FILING MEETING SUMMARY

Application number: BLA STN 125742/0
Product name: COVID-19 mRNA Vaccine (COMIRNATY)
Proposed Indication: Active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older
Applicant: BioNTech Manufacturing GmbH
Meeting date & time: June 29, 2021; 2:00 - 3:30 PM EDT
Committee Chair: Ramachandra Naik, Ph.D.
Meeting Recorders: CAPT Michael Smith, Ph.D. and Laura Gottschalk, Ph.D.

Ramachandra Naik -S
Digitally signed by Ramachandra Naik -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2001232361, cn=Ramachandra Naik -S
Date: 2021.07.26 10:58:23 -04'00'

Background:
This meeting was to discuss the new original BLA (STN 125742/0) from BioNTech Manufacturing GmbH (in partnership with Pfizer, Inc.) for COVID-19 mRNA Vaccine, for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older. This is a Rolling BLA submission. The first roll containing eCTD sections 2, 4, and 5 was submitted and received on May 6, 2021. The second and final roll containing eCTD Section 3 (and the rest of Section 1 items) was submitted and received on May 18, 2021. As agreed during the Pre-BLA interaction, the COVID-19 case strain sequencing report was submitted on June 7, 2021.

The purpose of this meeting was to discuss 1) the completeness of the BLA submission and 2) whether it is acceptable to be filed.

Table 1: Review Committee and Discipline Filing Decision Summary

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
Regulatory Project Managers (RPM)	CAPT Michael Smith, PhD Laura Gottschalk, PhD	✓ ✓	✓		
Chair	Ramachandra Naik, PhD	✓	✓		
Division Director - Clinical	Doran Fink, MD, PhD	✓	✓		
Division Director/Deputy (Acting) – Regulatory	Loris McVittie, PhD/ Kirk Prutzman, PhD	✓	✓		
Office Director/Deputy	Marion Gruber, PhD/ Philip Krause, MD, PhD	✓ ✓	✓		
Clinical Reviewers	Susan Wollersheim, MD CAPT Ann Schwartz, MD	✓ ✓	✓		
Toxicology Reviewer	Nabil Al-Humadi, PhD	✓	✓		
CMC Reviewers	Xiao Wang, PhD Anissa Cheung, MSc	✓	✓		

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
OCBQ/DMPQ Reviewers	Kathleen Jones, PhD Laura Fontan, PhD Gregory Price, PhD Zhongren Wu, PhD CDR Donald Ertel, MS Ekaterina Allen, PhD Cheryl Hulme Iryna Zubkova, PhD	✓ ✓ ✓	✓		
OCBQ/APLB Reviewers	CDR Oluchi Elekwachi, PharmD, MPH Dana Jones (Back up)	✓	✓		
OCBQ/BIMO Reviewer	Haecin Chun, MT (ASCP) SSB, MS	✓	✓		
OCBQ/DBSQC Reviewers	Hsiaoling Wang, PhD Emnet Yitbarek, PhD Karla Garcia, MS Anil Choudhary, PhD, MBA Esmeralda Alvarado, PhD Marie Anderson, PhD	 ✓ ✓ ✓ ✓	✓		
Statistical Reviewer of clinical and nonclinical data	Lei Huang, PhD	✓	✓		
Postmarketing Safety Epidemiological/ Pharmacovigilance Reviewer	Deborah Thompson, MD, MSPH	✓	✓		
Labeling Reviewer	Daphne Stewart	✓	✓		
CDISC Consult	Brenda Baldwin, PhD Kirk Prutzman, PhD		✓		

Other Attendees:
Maria Allende, Nicolette Devore, Maryna Eichelberger, John Eltermann, Karen Farizo, Theresa Finn, Sara Gagneten, Varsha Garnepudi, Dave Green, Marion Gruber, Hector Izurieta, Philip Krause, Lucia Lee, Robin Levis, Nicole Li, Carrie Mampilly, Narayan Nair, Manette Niu, Tim Nelle, Cassandra Overking, Tao Pan, Keith Peden, Lori Peters, Douglas Pratt, Joseph Quander, Carolyn Renshaw, Jeff Roberts, David Rouse, Muhammad Shahabuddin, Lisa Stockbridge, Elizabeth Sutkowski, Swati Verma and Jerry Weir

Review Timetable (PDUFA Milestones are in blue)

Review Milestone	Target Due Date
Submitted	
Roll 1 Submission:	06-MAY-2021
Roll 2 Submission (final):	18-MAY-2021
Received:	18-MAY-2021
Committee Assignment:	09-JUN-2021
First Committee Meeting:	03-JUN-2021
Filing checklist/reviews complete:	23-JUN-2021
Filing Meeting:	**29-JUN-2021**
Filing Action:	16-JUL-2021
Deficiencies Identified:	31-JUL-2021
Initial proprietary name review:	16-AUG-2021
Draft Primary Reviews & Reviewer Reports Due (4 days prior to Mid-Cycle meeting):	25-AUG-2021
Mid-Cycle Meeting (Internal):	31-AUG-2021
Mid-Cycle Communication:	13-SEP-2021
Final Draft Primary Reviews with Supervisory Concurrence (upload not required):	01-SEP-2021
PLI Inspections completed:	30-JUL-2021
BiMO Inspections completed:	30-JUL-2021
PeRC briefing materials due to PeRC:	27-JUL-2021
PeRC Meeting:	10-AUG-2021
Final reviews & addenda signed & uploaded:	15-SEP-2021
Lot release protocol & testing plan finalized:	30-AUG-2021
Notify OCOD of pending approval:	30-AUG-2021
Draft SBRA:	30-AUG-2021
Labeling Comments to Applicant:	30-AUG-2021
Notify Applicant of PMC/PMR:	30-AUG-2021
Targeted Action Due Date (ADD):	**30-SEP-2021**
PDUFA ADD:	**16-JAN-2022**

Table 2: Scheduled Meetings

PDUFA Meetings:
• **First Committee Meeting:** June 3, 2021, 4:00PM – 5:30PM
• **Filing Meeting:** June 29, 2021, 2:00PM – 3:30PM
• **Internal Mid-Cycle Meeting:** August 31, 2021, 2:00PM – 3:30PM
• **Mid-Cycle Communication:** September 13, 2021, 3:00PM – 4:00PM
Monthly Committee Meetings:
• July 15, 2021, 3:30PM – 5:00PM
• August 9, 2021, 1:30PM – 3:00PM
• September 10, 2021, 12:30PM – 2:00PM
Labeling Meetings:

• August 4, 2021, 3:00PM – 5:00PM
• August 6, 2021, 3:00PM – 5:00PM
• August 11, 2021, 3:00PM – 5:00PM
• August 16, 2021, 11:00AM – 12:30PM (Carton & Container)
• August 18, 2021, 3:30PM – 5:00PM (Carton & Container)
• September 2, 2021, 4:00PM – 5:30PM
• September 7, 2021, 2:00PM – 4:00PM
• September 21, 2021, 3:00PM – 5:00PM

DISCUSSION SUMMARY

The Chair highlighted updates that had taken place since the First Committee Meeting:

1. **No Filing Checklists are required**
   - ADRM agreed that the discipline reviewers don't need to complete the filing checklists for this BLA. However, the discipline reviewers were reminded to refer to the filing checklists to initiate the process and look for special items that should be included in the submission.
   - This exception to policy, not requiring filing checklists, is intended to help facilitate the expedient review of the application, but in no way alleviates reviewers from performing their due diligence to ensure that the application is complete for the purposes of filing.
   - Normally, major issues or IRs being drafted will be listed in Filing Checklists. However, as this is the Priority Review BLA with the short review timeline, the reviewers have already started sending IRs and inspecting the vaccine manufacturing facilities (see below for additional details).

2. **BLA License Number generated in advance of approval**
   - The Applicant requested a US License Number for BioNTech Manufacturing GmbH with agreement that they will not use it until after the BLA is approved.
   - Dr. Joneckis wrote a memo to the file authorizing release of the BLA license number in advance of the typical notification in the approval letter.
   - RIMS generated the license number which will be provided to the Applicant, after filing, in an email message.

3. **PeRC meeting is scheduled for August 10, 2021**

UPDATES FROM REVIEW DISCIPLINES:

1. **Chair** (Ram Naik):
   - See discussion summary above.

2. **Regulatory Project Managers** (Mike Smith and Laura Gottschalk):
   - The RPMs summarized the IRs and Amendments to the BLA to date (please see details at end of document).

- The BLA is fileable.
- To ensure the regulatory items were covered in the submission, the RPM Checklist was completed and will be uploaded to the file.

3. **Clinical** (Susan Wollersheim and Ann Schwartz):
    - The BLA is fileable and the clinical reviewers agree with the Priority Review designation.

4. **CMC** (Xiao Wang):
    - The BLA is fileable and no major issues have been identified that warrant discussion.
    - The CMC reviewer noted that she used the Filing Checklist during her review and no major deficiencies were identified.
    - A list of clarification Information Requests is being generated for the Applicant.

5. **DBSQC** (Hsiaoling Wang, Emnet Yitbarek, Karla Garcia, Anil Choudhary, Esmeralda Alvarado and Marie Anderson):
    - The BLA is fileable.

6. **Toxicology** (Nabil Al-Humadi):
    - The BLA is fileable.

7. **Statistics** (Lei Huang):
    - The BLA is fileable.

8. **Epidemiology/Pharmacovigilance** (Deborah Thompson):
    - The BLA is fileable.

9. **DMPQ** (Kathleen Jones, Laura Fontan, Gregory Price, Zhongren Wu, Donald Ertel, Ekaterina Allen, Cheryl Hulme and Iryna Zubkova):
    - The BLA is fileable.
    - Laura Fontan is currently in Belgium carrying out inspections of the Pfizer, Puurs facilities.
    - There will most likely be a waiver for inspections of the Pfizer, Kalamazoo site.
    - Kathleen Jones will be leading the inspections of the Pfizer, Andover site scheduled for July 19-23, 2021.

10. **BiMO** (Haecin Chun):
    - The BLA is fileable.
    - At this time, they are not planning on issuing inspections in support of this BLA (inspections of 9 clinical sites were conducted for Protocol C4590001 under the IND/EUA).

11. **APLB** (Oluchi Elekwachi):
    - The BLA is fileable.

12. **Container Labeling** (Daphne Stewart):
    - The BLA is fileable.
    - The labeling reviewer is finalizing an IR.

13. **CDISC** (Brenda Baldwin and Kirk Prutzman):
    - The BLA is fileable.
    - As previously noted, the datasets submitted with this BLA will not be validated since they were already validated under an amendment to EUA 27034.

UPDATES FROM MANAGEMENT:

1. **Advisory Committee Meeting**
    - The Office Director confirmed that, unless a significant new safety concern or other important issue is discovered during the review of the submission that would necessitate convening the VRBPAC, an Advisory Committee Meeting will not be needed for this BLA.

2. **Regular Updates to Management on Review Progress**
    - The Office Director noted that at this time, review progress updates provided during the Monthly Review Committee Meetings would suffice. This plan can be revisited during August and September to determine if more frequent updates to Managers should be provided.

REGULATORY CONCLUSIONS / DEFICIENCIES:

1. **Does the application, on its face, appear to be suitable for filing or is the application unsuitable for filing and require an RTF letter?**
   The application appears to be suitable for filing.

2. **If fileable, list any substantive deficiencies or issues that have significant impact on the ability to complete the review or approve the application**:
   No substantive deficiencies or issues have been identified that would have a significant impact on the ability to complete the review or approve the application.

3. **If RTF, list any substantive deficiencies or issues that would make this application unsuitable for filing:**
   NA

FILING MEETING DISCUSSION, IF FILED:

4. **Indicate any comments on the status of the proprietary name review (PNR).**
   The IND PNR memo for COMIRNATY was completed on November 9, 2020 and the decision was communicated to the Sponsor on November 20, 2020. The BLA PNR review memo is being finalized.

5. **Indicate whether the product sh/would be subject to lot release, surveillance, or exempt from lot release. Verify sample availability.**
   The product is subject to lot release. DBSQC's request for Lot Release Protocol, samples and reagents, was sent to the Applicant on June 25, 2021.

6. **Confirm review schedule for the application. If priority review, include justification from clinical reviewer filing review checklist. [Standard Review, Priority Review, or Expedited Review]**
   The review schedule for this BLA submission is an 8-month Priority Review with a PDUFA Action Due Date (ADD) of January 16, 2022. However, the targeted expedited ADD is September 30, 2021. The review timeline may be revised to address public health needs and as feasible. (See Review Timetable above for dates)

7. **Indicate the decision regarding the need for an Advisory Committee.**
   At this time, an Advisory Committee Meeting will not be needed for the BLA. Five Advisory Committee Meetings have occurred from October 22, 2020 to June 10, 2021 to discuss the development, Emergency Use Authorization and licensure of COVID-19 vaccines.

8. **Indicate whether the submission triggers PREA. If yes, a PeRC meeting is needed. Verify whether the applicant has an initial pediatric study plan (iPSP) in place.**
   The submission triggers PREA because it contains a new active ingredient, and a meeting with PeRC has been scheduled for August 10, 2021. The Applicant has an iPSP in place.

9. **Indicate whether the submission contains a proposed REMS. If yes, or if a REMS may be needed as a condition of approval, schedule an internal REMS meeting between the Product Office and OBE/DE.**
   The submission does not contain a proposed REMS.

10. **Is a comprehensive and readily located list of all clinical sites included or referenced in the application?**
    A comprehensive and readily located list of all clinical sites is included in the application.

11. **Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?**
    A comprehensive and readily located list of all manufacturing facilities is included in the application.

12. **Indicate any updates since the First Committee Meeting on pre-license inspection, pre-approval inspection, or BIMO sites requiring inspections (Is the establishment(s) ready for inspection?)**
    See updates from the DMPQ reviewers above.

BIMO is not issuing any inspections under this BLA; see updates from the BIMO reviewer above.

13. **If the application is affected by the Application Integrity Policy (AIP), has the division made a recommendation regarding whether an exception to the AIP should be granted to permit review based on medical necessity or public health significance?**
The application is not affected by the AIP.

14. **Is the product an Original Biological Product or a New Molecular Entity (NME) for an NDA?**
The product is an Original Biological Product.

FOR APPLICATIONS IN THE PDUFA PROGRAM (NME NDAs/Original BLAs), IF FILED:

15. **Confirm that any late submission components were submitted within 30 days. List any late submission components that arrived after 30 days.**
As agreed, a strain sequence analysis report for all COVID-19 cases was submitted in amendment 5 (sequence 0006) dated June 7, 2021. There were no late submission components that arrived after 30 days.

16. **Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?**
The application was complete upon submission.

ADMINISTRATIVE DETAILS, IF FILED:

17. **Review the Milestone Schedule and indicate if there are any issues with the schedule. Note: This is a confirmation to capture any changes made since the First Committee Meeting.**
No changes have occurred in the Milestone Schedule since the First Committee Meeting. Please see Review Timetable above.

INFORMATION REQUESTS (IRs):

1. 05/18/2021: Three questions regarding datasets (Response in 125742/0.3)

2. 05/20/2021: Four facilities questions and a request for a telecon on 5/25/21 or 5/26/21 to discuss production schedule and the shutdown activities planned for the Puurs, Belgium site (Response in 125742/0.4)

3. 06/08/2021: Three clinical questions regarding datasets and the PI (Response in 125742/0.6)

4. 06/09/2021: Clinical IR requesting dates for PREA deferred studies (Response in 125742/0.7)

5. 06/25/2021: DBSQC IR regarding the lot release protocol (LRP) template and samples and reagents (Awaiting response)

6. 06/25/2021: Clinical IR regarding the document titled “bnt162-01-intrim3-report-body” (Awaiting response)

AMENDMENTS:

1. 05/18/2021: Second roll and final piece of the BLA, which started the review clock. This amendment was not submitted in response to an IR.

2. 05/19/2021: Request for Proprietary Name Review. This amendment was not submitted in response to an IR.

3. 05/19/2021: Response to May 18, 2021, IR RE three dataset questions.

4. 05/24/2021: Response to DMPQ’s May 20, 2021, IR RE four facilities questions and a request for a t-con on 5/25/21 or 5/26/21 to discuss production schedules and the shutdown activities planned for the Puurs, Belgium site.

5. 05/24/2021: COVID-19 case strain sequencing data. This amendment was not submitted in response to an IR.

6. 06/16/2021: Response to June 8, 2021, clinical IR on three clinical questions regarding datasets and the PI.

7. 06/17/2021: Response to June 9, 2021, clinical IR requesting dates for PREA deferred studies.