U.S. FOOD & DRUG ADMINISTRATION

MARCH MONTHLY MEETING SUMMARY

Application number:	BLA STN 125742/45
Product name:	COVID-19 Vaccine, mRNA (COMIRNATY)
Proposed Indication:	Active immunization to prevent coronavirus disease 19 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older
Applicant:	BioNTech Manufacturing GmbH
Meeting date & time:	March 2, 2022; 1:00 - 2:00 PM EST
Committee Chair:	Ramachandra Naik, Ph.D.
Meeting Recorders:	CAPT Michael Smith, Ph.D. and Laura Gottschalk, Ph.D.

1. Background

COMIRNATY (COVID-19 Vaccine, mRNA) was originally approved on August 23, 2021, for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older. The current application, received on December 16, 2021, is an efficacy supplement from BioNTech Manufacturing GmbH (in partnership with Pfizer, Inc.) for COMIRNATY to extend the indication to adolescents 12 through 15 years of age.

The purpose of this meeting was to discuss the progress of the review, identify and present any issues, and plan the remainder of the review, including dates for further deliverables and interactions.

Table 1: Review Committee (meeting attendees are in bold font)

Review Responsibility	Committee Member	Team Leader/Supervisor	Division Director (and DDD)
Chair	**Ramachandra Naik, PhD**	BC: Elizabeth Sutkowski, PhD	**DD: Loris McVittie, PhD** **SA: Kirk Prutzman, PhD**
Regulatory Project Managers	**CAPT Mike Smith, PhD** **Laura Gottschalk, PhD**	BC: Elizabeth Sutkowski, PhD	**DD: Loris McVittie, PhD** **SA: Kirk Prutzman, PhD**
Clinical	**Susan Wollersheim, MD**	**TL: Lucia Lee, MD** BC: Maria Allende, MD	**DD: Doran Fink, MD, PhD** SA: Rebecca Reindel, MD **Douglas Pratt, MD**
DVP – CMC	**Xiao Wang, PhD**	LC: Keith Peden, PhD **Cc: Anissa Cheung, MSc**	DD: Jerry Weir, PhD **DDD: Robin Levis, PhD**
Statistics – Clinical (Immunogenicity and Safety)	**Ye Yang, PhD**	**TL: Lei Huang, PhD** **BC: Tsai-Lien, PhD**	**DD: John Scott, PhD** **DDD: Shiowjen Lee, PhD**
Epidemiological/Pharmacovigilance	**Deborah Thompson, MD, MSPH**	**BC: Manette Niu, MD**	**DD: Narayan Nair, MD** **DDD: Meghna Alimchandani, MD**

Benefit-Risk Assessment Real World Evidence	**Hong Yang, PhD** Osman Yogurtcu, PhD **Patrick Funk, PhD** **Yun Lu, PhD**	**Sup: Richard Forshee, PhD** **Sup: Richard Forshee, PhD**	
BIMO	**Kanaeko Ravenell** **Char-Dell Edwards**	**BC: Dennis Cato**	DD: Carrie Mampilly, MPH
APLB Labeling	**CAPT Oluchi Elekwachi, PharmD, MPH**	**BC: Lisa Stockbridge, PhD**	DD: Robert Sausville
CDSIC Consult	Brenda Baldwin, PhD	BC: Elizabeth Sutkowski, PhD	**DD: Loris McVittie, PhD** **SA: Kirk Prutzman, PhD**

Additional attendees: Karen Farizo, Theresa Finn and Hector Izurieta

Review Timetable (PDUFA Milestones are in blue)

Review Milestone	**Target Due Date**
Submitted:	16-DEC-2021
Received:	16-DEC-2021
Committee Assignment:	30-DEC-2021
First Committee Meeting:	06-JAN-2022
Filing reviews complete:	25-JAN-2022
Confirm BIMO (GCP) Inspection Sites	30-JAN-2022
Filing Meeting:	31-JAN-2022
Filing Action:	14-FEB-2022
Deficiencies Identified:	28-FEB-2022
Primary Draft Reviews & Reviewer Reports Due (4 days prior to Mid-Cycle meeting):	31-MAR-2022
Mid-Cycle Meeting (Internal):	06-APR-2022
Notify Safety Working Group (SWG)	18-APR-2022
PeRC Briefing materials due:	19-APR-2022
PeRC Meeting:	03-MAY-2022
Labeling Comments to Applicant:	18-MAY-2022
Final draft primary reviews with supervisory Concurrence (upload not required):	18-MAY-2022
Notify OCOD of pending approval:	18-MAY-2022
Notify Applicant of PMC/PMR:	18-MAY-2022
Final reviews & addenda signed & uploaded:	12-JUN-2022
PDUFA ADD:	**17-JUN-2022**

Table 2: Scheduled Meetings

PDUFA Meetings:
First Committee Meeting: January 6, 2022 (by email)
Filing Meeting: January 31, 2022, 12:00PM – 1:00PM
Internal Mid-Cycle: April 6, 2022, 1:00PM-2:30PM
Monthly Committee Meetings:
March 2, 2022; 1:00 – 2:00 pm
May 17, 2022; 3:00 – 4:00 pm
Labeling Meetings:

April 8, 2022 (w/o MGMT); 12:30 – 2:00 pm
April 11, 2022 (w/o MGMT); 1:00 – 3:00 pm
April 20, 2022; 2:00 – 4:00 pm
April 21, 2022; 3:00 – 5:00pm
May 3, 2022; 3:00 – 5:00pm
May 11, 2022; 2:00 – 4:00pm

2. Discussion Topics

2.1 Opening remarks from the Chair and RPMs

The Chair informed that the PeRC meeting is scheduled for May 3, 2022, and therefore, the PeRC materials due on April 19, 2022. He asked the reviewers to inform the regulatory team if any reviewer is planning to present the review summary at the Mid-Cycle meeting.

2.2 Review of milestones and internal/projected target dates

2.3 Status update (including any major concerns that have been identified so far) from each member of the review committee

2.3.1 Clinical (Susan Wollersheim):

The clinical review is ongoing, and two IRs are currently being drafted with the statistical reviewer. The first is regarding the immunogenicity endpoints and lower limit of quantification that was discussed briefly during the review of the EUA amendment for use of the Pfizer-BioNTech COVID-19 Vaccine in children 6 months to <5 years of age. The second IR is to address the slight differences in the solicited adverse reactions submitted for the 6-month data.

2.3.2 Statistics (Ye Yang):

The statistical review is still ongoing, and the two IRs mentioned by the clinical review are currently being drafted.

2.3.3 Benefit-Risk assessment (Hong Yang, Osman Yogurtcu and Patrick Funk):

It hasn’t been decided yet if a benefit-risk assessment will be required for this supplement. Additionally, data may not be available for this age group in BEST since it is for adolescents 12 through 15 years of age. The team will check to see if BEST data available for this age group or 17 years of age and younger and will let the rest of the review team know as soon as possible or at the Mid-Cycle meeting.

2.3.4 Real World Evidence (Yun Lu):

The reviewer noted that she will review the RWE publications that are referenced in parts of this supplement. During the review of the original

Comirnaty BLA for individuals 16 years and older, we asked the Applicant to include 12-15 years old individuals in the post-marketing safety and effectiveness studies, so this age-group has already been covered in the existing PMRs and PMCs.

2.3.5 Epidemiology/Pharmacovigilance (Deborah Thompson):
The PVP plan is currently under review and there have been no major issues identified at this time.

2.3.6 BiMO (Kanaeko Ravenell and Char-Dell Edwards):
Three clinical inspections were issued on February 17, 2022. The first will start on March 7, 2022. The due date for the inspections is April 6, 2022, and no additional inspections are anticipated for this submission.

2.3.7 CMC (Xiao Wang):
The review is ongoing with no issues identified at this time.

2.3.8 APLB (Oluchi Elekwachi):
The review is ongoing, and a draft review should be completed by March 31, 2022.

2.3.9 CDISC (Brenda Baldwin):
The CDISC reviewer was not able to attend the meeting, but no issues have been identified at this time.

3. Information Requests:

1. 01/19/2022: Three questions regarding datasets.

2. 01/25/2022: Request for an updated FDA form 356h and an Environmental Assessment or claim of Categorical Exclusion.

3. 02/23/2022: Two questions on cumulative analysis of post-authorization adverse event reports.

4. Amendments:

1. STN 125742/45.1 (01/28/2022) – Response to January 25, 2022 request regarding submitting (1) updated Form 356h to include information regarding all establishments and manufacturing facilities, and (2) an Environmental Assessment or Claim of Categorical Exclusion.

2. STN 125742/45.2 (02/02/2022) – Response to January 19, 2022 request regarding datasets.

3. STN 125742/45.3 (3/1/2022) – Response to February 23, 2022 request regarding cumulative analysis of post-authorization adverse event reports.

5. Action Items

- The clinical and stats teams will finalize their two IRs to be communicated to the Applicant.
- The benefit-risk team will check to see if there are any updated data for this age group.