



LATE-CYCLE MEETING MATERIALS

July 26, 2023

Our STN: BL 125768/0

Pfizer Inc.
Attention: Nirvana Moodley
500 Arcola Road
Collegeville, PA 19426

Dear Ms. Moodley:

Please refer to your Biologic License Application (BLA) submitted under section 351(a) of the Public Health Service Act for Respiratory Syncytial Virus Vaccine, ABRYSV0, for the prevention of lower respiratory tract disease and severe lower respiratory tract disease caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age by active immunization of pregnant individuals.

Attached are our meeting materials, including our agenda, for the Late-Cycle Meeting (LCM) scheduled for 3:30 PM – 5:00 PM, Friday, July 28, 2023.

If you have any questions, please contact the Regulatory Project Manager Managers, Paul Keller, Ph.D. (Paul.Keller@fda.hhs.gov), Ms. Laura Montague (Laura.Montague@fda.hhs.gov), and Vera Stupina, Ph.D. (Vera.Stupina@fda.hhs.gov).

Sincerely,

Loris McVittie, Ph.D.
Deputy Director - Regulatory
Division of Vaccines and Related Products
Applications
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research

ENCLOSURE:
Late-Cycle Meeting Materials

Late-Cycle Meeting Materials

Meeting Date and Time:	3:30 PM – 5:00 PM, Friday, July 28, 2023
Meeting Location:	Teleconference (Zoom.Gov)
Application Number:	BLA 125768/0
Product Name:	Respiratory Syncytial Virus Vaccine, ABRYSV0
Indication:	For the prevention of lower respiratory tract disease and severe lower respiratory tract disease caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age by active immunization of pregnant individuals.
Applicant Name:	Pfizer Inc.

INTRODUCTION

The purpose of a Late-Cycle Meeting (LCM) is to share information and to discuss any substantive review issues that we have identified to date, and our objectives for the remainder of the review. The application has not yet been fully reviewed by the signatory authorities, division directors, and application Chair. Therefore, the meeting will not address the final regulatory decision for the application. We are sharing this material to promote a collaborative and successful discussion at the meeting.

During the meeting, we may discuss additional information that could be submitted to address any identified issues. We may also discuss whether the submission of such information would be expected to trigger an extension of the PDUFA goal date if the Review Committee should decide, upon receipt of the information, to review it during the current review cycle.

Please note: If you submit any new information in response to the issues identified in this background package prior to this LCM, we may not be prepared to discuss that information at this meeting.

1. Substantive Review Issues to be discussed during the LCM

SUBSTANTIVE REVIEW ISSUES HAVE BEEN IDENTIFIED

The following substantive review issues have been identified to date:

Benefit-Risk Assessment: As communicated in our July 19, 2023, information request, our assessment is that administration of ABRYSV0 between 24 to 36 weeks gestation has an unfavorable overall benefit/risk profile. The potential risks of pre-term deliveries/births and maternal adverse events, such as pre-eclampsia, which are numerically higher in the vaccine group, outweigh the potential benefits for your proposed indication of “the prevention of lower respiratory tract disease and severe lower respiratory tract disease caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age by active immunization of pregnant individuals”.

We are considering whether restricting vaccination to later in pregnancy (e.g., 32-36 weeks gestation) might have a more favorable overall benefit/risk profile. To reach alignment on a possible favorable path forward, CBER and Pfizer will need to reach agreement on a number of specific issues, including but not limited to: revision of your proposed indication to restrict vaccination to later in pregnancy, consideration for the revision of the indication for prevention of severe LRTD to reflect the pre-specified efficacy endpoint criterion that was met, review of additional post-hoc subgroup analyses to support changes to an indication statement, review of PMRs/PMCs, and discussion of review timeline.

2. Advisory Committee Meeting

An Advisory Committee meeting took place on May 18, 2023. An additional meeting is not planned.

3. Risk Management Actions (e.g., REMS, the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk)

A. REMS ACTIONS HAVE NOT BEEN IDENTIFIED

We do not believe that a Risk Evaluation and Mitigation Strategy (REMS) is needed at this time.

B. RISK MANAGEMENT ACTIONS HAVE BEEN IDENTIFIED

As communicated previously, you will be required to conduct enhanced pharmacovigilance for preterm birth in the postmarketing period and submit reports of preterm birth as expedited (15-day) reports to VAERS, conduct follow-up on spontaneous reports of preterm birth using a targeted questionnaire, and provide your assessment for preterm birth (based on aggregate and interval data) in periodic safety reports. Your proposed pregnancy studies are under ongoing review and FDA will provide additional recommendations, as needed. If approved, we are considering a 505(o) Safety PMR trial to evaluate the risk of pre-term birth in a prospective, randomized, placebo-controlled trial designed for a finding of "non-inferiority" with respect to placebo administration, with an ethically appropriate trial design allowing for ABRYSV0 vaccine administration for all subjects enrolled in the trial, for example, as week 36 gestation approaches. In addition, we are considering a 505(o) Safety PMR evaluation of maternal adverse reactions of pre-eclampsia and gestational hypertension, which has potential to be evaluated in the context of one prospective PMR trial to evaluate these safety concerns (pre-term births, pre-eclampsia, gestational hypertension).

LCM AGENDA

1. Introductory Comments – 5 minutes, Goutam Sen, Chair

Welcome, Introductions, Ground rules, Objectives of the meeting

2. Discussion of Substantive Review Issues – 40 minutes:

Each issue will be introduced by FDA and followed by a discussion.

- The risk of pre-term births and the response to IR sent on July 19, 2023 regarding benefit/risk for infants and for pregnant individuals of restricting vaccination to later in pregnancy (e.g., 32-36 weeks gestation).
- The risk of maternal complications of pre-eclampsia and gestational hypertension.
- Recommendation to conduct additional post-hoc analyses based on different subgroups of the timing of vaccination by gestational age, including analyses of risk and benefit to inform revisions to your proposed indication and population to restrict vaccination to later gestational ages in pregnancy.
- To revise your proposed indication to "prevention of severe LRTD" only.

3. Additional Clinical Data – 10 minutes **(Applicant)**

4. Information Requests – One outstanding IR

5. Risk Management Actions (e.g., REMS, the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk) – 5 minutes

- You will be required to conduct enhanced pharmacovigilance for preterm birth in the postmarketing period and submit reports of preterm birth as expedited (15-day) reports to VAERS, and to provide your assessment for preterm birth (based on aggregate and interval data) in periodic safety reports. Additional recommendations will be provided as needed.

6. Postmarketing Requirements/Postmarketing Commitments – 5-10 minutes

- Your proposed pregnancy studies are under ongoing review and FDA will provide additional recommendations as needed. As noted above, we anticipate having discussions with you about a prospective, randomized, placebo-controlled trial as a safety PMR trial.

7. Major labeling issues – 5 minutes

- Labeling updates (PI) will likely be needed based on decision(s) regarding proposed indication and post-hoc risk and benefit analyses.
- As a risk management action to describe in labeling, we are considering a Warning and Precaution for the risk of pre-term birth with statements included in safety labeling to avoid use in persons at risk for pre-term birth, such as persons who have pre-eclampsia, gestational hypertension or are at risk for these maternal complications. Labeling should also provide for information on the risk of pre-eclampsia and the risk of gestational hypertension that were observed in the clinical trial database.

8. Review Plans – 5 minutes

We anticipate sending an information request to you within the next week on additional analyses of efficacy and safety data for you to provide to the BLA. This information is likely to be considered in the context of a major amendment to the BLA.

9. Applicant Questions – 5 minutes

10. Wrap-up and Action Items – 5 minutes