First Committee Meeting Summary

Application number: BLA STN 125752
Product name: COVID-19 Vaccine, mRNA (SPIKEVAX)
Proposed Indication: Active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.
Applicant: ModernaTX, Inc.
Meeting date & time: September 9, 2021 (2:00 PM-3:30 PM EST)
Committee Chair: Sudhakar Agnihothram, Ph.D.
Meeting Recorders: Josephine Resnick, Ph.D.
Joseph Kulinski, Ph.D.

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

Review responsibility	Committee Member	Team Leader/Supervisor	Division Director
Chairperson	**Sudhakar Agnihothram,** PhD	**TL: Timothy Fritz,** PhD **BC: Rakesh Pandey,** PhD	DD: **Loris McVittie,** PhD SA (Acting): Kirk Prutzman, PhD
Regulatory Project Managers	**Joseph Kulinski,** PhD **Josephine Resnick,** PhD	**TL: Timothy Fritz,** PhD **BC: Rakesh Pandey,** PhD	DD: **Loris McVittie,** PhD SA (Acting): Kirk Prutzman, PhD
Clinical	**Rachel Zhang, MD**	**TL: Anuja Rastogi,** MD **BC: Maria Allende,** MD	DD: **Doran Fink,** MD, PhD
Product/(CMC) Clinical Assay DVP Regulatory coordinator	**Alena Dabrazhynetskaya,** PhD **Keith Peden**, PhD Swati Verma, PhD **Sara Gagneten,** PhD	BC: **Keith Peden,** PhD	DD: **Jerry Weir,** PhD DDD: **Robin Levis,** PhD
Pre-clinical	**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 LRP and Testing Plan Dev. Lot Release Protocol	Hsiaoling Wang, PhD **Emnet Yitbarek,** PhD LCDR Yen Phan, MLS(ASCP) Most Nahid, Parvin, PhD **Marie Anderson,** PhD	TL: **Tao Pan,** PhD TL: **Tao Pan,** PhD TL: **CAPT James Kenney,** DSc TL: Muhammad Shahabuddin, PhD	DD: **Maryna Eichelberger,** PhD DDD: N/A
Toxicology	Ching-Long Sun, PhD	BC: **Martin Green,** PhD	DD: **Doran Fink,** MD, PhD
Statistics, both Clinical data & assays	Ye Yang, PhD	TL: **Lei Huang,** PhD BC: **Tsai-Lien Lin,** PhD	DD: **John Scott,** PhD DDD: **Shiowjen Lee,** PhD
Epidemiology/ Pharmacovigilance	**CDR Jane Baumblatt,** MD	BC: **Manette Niu,** MD	DD: Narayan Nair, MD DDD: Meghna Alimchandani, MD
Real World Evidence	**Yun Lu, PhD**		AD: Richard Forshee, PhD
DMPQ Reviewer and Inspector DMPQ Inspector DMPQ Inspector DMPQ RPM DMPQ PRB (Lot Release)	**Obinna Echeozo,** MPH, MBA **Pete Amin** **Christian Lynch** **Debra Vause,** RN, BSN **Cheryl Hulme**	TL: Jie He, PhD BC**: Anthony Lorenzo** BC: James Crim BC: **Joseph Quander**	DD: **John Eltermann,** RPh, MS DDD: Carolyn Renshaw
BIMO	**Bhanu Kannan,** MS	BC: Dennis Cato	DD: Carrie Mampilly, MPH
APLB Labeling reviewer	**CDR Oluchi Elekwachi, PharmD,**	BC: **Lisa Stockbridge**	DD: Robert Sausville
Container and Carton Labeling	**Daphne Stewart**	BC: Timothy Nelle, PhD	DD: **Loris McVittie, PhD**

Review responsibility	Committee Member	Team Leader/Supervisor	Division Director
Electronic integrity	CDR David Schwab, MSIS		DD: **Loris McVittie,** PhD
CDISC consult Clinical Data Validation	**Brenda Baldwin,** PhD Kirk Prutzman, PhD Jainmin (Jack) Zhang, PhD Lisa Lin, PhD Virginia Hussong, PhD Shifu Zhao, PhD	BC: **Elizabeth Sutkowski,** PhD	DD: **Loris McVittie,** PhD

Other Attendees:
Anissa Cheung, MS
David Cho
David Rouse
Douglas Pratt
Helen Gemignani
Konstantin Virnik, PhD
Leslie Taylor
Marion Gruber, PhD
Mark Coelho
Maureen Hess
Theresa Finn, PhD
Varsha Garnepudi
Vera Stupina
Karen Farizo

Background and Purpose:
This meeting was to discuss the new original BLA (STN 125752/0) from ModernaTX, Inc. for Spikevax (COVID-19Vaccine, mRNA) for active immunization against coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older. This is a Rolling BLA submission and will be handled in RMS-BLA. The first submission containing eCTD module 4, was submitted and received on May 28, 2021. The second submission containing eCTD module 3 was submitted and received on August 16, 2021. The final submission containing all remaining modules in completion was submitted and received on August 24, 2021.

The purpose of this First Committee Meeting was to discuss the milestones (Table 2 below), scheduled meetings (Table 3 below), roles and responsibilities of each member of the review team.

Review Timetable

Table 2: Tentative Review Timeline (based on a compressed 5-month schedule with an ADD of January 31, 2021). Milestones from RMS-BLA (and respective dates for 5M review) are in bolded font.

Milestone (Total Review Clock 183 days)	Priority 8mth PDUFA timeline	Target 5M Date	Actual Scheduled/Completed Date
Application Receipt Date			24-Aug-21
Acknowledgement Letter	7-Sep-21		9-Jun-21
Committee Assignment	**14-Sep-21**	**6-Sep-21**	**27-Aug-21**
First Committee Meeting	**14-Sep-21**	**6-Sep-21**	**9-Sep-21**
Proper-name Designation	14-Sep-21	6-Sep-21	6-Sep-21
Late minor components received (due by day 30; may be RTF issue)	23-Sep-21	11-Sep-21	
Filing checklist/reviews complete	3-Oct-21	18-Sep-21	
Filing meeting	**8-Oct-21**	**21-Sep-21**	**28-Sep-21**
Filing Letter	**23-Oct-21**	**30-Sep-21**	
Deficiencies/Day 74 letter	**6-Nov-21**	**9-Oct-21**	
Initial Proprietary Name Review	22-Nov-21	19-Oct-21	
Reviewer reports/draft reviews complete (Due to RPM 4 days prior to mid-cycle)	4-Dec-21		
Internal Mid-cycle meeting	**8-Dec-21**	**29-Oct-21**	**27-Oct-21**
Mid-cycle communication with applicant (Due 14days after internal Mid-cycle meeting)	**22-Dec-21**	**7-Nov-21**	
Final draft primary reviews w/supervisory concurrence (upload not required)	23-Feb-22	15-Dec-21	
Internal Late-cycle meeting			
Late cycle briefing pkg to applicant 12 days before LC meeting)	21-Feb-22	7-Dec-21	
Late cycle meeting (NLT 60 days before ADD)	**23-Feb-22**	**15-Dec-21**	
VRBPAC	NA		
PeRC briefing materials due to PeRC (14 days prior to PeRC meeting)	9-Feb-22	2-Dec-21	8-Oct-21
PeRC Meeting date (approximation, no later than T-60 days but after VRBPAC) [enter actual date]	23-Feb-22	16-Dec-21	12-Oct-21
PLI Inspections completed (by T-60days)	23-Feb-22	16-Dec-21	
BIMO Inspections completed (by T-60days)	23-Feb-22	16-Dec-21	
Draft PMR/PMC in approval letter (notify OVRR SWG Rep as soon as identified)	23-Feb-22	16-Dec-21	
Employee Officer list memo	23-Feb-22	16-Dec-21	
Press release - contact Maureen Hess	5-Mar-22	22-Dec-21	
Final reviews & addenda signed & uploaded	25-Mar-22	4-Jan-22	
Notify OCOD of pending approval	25-Mar-22	4-Jan-22	
Lot Release Protocol & Testing plan finalized (draft by mid-cycle)	25-Mar-22	4-Jan-22	

Milestone (Total Review Clock 183 days)	Priority 8mth PDUFA timeline	Target 5M Date	Actual Scheduled/Completed Date
Labeling comments to applicant	**25-Mar-22**	**4-Jan-22**	
PMC/PMR notify applicant	**25-Mar-22**	**4-Jan-22**	
Draft SBRA	25-Mar-22	4-Jan-22	
Prepare & circulate electronic action package (include documentation review memo)	10-Apr-22	14-Jan-22	
Final draft labeling	10-Apr-22	14-Jan-22	
Action Due Date	**24-Apr-22**	**31-Jan-22**	**31-Jan-22**

Table 3: Scheduled Meetings

Monthly Committee Meetings (MCM):
• September 28, 2021, 11:00AM – 12:30 PM (Filing /MCM)
• October 27, 2021, 1:00PM – 2:30PM (Internal Midcycle/MCM)
• November 23, 2021, 1:00PM – 2:30PM
• December 17, 2021, 11:00AM -12:30PM
Labeling Meetings:
• September 29, 2021, 1:30PM – 3:30PM (CMC & Toxicology sections)
• October 1, 2021, 12:00PM – 2:30PM (CMC & Toxicology sections)
• October 5, 2021, 9:30AM – 11:30PM (CMC & Toxicology sections)
• October 12, 2021, 1:30PM – 3:30PM (Clinical)
• October 15, 2021, 11:30PM – 1:30PM (Clinical)
• October 19, 2021, 2:00PM – 4:00PM (Clinical)
• October 22, 2021, 10:00PM – 12:30PM (Clinical)
Other Meetings:
• Meeting between DVP and DBSQC to discuss tests to support licensure and lot release of SPIKEVAX: September 22, 1:00PM – 2:30PM

Discussion Summary:

- **Chair (Sudhakar Agnihothram)**

  The Chair provided a brief overview of the submission, reviewed the regulatory milestones and meetings schedule and highlighted several important points of the BLA review:

  - 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 reviewers were also asked whether they have received the appropriate

documents or electronic links and have a clear understanding of all their responsibilities.

- The submission is an 8-month Priority Review BLA with a PDUFA Action Due Date (ADD) of April 24, 2022. However, the targeted ADD is January 31, 2022. The adjusted 5-month compressed timeline and milestones were reviewed.

- The Mid-Cycle and Late-Cycle communications with the company will likely not take place since the team anticipates being in close communication with the company throughout the review cycle, and since this will be reviewed on a compressed priority schedule.

- Filing Checklists will not need to be uploaded for this submission, but it was recommended that the review team utilize them as a guide to check for completeness of the submission and any potential filing issues.

- It was confirmed that an Advisory Committee Meeting will not be needed for the BLA.

- Monthly meetings as well as PeRC and several labeling meetings have already been scheduled as shown in Table 3. In addition, DBSQC has scheduled a meeting with DVP to discuss testing and lot release requirements.

- Committee was notified about the following requests submitted by Moderna

    - A request for an exception to the requirement to include a preservative in the vaccine multiple-dose containers

    - Waiver request to be placed on routine lot surveillance in lieu of lot release

    - Request for Priority Review Designation

    - Request for Medical Threat Medical Countermeasure Priority Review Voucher

- **Clinical (Rachel Zhang):**

  The clinical team noted that they are waiting on completed shell tables to be submitted to the BLA. No major issues have been identified so far, and the team is preparing for a PeRC review of the iPSP to be held on October 12, 2021. The team noted that PeRC may request an update on the status of the adolescent EUA, and asked that the epidemiology team provide an update on recent safety data as soon as it becomes available.

- **CMC (Alena Dabrazhynetskaya):**

  No major issues have been identified so far. Minor issues will be addressed through information requests.

- **DBSQC (Hsiaoling Wang, Emnet Yitbarek, Yen Phan, Most Nahid Parvin, Marie Anderson):**

  Maryna provided an update for the team, noting that one DBSQC representative will be assigned to provide updates for DBSQC at meetings and to write a consolidated review memo. Test assays and methods as well as lot release protocols will be reviewed by DBSQC. Marie Anderson will develop a testing plan and will work with Cheryl Hulme (DMPQ/PRB) to review the lot release protocol template, and to obtain samples for in-support testing. Information requests will be reviewed internally with input from the product office, as needed, and concurred by Mary Malarkey prior to being sent to the RPMs. An information request for updates to the LRP template will likely be submitted shortly.

- **Toxicology (Joe Sun):**

  An update from the toxicology reviewer was obtained via email after the meeting. The toxicology reviewer noted that three of the six genotoxicity studies of the LNP components that were included in the BLA have not been reviewed under IND 19745 and will be reviewed under the BLA. No major issues have been identified.

- **Statistics (Ye Yang):**

  There are no issues currently identified with the submitted datasets. They will contact the CMC team to discuss aspects of the non-clinical review.

- **Real World Evidence (Yun Lu):**

  The revised Postmarketing safety protocol P903 and responses to CBER's July 14, 2021 comments on the Postmarketing safety protocol are currently under review. It is expected that an additional information request will be sent to the company.

- **Epidemiology/Pharmacovigilance (Jane Baumblatt):**

  The Risk Management Plan (RMP) was provided in the submission and appears to be complete with all the necessary information and pharmacovigilance plan. AEs of potential concern are all listed. No major issues have been identified at this time.

- **DMPQ (Obinna Echeozo, Pete Amin, Christian Lynch, Debra Vause):**

No major issues currently identified. The current focus is arrangement of pre-license inspections. Three facilities involved in manufacturing of mRNA-1273 LNP drug substance (DS) have been identified so far for inspections – Aldevron LLC, Fargo, ND; ModernaTX Inc., Norwood, MA; and Lonza Biologics Inc., Portsmouth, NH. The production schedule has been requested for these facilities, and inspection dates will be finalized shortly. Pete (lead inspector) and Obinna will inspect the Norwood and Portsmouth facilities. Christian Lynch (newly assigned from CBER OD) will lead the inspection for the Fargo facility. DVP will provide details of their personnel to be involved in these facility inspections.

- **DMPQ-PRB (Cheryl Hulme):**

  PRB will work with Marie to finalize the LRP template and will handle the receipt of samples submitted for lot-release testing.

- **BIMO (Bhanu Kannan):**

  All required datasets are present and accessible in the submission. Transfer obligations have been reviewed and are satisfactory. BIMO will consult with the clinical team regarding potential BIMO inspection sites.

- **APLB (Oluchi Elekwachi):**

  Labeling was submitted and is in the correct format. Review of the labels and the PNR has started, no major issues currently identified.

- **Carton & Container Labeling (Daphne Stewart):**

  The carton and container labels were submitted and are under review. No major issues have been identified, and it is likely that only minor changes will be requested.

- **CDISC (Brenda Baldwin and Kirk Prutzman):**

  A meeting to discuss the data validation results will be held on September 10th.

Other First Committee Meeting Agenda Items/Responses Discussed:

1. *Confirm that the application is compliant with 21 CFR 601.2 for BLAs and 21 CFR 314.101 for NDAs.*

   The Biological License Application STN 125752 appears to be compliant with 21 CFR 601.2. A more comprehensive review will be completed prior to the filing meeting to identify any deficiencies and non-compliance with the CFR.

2. *Confirm whether the product falls within the PDUFA Program, if a PDUFA product.*
   Yes. The product falls within the PDUFA program.

3. *Review all future meeting dates, e.g., Mid-Cycle, Late-Cycle.*
   All the future meetings dates listed in the Tables 2 and 3 were reviewed during the meeting

4. *Review/confirm if Orphan Drug designation was granted.*
   This item is not applicable to the review of STN 125752 BLA.

5. *Review/confirm if PREA is triggered and discuss the timeframe for scheduling a PeRC meeting.*
   PeRC review is scheduled for October 12, 2021.

6. *Document if an Advisory Committee Meeting is likely and review the appropriate Advisory Committee Meeting schedule for a potential date. If an Advisory Committee Meeting will likely not be needed, include the rationale/reasons in the meeting summary.*
   It was determined that STN 125752 will not be discussed at an Advisory Committee Meeting.

7. *Document any potential issues found in the early review, categorized by discipline, including identification of data sets submitted incorrectly, use of data standards, problems encountered opening data tables or absent data sets, etc. If not completed during the meeting, document that "Any potential issues should be identified by Day 45 of the review."*
   Reviewers were notified to keep the committee chair and RPMs informed about any potential issues that may arise during the review of STN 125752.

8. *Document whether pre-license or pre-approval inspections are necessary. If not completed during the meeting, document that "the need for pre-license or pre-approval inspections will be determined by day 45 of the review."*
   Details regarding the pre-license inspections were discussed as a part of the updates provided by DMPQ reviewers. Please refer to the discussion summary above.

9. *Discuss whether BIMO inspection(s) will be required. If not completed during the meeting, document that "need for BIMO inspection(s) will be determined by Day 45 of the review."*
   Details on BIMO inspections were discussed as a part of the update provided by the BIMO reviewer. Please refer to the discussion summary above.

10. *Identify activities to be completed before the Filing Meeting*.
    Reviewers were asked to ensure that the modules appropriate to their review discipline are complete. The reviewers were notified that filing checklists do not need to be uploaded for this BLA, but all reviewers are encouraged to use the

filing checklists as a guide to ensure all necessary components have been submitted.

11. *Confirm meeting date for Filing Meeting and discuss expectations for the Filing Meeting.*

    The Filing Meeting has been scheduled for September 28, 2021. Reviewers were notified that the purpose of the filing meeting is to discuss any deficiencies and/or issues that have arisen during the initial review of the submitted material.

Communication Plan

Several methods such as telecon, secure e-mail, and letter are available to communicate with the applicant. 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 **Sudhakar Agnihothram** (Chair), **Josephine Resnick** and **Joseph Kulinski** (RPMs) if you need to communicate with the applicant.
- 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 (this allows for more effective communication with internal upper-level management and the applicant when necessary).
- Supervisory concurrence is necessary prior to sending communications to the applicant (e.g., memos with request for information, providing advice, etc.). An information request template will be provided to the team to help facilitate the process.

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 or not 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 be in attendance at 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. The CDTL, as referred to in the Program of PDUFA V is the same as the Chair within CBER. The Chair is responsible for preparing the Summary Basis of Regulatory Action.
- **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 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 RMS/BLA. Throughout the review cycle, the RPM ensures all FDA documents are uploaded into CBER Connect 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 keep management, including senior management, abreast of any significant review issues

- **Supervisors** – Ensures 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.