First Committee 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
Applicant: BioNTech Manufacturing GmbH
Meeting date & time: June 3, 2021; 4:00PM - 5:30PM EDT
Committee Chair: Ramachandra Naik, Ph.D.
Meeting Recorders: CAPT Michael Smith, Ph.D. and Laura Gottschalk, Ph.D.

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

Review responsibility	Committee Member	Team Leader / Supervisor(s)	Division Director
Chairperson	**Ramachandra Naik,** PhD	TL: **Kirk Prutzman,** PhD BC: **Elizabeth Sutkowski**, PhD	DD: **Loris McVittie**, PhD SA: **Kirk Prutzman,** PhD (acting)
Regulatory Project Managers	**CAPT Mike Smith,** PhD **Laura Gottschalk,** PhD	TL: **Kirk Prutzman,** PhD BC: **Elizabeth Sutkowski,** PhD	DD: **Loris McVittie,** PhD SA: **Kirk Prutzman,** PhD (acting)
Clinical	**Susan Wollersheim,** MD **CAPT Ann Schwartz,** MD	TL: **Lucia Lee,** MD BC: **Maria Allende,** MD	DD: **Doran Fink,** MD, PhD
Product (CMC) DVP Regulatory coordinator, DVP Product Specialist	**Haruhiko Murata,** MD, PhD **Xiao Wang,** PhD **Anissa Cheung,** MSc	BC: **Keith Peden,** PhD BC: **Keith Peden,** PhD	DD: **Jerry Weir,** PhD DDD: **Robin Levis,** PhD
DS and DP release assays DS and DP release assays DS and DP release assays DS and DP release assays DS and DP release assays LRP and Testing Plan Dev.	**Hsiaoling Wang,** PhD **Emnet Yitbarek,** PhD **Karla Garcia,** MS **Anil Choudhary,** PhD, MBA **Esmeralda Alvarado,** PhD **Marie Anderson,** PhD	TL: **Tao Pan,** PhD TL: **Tao Pan,** PhD BC: **CDR James Kenney,** DSc BC: Muhammad Shahabuddin, PhD BC: Muhammad Shahabuddin, PhD **Maryna Eichelberger,** PhD	DD: **Maryna Eichelberger,** PhD DDD: N/A
Toxicology	Nabil Al-Humadi, PhD	BC: Martin Green, PhD	DD: **Doran Fink,** MD, PhD
Statistics, both Clinical data & assays	**Lei Huang,** PhD	BC: **Tsai-Lien Lin**, PhD	DD: **John Scott**, PhD DDD: Shiowjen Lee, PhD
Epidemiology/ Pharmacovigilance	**Deborah Thompson,** MD, MSPH	TL: LCDR Jane Baumblatt, MD BC: **Manette Niu,** MD	DD: Narayan Nair, MD DDD: Meghna Alimchandani, MD
DMPQ Reviewer/Inspector DMPQ Reviewer/Inspector DMPQ Reviewer DMPQ Inspector DMPQ Inspector DMPQ Inspector Lot Release DMPQ RPM	**Kathleen Jones,** PhD **Laura Fontan**, PhD **Gregory Price,** PhD **Zhongren Wu,** PhD **CDR Donald Ertel**, MS **Ekaterina Allen**, PhD **Cheryl Hulme** **Iryna Zubkova,** PhD	TL: **Nicole Li** BC: **Lori Peters,** MS TL: **CDR Donald Ertel**, MS BC: **Lori Peters**, MS BC: Anthony Lorenzo BC: **Joseph Quander** BC: James Crim	DD: **John Eltermann,** RPh, MS DDD: **Carolyn Renshaw**
BIMO	**Haecin Chun,** MT(ASCP)SBB, MS	BC: **Dennis Cato**	DD: **Carrie Mampilly,** MPH
APLB Labeling reviewer	**CDR Oluchi Elekwachi,** PharmD, MPH **Dana Jones**	BC: **Lisa Stockbridge,** PhD	DD: Robert Sausville
Container Labeling	**Daphne Stewart**	BC: Timothy Nelle, PhD	DD: **Loris McVittie**, PhD
Electronic integrity	CDR David Schwab, MSIS	**Loris McVittie**, PhD	DD: **Loris McVittie,** PhD
CDISC consult	**Brenda Baldwin,** PhD **Kirk Prutzman,** PhD	BC: **Elizabeth Sutkowski,** PhD	DD: **Loris McVittie,** PhD

Other attendees that were not listed in the review committee table: Maureen Hess, Leslie Taylor, Laura Montague, Konstantin Vernik, Cassandra Overking, David Cho, Varsha Garnepudi, Hector Izurieta, Jeff Roberts, Joseph Kulinski, Nicki DeVore, Douglas Pratt, Sara Gagneten, David Rouse, Sudhakar Agnihothram, Tatiana ClarodaSilva, Swati Verma and Nadine Kaelber

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
Proper name designation:	08-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
Primary Draft 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:** 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

Background and Purpose:
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 (COMIRNATY, pronounced “koh-MER nah-tee”), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age. This is a Rolling BLA submission, so it will be handled in RMS-BLA, not eMRP. 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.

The purpose of this First Committee Meeting was to discuss the milestones, roles and responsibilities of each member of the review team.

Discussion Summary:

The Chair provided a brief overview of the submission and highlighted several important points for the review of the BLA.

- A table of the full review committee and their corresponding team leaders, managers and directors, was included in the agenda for the meeting. The review committee was asked to review it and let the regulatory review team know if anything needs to be corrected.

- The submission is an 8-month Priority Review BLA with a PDUFA Action Due Date (ADD) of January 16, 2022. However, the targeted ADD is September 30, 2021.

- The Chair summarized the review milestones (as shown on page 2).

- A Late Cycle Meeting (LCM) will likely not take place since the PDUFA deadline for the LCM is November 1, 2021, and this is after the Target Action Due Date of September 30, 2021.

- In an effort to reduce the burden for reviewers, the Chair questioned whether Filing Checklists should be completed for this submission. Management said that they will check with CBER IOD about the requirement for Filing Checklists and let the review team know.

- It was confirmed that an Advisory Committee Meeting will not be needed for the BLA since five Advisory Committee Meetings would have occurred from October 22, 2020 to June 10, 2021 to discuss the development, Emergency Use Authorization and licensure of COVID-19 vaccines.

- The Chair asked about the best method for the review team to provide regular status updates to Management. Management will discuss this internally and will provide an answer to the review team soon.

- The Chair announced that an internal meeting is scheduled for Friday, June 4, 2021, with the DVP and DBSQC teams to discuss tests that will be part of the lot release protocol and in-support testing.

Updates from Discipline Reviewers:

1. Chair (Ramachandra Naik):

    - See discussion summary above.

2. Clinical (Susan Wollersheim and Ann Schwartz):

    - The clinical reviewers have found the review to be more burdensome than expected since much of the clinical information is referenced from the prior IND and EUA, plus the clinical information was not well organized and a summary document would be helpful. They will discuss internally to see if there is something that can be requested from the Applicant that can aid them in their review, including potentially having a teleconference with the Applicant. The clinical team thought they will likely have a safety data information request, but they were going to discuss with the statistical team first.

3. CMC (Haruhiko Murata and Xiao Wang):

    - No issues have been identified.

4. DBSQC (Hsiaoling Wang, Emnet Yitbarek, Karla Garcia, Anil Choudhary, Esmeralda Alvarado and Marie Anderson):

    - No issues have been identified. However, the Lot Release Protocol appears to be missing and an information request will be sent to the Applicant to request this document.

5. Toxicology (Nabil Al-Humadi):

    - Dr. Green informed the regulatory team prior to the meeting that the toxicology team will not be able to attend the meeting, but no issues have been identified and there should be no problem making the deadlines.

6. Statistics (Lei Huang):

    - No issues have been identified.

7. Epidemiology/Pharmacovigilance (Deborah Thompson):

    - The reviewer noted that a pregnancy registry was mentioned in the submission, and it will need to be determined if it will be considered a PMC.

8. DMPQ (Kathleen Jones, Laura Fontan, Gregory Price, Zhongren Wu, Donald Ertel, Ekaterina Allen, Cheryl Hulme and Iryna Zubkova):

    - No issues have been identified and inspections for Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC (FEI: 1222181, referred to as Pfizer, Andover) and Pfizer Manufacturing Belgium NV (FEI: 100654629, referred to as Pfizer, Puurs) sites are tentatively being planned for July 19th – 23rd and June 24th - July 2nd, respectively. They are waiting on the EIR from the Pharmacia & Upjohn Company (FEI: 1810189, referred to as Pfizer, Kalamazoo) site that was issued by TeamBio to see if the inspection can be waived since the site was recently inspected (May 11-20, 2021).

9. BiMO (Haecin Chun):

    - BiMO is not planning on issuing any more inspections since inspections of 10 study sites were already conducted under the IND and EUA, under 2 protocols. The BiMO team stated that the inspections that occurred under the IND and EUA did not inspect data integrity because there wasn't anything to inspect at the time. However, if the clinical and statistical reviewers encounter issues relevant to data integrity, BIMO should be made aware as soon as possible so that arrangements for inspections can be made. Lastly, the BiMO team noted that the agenda for this meeting included a BiMO inspections completed milestone of July 30, 2021, and

they mentioned that this is not feasible and too early in the review cycle if inspections were to be assigned.

10. APLB (Oluchi Elekwachi):

    - No issues have been identified and the propriety name review will be similar to what was submitted under the IND.

11. Container Labeling (Daphne Stewart):

    - The reviewer noted that she will have a few minor comments on the carton and container labels early next week.

12. CDISC (Brenda Baldwin and Kirk Prutzman):

    - 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 amendment.

Action Items:

- Management
  - Find out if Filing Checklists will be required.
  - Determine the best method for the review team to keep management apprised of the review progress.
- Clinical
  - Determine, as soon as possible, if there are issues that will prevent the review from being completed on time and keep management informed on what is decided.

Post-meeting updates:

- CBER IOD informed the regulatory team that discipline reviewer checklists do not need to be completed for this BLA. The reviewers were informed of this decision on June 7, 2021 and encouraged to refer to the checklists for guidance during the review of the BLA. The RPM filing checklist will be completed and uploaded to RMS-BLA/EDR.

Explanation of Milestones

First Committee Meeting: Committee must meet by this date to discuss the review of the BLA.

Filing Meeting: Meeting at which the review committee determines whether the BLA can be filed. Reviewers must determine whether the information included in the BLA is sufficient to allow the reviewer to conduct an adequate review. The purpose is not

	to determine the acceptability of the data but rather to determine whether the appropriate information was submitted to allow the reviewer to conduct a meaningful review.
Filing Action:	Date by which a filing letter (either accepting or refusing to file the BLA) must be issued.
Deficiencies Identified:	Date by which a letter must be issued in which review issues identified to date are conveyed to the applicant.
Mid-cycle Meeting:	Meeting at which each reviewer is expected to document their review progress and discuss the relevant content of the submission and present an overview. A draft review memorandum identifying key issues should be completed by the time of the meeting. First line supervisors for each review discipline as well as the Director and Deputy Director for DVRPA and OVRR, or their representative, should attend the meeting.
Action Due Date:	Date by which final action regarding the BLA must be conveyed to the applicant (issue Approval or Complete Response letter, depending on review decision). All review memos, regardless of the Action being taken, must be signed and uploaded to the EDR prior to the date of Action.

Explanation of Roles and Responsibilities (See CBER SOPP 8401 for more detail)

- Chair – Manages the administrative processing of reviews and ensures the regulatory and scientific content of submissions and their reviews are appropriate.
- Director and/or Deputy Director – the Signatory Authority who signs action letters and is responsible for content of reviews.
- Regulatory Project Manager (RPM) – Manages the review of submissions, including reviewing assigned portions, performing quality control checks, capturing review committee communications, and ensures that the review and review file is administratively complete. The RPM(s) works in tandem with the Chair to ensure that amendments are disseminated to the appropriate reviewers and that a meaningful short summary is entered into eMRP. Throughout the review cycle, the RPM ensures that all FDA documents are uploaded into the EDR as they are generated, and the documentation review memo is maintained in real-time.
- Review Committee – Perform review of all assigned areas of submissions, participate in review meetings, and perform and document a review of the submission that is scientifically sound and follows Good Review Management Principles. Documentation of a discipline review may be in the form of a

primary review, discipline review letter, and a review addendum. It is imperative that the review committee endeavor to follow the review timetable and finish reviews in a timely manner to allow for adequate supervisory review. It is critical that the review committee keeps management, including senior management, abreast of any significant review issues.

- Supervisors – Ensure the overall content of reviews are appropriate, all administrative processing steps are being completed, including database data entry, and all deadlines are met. Reviews and approves employees' review memorandums and other submission documents per CBER policies and procedures. Supervisory review is considered the Secondary Review.

Documentation of Review

Each discipline reviewer is expected to prepare a written review documenting their review of the file. Timely submissions are imperative to allow time for adequate management review. The following is recommended:

- Identify all materials assigned for review and include an executive summary in each final or complete review memo.
- List and summarize all material reviewed. The summary should identify each amendment reviewed and include a list of the submission dates, sections and page numbers etc., as applicable.
- A list of questions communicated to the applicant, in letter-ready format, along with the responses received and reviewed should be clearly identified.
- A recommendation for action, approval or CR, based upon the review summary should be clearly stated.
- Draft reviews should be prepared and discussed with the reviewer's supervisor and a copy should be given to the Chair by the draft due date(s). Draft reviews should not be uploaded to the EDR.
- Reviewer's and supervisor's electronic signatures should be placed on the final PDF version of the review. A Word version should be attached, and the PDF should be certified and locked to prevent modification. The review should be entered into eMRP using the date of the Reviewer's approval stamp as the date of the memo and the certified PDF should be uploaded into the EDR.
- If a Complete Response (CR) Letter is issued, a complete written review is expected and should reflect all amendments that have been reviewed through the date of the CR decision. The final signed and certified PDF version of the review should be uploaded by the date of the CR action.

Communication Plan

We can communicate with the applicant via several methods such as telecon, secure e-mail, and letter. The following is recommended:

- All communication regarding requests for information or advice for the applicant will be coordinated by the RPMs and communicated either via telecon or secure email. Please contact **Ramachandra Naik** (Chair), **Mike Smith** and **Laura Gottschalk** (RPMs) if you need to communicate with the applicant.

- Although every effort should be made to include the RPMs and/or Chair when communicating with the applicant, in rare instances it may be appropriate, with permission from Ramachandra Naik and/or Laura Gottschalk and Mike Smith, to communicate some requests for information (e.g., something that is relatively simple) to the applicant via a telecon. Please ensure that all such communication is formally documented (i.e., write up a telecon memo and send it to the RPMs to include in the file).
- Formal telecons with the applicant can be scheduled to address issues for which a direct discussion is helpful. The RPMs will coordinate this if/when it is needed.
- Letters can also be used to communicate review issues to the applicant. Although both secure e-mail and letters provide the necessary documentation for the file, letters are a more formal process than secure e-mail (letters must go through more levels of supervisory review and concurrence) so typically letters are reserved for communication of policy or serious review issues.
- Please “cc” the Chair on significant e-mail communication and meetings (internal and external). It is helpful for the Chair to have a general overview of the review status and review issues in the various disciplines (allows for more effective communication with internal upper level management and the applicant when necessary).
- Supervisory concurrence will be sought, when appropriate, prior to sending communications to the applicant (e.g., memos with request for information, providing advice, etc.).