DATE: June 10, 2022

FROM: Kanaeko R. Ravenell, MS
Bioresearch Monitoring Branch (BMB)
Division of Inspections and Surveillance (DIS)
Office of Compliance and Biologics Quality (OCBQ)

THROUGH: Dennis Cato, Chief, BMB Dennis Cato -S Digitally signed by Dennis Cato -S Date: 2022.06.10 11:55:14 -04'00'

THROUGH: Carrie M. Mampilly, MPH, Director, DIS Carrie M. Mampilly -S Digitally signed by Carrie M. Mampilly -S Date: 2022.06.10 12:22:08 -04'00'

TO: Ramachandra Naik, PhD, Committee Chair
Susan Wollersheim, MD, Clinical Reviewer
Laura Gottschalk, PhD, RPM
Michael Smith, PhD, RPM

SUBJECT: Bioresearch Monitoring Final Discipline Review

SPONSOR: BioNTech Manufacturing GmbH
PRODUCT: COVID-19 mRNA vaccine (nucleoside modified) COMIRNATY
sBLA: STN 125742/45

FINAL SUMMARY STATEMENT:
Bioresearch Monitoring (BIMO) inspections were issued for three US clinical investigators who participated in the conduct of protocol C4591001. The inspections did not reveal substantiative issues that impact the data submitted in this supplemental Biologics License Application (sBLA).

BACKGROUND:
Three US clinical study sites for protocol C4591001 were identified for BIMO inspections. The sBLA review committee concurred with the proposed sites. The sites were selected based upon sponsor-reported adverse events, protocol deviations, total number of subjects enrolled, and previous BIMO inspection histories. The inspections were conducted in accordance with FDA's Compliance Program (CP) 7348.811, Inspection Program for Clinical Investigators. Information submitted in the sBLA was compared to source documents at each inspected site. The inspection assignment also included specific questions concerning the clinical study.

PROTOCOL:
Protocol C4591001: *A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals*

This supplement and the included data only encompass the phase 2/3 portion of the protocol for vaccine BNT162b2 that is indicated for adolescents 12 through 15 years of

age. Approximately 2260 subjects were randomized so that an equal number of participants received the vaccine and the placebo. At Visits 1 and 2, participants were vaccinated with either a single 30 µg dose of BNT162b2 or placebo, approximately 21 days apart. Follow-up visits were conducted at one and 6 months. Participants that were originally assigned to the placebo group, who become eligible for receipt of BNT162b2, were given the opportunity to receive the vaccine at the 6-month visit.

BIMO INSPECTIONS SUMMARY:

No significant BIMO inspectional findings were noted. The below table summarizes site information and outcomes from the BIMO inspections:

Site ID	Firm Name	Location	FDA Form 483 Issued	Final Classification*
1039	Gretchen Crook, M.D.	Austin, TX	No	NAI
1140	Stephen Thomas, M.D.	Syracuse, NY	No	NAI
1156	Hector Rodriguez, M.D.	Miami, FL	No	NAI

*No Action Indicated (NAI)

SPONSOR MONITORING ISSUES:

No significant sponsor or monitoring issues were identified during the above inspections.

FINANCIAL DISCLOSURE:

The Clinical Investigator Compliance Program directs the FDA investigator to ask the clinical investigator if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouse(s), and dependent children, as well as if and when the information was updated. The information submitted to the sBLA was verified for each of the inspected clinical study sites.

ADMINISTRATIVE FOLLOW-UP

Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at (240) 402-8423.

Kanaeko R. Ravenell -S

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Date: 2022.06.10 16:14:31 -04'00'

Kanaeko R. Ravenell, MS
Consumer Safety Officer

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Ramachandra Naik
Susan Wollersheim
Laura Gottschalk
Michael Smith
Carrie Mampilly
Dennis Cato
ChronFile
cberbimonotification@fda.hhs.gov