Application Information	
BLA STN#	125742/0
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 mRNA Vaccine
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
If foreign applicant, is a U.S. Agent identified?	Yes
Date of Application:	May 18, 2021
Date of Receipt:	May 18, 2021
Date clock started after Refusal to Accept for Filing (UN):	N/A
PDUFA Goal Date:	January 16, 2022
Action Goal Date (if different):	September 30, 2021
Date of Filing Meeting:	June 29, 2021
Filing Date:	July 17, 2021
Proposed indication:	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.
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
	Resubmission after refuse to file

Application Information	
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)]
	PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)]

Application Information	
	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 **N/A**
List referenced IND Number(s):	IND 19736 & EUA 27034

IS THE APPLICATION FILEABLE? _X_ Yes / ___ No

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?		✓		Non-standard approach (e.g., a Mid-Cycle Communication will be scheduled, but a Late-Cycle Meeting will not be scheduled). Other typical ad-hoc interactions that occur during the review process will occur.
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	✓			BLA is a priority review.

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.		✓		

	Application Integrity Policy	YES	NO	NA	Comment
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:* **User Fee Paid: $2,875,842.00**
		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.***			✓	Cross-reference letters to authorize review information regarding vials and stoppers: IND 19736, DMF 012683, DMF 9543, DMF 15209, DMF 011793, DMF 011820, DMF 011321, DMF 10953

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?	✓			Strain sequence analysis of all COVID-19 cases will be provided by June 7, 2021.
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.)***	✓			Submitted in amendment 5 (sequence 0006) dated June 7, 2021.

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, Elisa Harkins, 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?	✓			Lists of clinical sites are included in section 5.3.5.1 for each individual study under APPENDICES. Also, sites are listed in FDA form 3454 in section 1.3.4.
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 form 3454 (page 1) signed by J. R. Meloro (Pfizer). The Phase 1/2 study BNT162-01 was conducted by BioNTech SE; they also submitted the form 3454 signed by Dr. Christopher Marshallsay (page 78).

Table 8: Clinical Trials Database and Study Data

	Clinical Trials Database & Study Data	YES	NO	NA	Comment
	Is form FDA 3674 included with authorized signature? If yes, ensure that the application is also coded with the supporting document category, "C***ertification 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).***	✓			

	Clinical Trials Database & Study Data	YES	NO	NA	Comment
22.	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), and NCT04380701 (Study BNT162-01) are entered in RMS-BLA
23.	Determine if Study Data Tabulation Model (SDTM), Analysis Data Model (ADaM) data, Standard for Exchange of Nonclinical Data (SEND) or CTD datasets - Module 5 are present. ***If yes, notify CBER's Clinical Data Interchange Standards Consortium (CDISC) representative and request that a CDISC format validation be performed. Email*** *CBER.CDISC@fda.hhs.gov.* ***Note****: CDISC will email validation reports to the RPM upon completion for upload to the EDR.* ***Refer to*** *CBER JA 900.18: Study Data Validation Process****.***	✓			

	Clinical Trials Database & Study Data	YES	NO	NA	Comment
24.	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.*	✓			Dataset validation will not be done for this BLA. The included datasets are the same as those in the EUA amendment for adolescents 12 through 15 years of age, which were validated during the review of the EUA 27034 amendment 132.

Table 9: Debarment Certification

	Debarment Certification	YES	NO	NA	Comment
25.	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
26.	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***		✓		
27.	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*			✓	
28.	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.***	✓			

	Exclusivity	YES	NO	NA	Comment
29.	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
30.	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****: Follow the job aid and complete the checklist for the voucher type requested (see links below).*		✓		
31.	**Rare pediatric disease (RPD)** Follow: JA900.19 RPD PRV C900.03 RPD PRV Eligibility Checklist		✓		
32.	**Material Threat Medical Counter Measures (MCM)** Follow: JA900.20 MTMCM PRV C900.01 MTMCM PRV Eligibility Checklist		✓		
33.	**Tropical disease (TD)** Follow: JA900.21 TD PRV C900.02 – TD PRV Eligibility Checklist		✓		

Table 12: Pediatrics

	Pediatrics	YES	NO	NA	Comment
34.	**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.*	✓			

	Pediatrics	YES	NO	NA	Comment
	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.***	✓			
35.	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.***		✓		

Table 13: Proprietary Name

	Proprietary Name	YES	NO	NA	Comment
36.	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
37	Is a REMS submitted?		✓		

Table 15: Prescription Labeling-1

38.	Prescription Labeling	Check all types of labeling submitted.
a.	Package Insert (PI)	✓
b.	Patient Package Insert (PPI)	
c.	Patient Oriented Labeling (POL)	
d.	Instructions for Use (IFU)	
e.	Medication Guide (MedGuide)	
f.	Carton labels	✓ (BLA includes 25- and 125-dose carton labels for both Puurs and Kalamazoo packaging sites).
g.	Immediate container labels	✓ (BLA includes vial labels for both Puurs and Kalamazoo packaging sites).
h.	Diluent	✓
i.	Other (specify):	

Table 16: Prescription Labeling-2

	Prescription Labeling	YES	NO	NA	Comment
39	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.***	✓			

	Prescription Labeling	YES	NO	NA	Comment
40	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.***	✓			
41	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
42	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 the EDR

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

	Meeting Minutes in the EDR	YES	NO	NA	Comment
44.	Pre-BLA/Pre-NDA/Pre-Supplement meeting? **Date: 4/16/2021** ***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: We provided feedback regarding clinical/nonclinical questions on March 9, 2021 and provided feedback regarding CMC/facilities questions on March 31, 2021. During the 4/16/2021 teleconference, we discussed all the unresolved issues related to both clinical and CMC/facilities disciplines.
45.	Any Special Protocol Assessments (SPAs)? ***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: http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499 for 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. Access C 905.01.01 here: https://fda.sharepoint.com/sites/CBER-Review-Resources/SOPPsJAsTemplatesOther_References/C-905.01.01.docx

RPM FILING REVIEW CONCURRENCE

Application number: STN 125742/0

Laura B. Gottschalk -S
2021.06.30 14:01:34 -04'00'

Michael J. Smith -S4
Digitally signed by Michael J. Smith -S4
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1400480934, cn=Michael J. Smith -S4
Date: 2021.06.30 14:37:09 -04'00'

06/30/2021

RPMs (Laura Gottschalk and Mike Smith) Date

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

Elizabeth M. Sutkowski -S
Digitally signed by Elizabeth 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: 2021.06.30 20:36:26 -04'00'

06/30/2021

Branch Chief Date

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

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: 2021.07.01 11:05:07 -04'00'

07/01/2021

Division Director (or equivalent second line supervisor) Date