

**To:** Administrative File BL STN 125807/0.57

**From:** Ou Olivia Ma, CMC/Facility Reviewer, CBER/OCBQ/DMPQ/MRB2

**Through:** Anthony Lorenzo, Branch Chief, CBER/OCBQ/DMPQ/MRB2  
Lori Peters, Acting Division Director, CBER/OCBQ/DMPQ

**CC:** Christine Harman, Team Lead, CBER/OCBQ/DMPQ/MRB2  
Iryna Zubkova, RPM, CBER/OCBQ/DMPQ  
Shalini Seetharaman, RPM, CBER/OTP/ORMRR/DRMRR2/RRB2

**Applicant:** Abeona Therapeutics, Inc.

**Facility:** Abeona Therapeutics, Inc, Cleveland, OH; FEI# 3008334517

**Product:** prademagene zamikeracel / ZEVASKYN

**Subject:** Review Memo for Response to the Complete Response (CR) Letter issued on April 16, 2024, for the Biologic License Application (BLA) STN 125807/0 submitted to provide for the approval of prademagene zamikeracel indicated for the treatment of wounds associated with recessive dystrophic epidermolysis bullosa (RDEB).

**ADD:** April 29, 2025

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## RECOMMENDATION

Approval of the BLA is recommended from DMPQ perspective with the following Post-Marketing Commitment (PMC) and the inspectional considerations:

### PMC:

Abeona Therapeutics, Inc. commits to providing the results of an updated (b) (4) study in a Final Study Report Submission by October 29, 2025.

Study Protocol Submission: July 29, 2025

Final Study Report Submission: October 29, 2025

### Inspectional Considerations:

CBER understands that the recommendations below may or may not be taken (based on risk and available resources) and is not requesting documentation to be submitted as evidence of completion.

*Rationale of the Inspectional Considerations recommendation:*

(b) (4)

## EXECUTIVE SUMMARY

Abeona Therapeutics, Inc. (hereafter Abeona) submitted this supplement to respond to the complete response (CR) letter issued for BLA 125807/0 on April 16, 2024. CBER/DMPQ issued five deficiencies in the CR letter, including deficiencies in sterile filtration validations and container closure integrity testing. The responses to these deficiencies are reviewed and documented in this memo.

Submissions reviewed include the following:

Date Received	Submission	eCTD #	Comments/ Status
October 28, 2024	STN 125807/0.57	0058	Complete Response
February 11, 2025	STN 125807/0.62	0063	Response to DMPQ IR
March 5, 2025	STN 125807/0.67	0068	Response to OTP IR regarding sterility test nonconformance of stability study samples
March 13, 2025	STN 125807/0.70	0071	Response to DMPQ IR
March 21, 2025	STN 125807/0.75	0076	Response to OGT/DMPQ joint IR regarding CCIT as a one-time testing for the next (b) (4) batch
March 24, 2025	STN 125807/0.77	0078	PMC
March 27, 2025	STN 125807/0.78	0079	Response to DMPQ IR

## Complete Response Review

On April 16, 2024, a CR letter was issued to Abeona regarding BLA 125807/0 which included twelve deficiencies. The CR response was submitted on October 28, 2024 (STN 125807/0.57, eCTD# 0058).

Deficiencies #8, 9, 10, 11 and 12 were issued by DMPQ. Deficiencies #6 and #17 were issued by CMC reviewers, but the responses to deficiencies #6 and #17 include information under DMPQ purview, and therefore are also reviewed in this memo.

(The original CR deficiency is in **bold**, summary of the CR response is in normal font, and reviewer's comment is in *italic*.)

### CR Deficiency #8 and Response Review

**8. Your corrections to FDA's inspectional observations issued to you at the conclusion of the inspection conducted between February 19 and March 1, 2024, of your Cleveland, OH facility are still ongoing.**

***Reviewer's Comment:** Please note that deficiency #8 was included in the CR letter to document that classification of the pre-license inspection (PLI) of Abeona Therapeutics facility at Cleveland, OH was pending at the time of the CR letter issuance. Refer to the Establishment Inspection Report (EIR) and the 483 response review memo for evaluation of the PLI and the firm's response to the 483 observations. The firm has addressed this CR item. The firm's response to the 483 is acceptable and the inspection is classified as Voluntary Action Indicated (VAI). No further action is needed.*

### CR Deficiency #9 and Response Review

(b) (4)

2 pages have been determined to be not releasable: (b)(4)

(b) (4)

#### **CR Deficiency #6 and #10 and Response Review**

**6. You manufacture several media and reagents at your manufacturing facility which are used in the aseptic manufacturing of PZ DP. (b) (4) of the reagents, (b) (4) is not adequately evaluated for (b) (4) (b) (4) To address this concern, you proposed to (b) (4)**

(b) (4) However, as this proposed change was made after completion of your process performance qualification (PPQ), you did not provide adequate data to support the change in reagent. Therefore, in order to replace the (b) (4) reagent with (b) (4) (b) (4) please submit data to demonstrate that the reagent change does not impact the final DP.

10. You use media and buffers (b) (4) in the aseptic manufacturing process of PZ, and the (b) (4) (b) (4) However, you have not validated the (b) (4) used in the preparation of the media and buffers, and you have not established (b) (4) (b) (4) Additionally, you do not test the (b) (4) of the (b) (4) (b) (4) after use.

Because the media and buffers will be used directly in the aseptic manufacturing process of PZ, the (b) (4) of the media and buffers must be assured. Therefore, the (b) (4)

This deficiency was noted on the FDA Form 483 that was issued on March 1st, 2024. You indicated in the responses to the 483 observations that the studies will be completed between May 14 and July 31, 2024; however, these timeframes are insufficient for a review of the information prior to the BLA action due date.

Please provide (b) (4) validation studies for (b) (4) used for the media and components. In addition, please provide the established (b) (4) (b) (4) and a description of the (b) (4) testing that will be implemented. Please note that if the (b) (4) used for (b) (4) are adequately validated, (b) (4) components may not be necessary.

CR response is summarized below:

Abeona-manufactured medias/reagents are (b) (4)

(b) (4)

5 pages have been determined to be not releasable: (b)(4)

(b) (4)

**CR Deficiency #17 and Response Review**

17. In section 3.2.S.7 of your BLA submission, you propose a shelf-life of (b) (4) for your LZRSE-Col7A1 RVV. Your proposed LZRSE-Col7A1 RVV shelf-life is still under review, pending FDA receipt of additional stability data. In your resubmission, please include any stability data collected prior to the resubmission date, including but not limited to the following:



- a. Data collected from stress and in-use stability studies you proposed in amendment 33 received on March 1, 2024, which was expected to be submitted to the FDA by June 30, 2024.
- b. Any additional long-term stability data collected according to your stability protocols STA-DS-000001 and STA-DS-000003.

CR response under DMPQ purview is summarized below:

(b) (4)

2 pages have been determined to be not releasable: (b)(4)