBER's assessment and request a corrected form 356h.*	*If yes, indicate by using **Bold** which type of combination product and contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults (if applicable).* ***Note 2*** *: Notification of OCP should only be done after verification and applicant notification as explained in Note 1.*
	CPN - Not a Part 3 Combination Product
	CP1 - Convenience Kit of Co-package
	CP2 - Prefilled Drug Delivery Device/System (syringe, patch, etc.)
	CP3 - Prefilled Biologic Delivery Device/System (syringe, patch, etc.)
	CP4 - Device Coated/Impregnated/Otherwise Combined with Drug
	CP5 - Device Coated/Otherwise Combined with Biologic
	CP6 - Drug/Biologic Combination
	CP7 - Separate Products Requiring Cross-Labeling
	CP8 - Possible Combination Based on Cross Labeling or Separate Products
	CP9 - Other Type of Part 3 Combination Product (e.g. Drug/Device/Biologic Product)
What is the Application Type?	*Indicate the type by using **Bold***
	Fast Track
	Rolling Review
	Orphan Designation (for this indication)
	Rare disease
	Breakthrough Therapy Designation
	Triggers PREA
	Other:
PMR response:	*Indicate by using **Bold** the type of PMR response*
	FDAAA [505(o)]

Application Information	
	PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)]
	Accelerated approval confirmatory studies [21 CFR 314.510/21 CFR 601.41]
	Animal rule postmarketing studies to verify clinical benefit and safety [21 CFR 314.610/21 CFR 601.42]
PMC response:	*Indicate by using **Bold** the type of PMC response*
	Clinical Safety [506B PMC]
	Clinical Efficacy [506B PMC]
	Clinical Pharmacology [506B PMC]
	Non-Clinical Toxicology [506B PMC]
	CMC or Stability related [non-506B PMC]
Has the Office PMR/PMC Coordinator been notified that submission is in response to PMC or PMR?	*Indicate by using **Bold** either yes or no.* **Yes** No
Was either an Environmental Assessment or Claim of Categorical Exclusion included (refer to Job Aid 910.20 for more information)?	*Indicate by using **Bold** either yes or no.* **Yes** No Note: Included in STN 125742/45.1 submitted January 28, 2022.
List referenced IND Number(s):	

IS THE APPLICATION FILEABLE? _X_ Yes / ___ No

If the application is not fileable from the RPM perspective, state the rationale for your recommendation and provide letter ready comments to be sent to the Applicant in the refuse to file letter.

Rationale:

Please also identify and list any potential review issues in letter ready comment format to be forwarded to the Applicant in the filing letter or the Deficiency Identified (DI) letter (74-day letter).

Table 1: Goal Dates/ Product Names/ Classification Properties

	Goal Dates/ Product Names/ Classification Properties	YES	NO	NA	Comment
1.	PDUFA and Action Goal dates correct in tracking system?	✓			
2.	Is there a formal communication plan? Have the dates been captured in the appropriate regulatory system?		✓		
3.	Are the proprietary, established/proper, and applicant names correct in tracking system?	✓			
4.	Is the review schedule standard or priority (S or P) and are all classifications/properties entered in the appropriate regulatory system (e.g., workload management, review schedule, STN characteristics)? If unable to make corrections, contact CBERRIMS@fda.hhs.gov	✓			Priority

Table 2: Application Integrity Policy

	Application Integrity Policy	YES	NO	NA	Comment
5.	Is the application affected by the Application Integrity Policy (AIP)? ***Check the AIP list at:*** https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/application-integrity-policy **If yes**, explain in comment column and discuss with immediate supervisor.		✓		
6.	**If affected by AIP**, has DMPQ & BiMo been notified of the submission? **If yes,** date notified:			✓	

Table 3: User Fees
SOPP 8406 CBER Processing of PDUFA Application Payments

	User Fees	
7.	Is Form 3397 (User Fee Cover Sheet) included with authorized signature? *[See SOPP 8406 for details on which products require a coversheet].*	*Indicate by using* ***Bold***
		YES
		NO
		N/A
		Comment
8.	Is the applicant attempting to **redeem** a priority review voucher with this application? ***Notify*** *CBERPDUFAStaff@fda.hhs.gov* ***to confirm payment of priority review voucher fee.*** ***NOTE****: If the applicant is requesting to receive a priority review voucher, see Table 12.*	No
9.	**User Fee Status** ***Verify payment status with*** *CBERPDUFAStaff@fda.hhs.gov*. ***If a user fee is required and it has not been paid, the application is unacceptable for filing following a 5-day grace period. Review stops. Send Unacceptable for Filing (UN) letter and contact user fee staff [See SOPP 8406].*** ***Note****: CBER PDUFA Staff will monitor arrears status daily and proactively alert affected Offices that applications and supplements should not be received if a firm is in arrears.*	*Indicate the payment for this application by using BOLD:*
		Paid
		Exempt (orphan, government)
		Waived (e.g., small business, public health)
		Not required

Format and Content

Table 4: Overall Format/Content

	Overall Format/Content	YES	NO	NA	Comment
10.	Does electronic submission follow the eCTD guidance? *Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* **If not,** explain (e.g., waiver granted).	✓			
11.	**Index:** Does the submission contain an accurate comprehensive index? (e.g., table of contents)	✓			
12.	Is the submission complete as required under 21 CFR 314.50 (*NDAs/NDA efficacy supplements*) or under 21 CFR 601.2 (*BLAs/BLA efficacy supplements*) including: ** RTF issues, a "No" means the application is unacceptable for filing*. **If any of the following are "no"**, explain why (i.e., datasets are not in correct format)				
a.	• Legible*	✓			
b.	• English* (or translated into English)	✓			
c.	• Pagination	✓			
d.	• Navigable hyperlinks* (electronic submissions only)	✓			
e.	• Datasets present in software compatible format*	✓			
f.	• All sections are present*	✓			

	Overall Format/Content	YES	NO	NA	Comment
13.	Companion application received if a shared or divided manufacturing arrangement (***BLA only***) or, cross-reference to Master File received for proprietary information not included with submission. If yes, insert companion application BLA # or cross-referenced Master File # ***If missing, this may be a Refuse to file issue, discuss with review team and management.***			✓	

Table 5: Applications in The Program (PDUFA)

	Applications in The Program (PDUFA)	YES	NO	NA	Comment
14.	Were there agreements made at the applicant's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application?		✓		
15.	• If so, were the late submission components all submitted within 30 days? List any late submission components which arrived after 30 days in the comments box. ***(This is an RTF issue, discuss with review team and management.)***			✓	

Forms and Certifications

16. ***Electronic*** *forms and certifications with electronic signatures (scanned, digital, or electronic) are acceptable.* ***Forms*** *include user fee cover sheet (3397), application form (356h), financial disclosure (3454/3455), and clinical trials (3674);* ***Certifications*** *include: debarment certification and pediatric certification on Pediatric Plan for waived or deferred Pediatric studies.*

Table 6: Application Form

	Application Form	YES	NO	NA	Comment
17.	Is form FDA 356h included with authorized signature per 21 CFR 601.2(a) (BLAs) or per 21 CFR 314.50(a) (NDAs)?	✓			
18.	If foreign applicant, has a U.S. agent signed the form [see 21 CFR 314.50(a)(5)]?	✓			BioNTech Manufacturing GmbH is the foreign applicant and the U.S. Agent, Amit Patel, Pfizer, Inc. signed the form.
19.	Is a comprehensive and readily located list of all clinical sites listed on the form or attached to the form?	✓			Included in section 5.2
20.	Are all establishments and manufacturing facilities, along with their registration numbers, listed on the form or attached to the form?	✓			

Table 7: Financial Disclosure

	Financial Disclosure	YES	NO	NA	Comment
21.	Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)? ***Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].*** ***Note:*** *Financial disclosure is required for bioequivalence studies that are the basis for approval.*	✓			The Phase 1/2/3 study C4591001 was conducted by Pfizer; therefore, Pfizer submitted the forms 3454 and 3455 signed by (b) (6) (b) (6) (Pfizer).

Table 8: Clinical Trials Database and Study Data

	Clinical Trials Database & Study Data	YES	NO	NA	Comment
22.	Is form FDA 3674 included with authorized signature? ***If yes, ensure that the application is also coded with the supporting document category, "Certification Form 3674."*** ***If no, ensure that language requesting submission of the form is included in the STN Assignment Application letter (also called the Acknowledgement Letter).***	✓			In form 3674, Pfizer checked box C in item 9 – Certification Statement.
23.	Are National Clinical Trial (NCT) Numbers included on 3674? ***If yes, enter in the appropriate regulatory tracking database (RMS/BLA).*** ***If no, request in either the Filing or Filing Issues (also called the Deficiencies Identified (DI)) letters. The NCT numbers will be referenced in the final action letter.***	✓			NCT04368728 (Study C4591001)
24.	Determine if Study Data Tabulation Model (SDTM), Analysis Data Model (ADaM) data, Standard for Exchange of Nonclinical Data (SEND) or CTD datasets – Module 4 or Module 5 are present. ***If yes, refer to*** *CBER JA 900.18: Study Data Validation* Process. ***Note****: The Data Standards Representative will email the validation reports to the RPM upon completion. The email and validation reports should be attached to the filing checklist when uploading to the CER.*	✓			Please see attached email and validation reports.

	Clinical Trials Database & Study Data	YES	NO	NA	Comment
25.	Is study data acceptable based on the validation reports? ***Refer to CBER JA 900.18: Study Data Validation Process.*** ***Note 1****: If there are errors, collaborate with discipline reviewer(s) and the CDISC representative to draft an information request for minor corrections or a refuse to file letter as appropriate.* ***Note 2****: Review decision regarding acceptance of data should be documented in the filing review checklist or memo and in the discipline reviewer's review memo.*	✓			An IR regarding the datasets was sent to the applicant on January 19, 2022. However, the response will not preclude the submission from being fileable. STN 125742.45.2 was received on 2/2/22 in response to the dataset IR.

Table 9: Debarment Certification

	Debarment Certification	YES	NO	NA	Comment
26.	Is a correctly worded Debarment Certification included with authorized signature? ***Certification is not required for supplements if the debarment certification was submitted in the original application. If foreign applicant, both the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].*** ***Note:*** *Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e.,"[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application..." Applicant may* ***not*** *use wording such as, "To the best of my knowledge…"*	✓			

Table 10: Exclusivity

	Exclusivity	YES	NO	NA	Comment
27.	Does another product (same active moiety) have orphan exclusivity for the same indication? ***Check the Orphan Drug Designations and Approvals list at:*** *http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm* ***If yes, consult CBER Jurisdiction Officer.*** ***See Jurisdiction intranet site for current CBER contact:*** ***http://inside.fda.gov:9003/cber/officeofthedirector/associatedirectorforqualityassurance/ucm023543.htm***		✓		
28.	If another product has orphan exclusivity, is the product considered to be the same product according to the orphan drug definition of sameness [see 21 CFR 316.3(b)(13)]? ***If yes, consult CBER Jurisdiction Officer.*** ***See Jurisdiction intranet site for current CBER contact:*** *http://inside.fda.gov:9003/cber/officeofthedirector/associatedirectorforqualityassurance/ucm023543.htm*			✓	

	Exclusivity	YES	NO	NA	Comment
29.	Has the applicant requested **reference product designation and** 12-year exclusivity? ***(Applies to first licensed product under section 351(a) for Original BLAs/BLA supplements only, request protects against biosimilar applications under 351(k)(7))*** ***If yes, refer to*** *JA 900.11 Determining Exclusivity Period of Reference Product Based on First Licensure Date* ***for procedures and alert CMC reviewer.***	✓			The applicant has requested umbrella exclusivity to this supplemental BLA for COMIRNATY.
30.	Has the applicant requested pediatric exclusivity under BPCA? ***If yes, email CBER Pediatric Exclusivity Board RPM at:*** *CBERIOD-PEB@fda.hhs.gov*		✓		

Table 11: Priority Review Voucher Requests

	Priority Review Voucher Requests	YES	NO	NA	Comment
31.	Has the applicant requested a priority review voucher? ***If yes, notify:*** *CBERVoucherNotifications@fda.hhs.gov* ***that a voucher request has been received and select the type below?*** ***Note****: Contact your Office BPS representative for additional review process guidance.*		✓		
32.	**Rare pediatric disease**		✓		
33.	**Material Threat Medical Counter Measures (MCM)**		✓		
34.	**Tropical disease**		✓		

Table 12: Pediatrics

	Pediatrics	YES	NO	NA	Comment
35.	**Pediatric Research Equity Act (PREA)** Does the application trigger PREA? *BLAs/efficacy supplements for new active ingredients, new indications (not change of age range only), new dosage forms, new dosing regimens, or new routes of administration trigger PREA.*		✓		
	a. If yes, has the applicant included or referenced the agreed upon pediatric study plan (PSP)? This should have been submitted at least 210 days prior to submission of this application. [*See JA851.05 Instructions for Processing PSPs.*] If no agreed PSP is included or referenced in the submission, consider RTF. Discuss with your Supervisor.			✓	
	b. If yes, has the applicant submitted the pediatric assessment, or provided documentation requesting either a waiver and/or deferral in accordance with their agreed PSP? ***Note 1: All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.*** ***Note 2: If the applicant deviated from their agreed PSP discuss with Supervisor and Office representative to CBER Pediatrics Working Group.*** ***Note 3: Pediatric items are looked at by both the RPM and the Clinical Reviewer.***			✓	

	Pediatrics	YES	NO	NA	Comment
36.	Does the submission include a pediatric assessment in response to a deferred Pediatric study? ***All pediatric assessment studies must be reviewed by PeRC prior to approval of the supplement.***	✓			This supplement includes the pediatric assessment for children 12 through 15 years of age as described in PMR #1 of the August 23, 2021 approval letter for the original COMIRNATY BLA. *PMR #1: Deferred pediatric Study C4591001 to evaluate the safety and effectiveness of COMIRNATY in children 12 years through 15 years of age.*

Table 13: Proprietary Name

	Proprietary Name	YES	NO	NA	Comment
37.	Is a proposed proprietary name submitted? ***If yes, ensure that PNR is selected for this submission in the regulatory system.*** ***If no, include missing PNR in an information request.*** *[See SOPP 8001.4: Review of Proprietary Names for CBER Regulated Products and JA 910.02 Proprietary Name Review (PNR) Processing]*			✓	
a.	Are the PDUFA milestones correct for review of proprietary name?			✓	
b.	Has APLB reviewer been notified?			✓	

Table 14: REMS

	REMS	YES	NO	NA	Comment
38	Is a REMS submitted?		✓		

Table 15: Prescription Labeling-1

39.	Prescription Labeling	Check all types of labeling submitted.
a.	Package Insert (PI)	✓
b.	Patient Package Insert (PPI)	
c.	Patient Oriented Labeling (POL)	

39.	**Prescription Labeling**	Check all types of labeling submitted.
d.	Instructions for Use (IFU)	
e.	Medication Guide (MedGuide)	
f.	Carton labels	
g.	Immediate container labels	
h.	Diluent	
i.	Other (specify):	

Table 16: Prescription Labeling-2

	Prescription Labeling	**YES**	**NO**	**NA**	**Comment**
40	Is Electronic Content of Labeling (COL) submitted in SPL, PDF, and Word format? ***If no, request applicant to submit SPL and Word before the filing date.***	✓			
41	Is the PI submitted in Physicians Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR) format? ***If no, request applicant to submit labeling in corrected format (PLR and PLLR, as applicable) before the filing date.***	✓			
42	Was all labeling (e.g., PI, PPI, MedGuide, POL/IFU, carton and immediate container labels) consulted to APLB?	✓			

Table 17: Other Consults

	Other Consults	**YES**	**NO**	**NA**	**Comment**
43	Are additional consults needed? (e.g., CDER, CDRH) ***If yes, specify consult(s) and date(s) sent:***		✓		

Table 18: IND/Pre- BLA/NDA Meeting Minutes in CBER Connect

	Meeting Minutes in CBER Connect	**YES**	**NO**	**NA**	**Comment**
44.	End-of Phase 2 meeting(s)? **Date(s): _____** ***If yes, reference IND number where minutes can be found in the filing meeting agenda and summary.***		✓		

	Meeting Minutes in CBER Connect	YES	NO	NA	Comment
45.	Pre-BLA/Pre-NDA/Pre-Supplement meeting(s)? **Date(s):** 9/24/2021 and 11/12/2021 ***If yes, reference IND number where minutes can be found in the filing meeting agenda and summary. For PDUFA BLAs, check for any late components agreed upon during Pre-BLA meeting, if held, and a formal communication plan. All late components must be submitted by day 30 after the initial submission is received from the applicant.***	✓			IND 19736.434: We provided comments and advice regarding the supplemental BLA for adolescents 12 through 15 years of age on 9/24/2021 and request for shell tables on 11/12/2021.
46.	Any Special Protocol Assessments (SPAs)? **Date(s):**_____ ***If yes, reference IND number where minutes can be found in the filing meeting agenda and summary.***		✓		

Append *C 905.01.01* here, if submission contains 505(b)(2).

See 505(b)(2) Regulatory Program more information on 505(b)(2) and append *C 905.01.01: RPM FILING REVIEW CHECKLIST FOR 505(b)(2) APPLICATIONS (NDA and NDA Supplements only)* here prior to filing review.

RPM FILING REVIEW CONCURRENCE

Application number: STN 125742/45

Laura Gottschalk — Laura B. Gottschalk -S 2022.02.07 07:41:50 -05'00' — 2/7/2022

RPM — Date

Michael Smith — Michael J. Smith -S4 — Digita ly s gned by Michael J Sm th S4 DN c=US o=U S Government ou=HHS ou=FDA ou=People 0 9 2342 19200300 100 1 1=0014080934 cn=Michael J Sm th S4 Date 2022 02 07 07 59 10 05'00' — 2/7/2022

RPM — Date

I concur with the reviewers recommendation? _X_ Yes / ___ No If no, provide a justification.

Elizabeth Sutkowski — Elizabeth M. Sutkowski -S — Digitally signed by El zabeth M Sutkowski S DN c=US o=U S Government ou=HHS ou=FDA ou=People 0 9 2342 19200300 100 1 1=1300076199 cn=Elizabeth M Sutkowski S Date 2022 02 07 12 00 37 05 00' — 2/7/2022

Branch Chief — Date

I concur with the reviewer(s) recommendation? _X_ Yes / ___ No If no, provide a justification.

Loris McVittie — Loris D. Mcvittie -S — Digitally signed by Loris D. Mcvittie -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300064781, cn=Loris D. Mcvittie -S Date: 2022.02.07 14:06:18 -05'00' — 2/7/2022

Division Director (or equivalent second line supervisor) — Date