



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: STN125832/0

From: Hsiaoling Wang, Ph.D., CMC reviewer, CBER/OCBQ/DBSQC/LAC

Through: Kenneth S. Phillips, Ph.D., LAC Chief, CBER/OCBQ/DBSQC/LAC
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Product: PAPZIMEOS (zopapogene imadenovec)

Applicant: Precigen Inc.

Subject: Analytical Methods for the Lot Release of (b) (4) Drug Product

Recommendation: Approval

Summary:

The following analytical methods used for lot release of PAPZIMEOS (zopapogene imadenovec) (b) (4) drug product (DP) from Precigen Inc., and the associated validations and qualifications were reviewed:

1. Purity by (b) (4) DP)
2. (b) (4)
3. (b) (4)
4. (b) (4)
5. (b) (4)
6. pH (b) (4) DP)
7. Appearance (DP)
8. Volume in Container (DP)
9. (b) (4)
10. Particulates (DP)

Conclusion: The analytical methods and their validations and qualifications reviewed for PAPZIMEOS (b) (4) DP were found to be suitable for their intended use.

Documents Reviewed

Rolling submission, dated December 23, 2024:

- Cover letter
- Form 356h

- Sections describing control of (b) (4) DP (3.2.P.5), including descriptions of (b) (4) DP specifications, analytical procedures of (b) (4) DP, qualifications of these analytical procedures, and (b) (4) DP batch analyses.

Amendment 26, dated April 18, 2025

- Response to 4Apr2025 IR (IR19, DBSQC IR)
- Document QCR-036: Analytical Method Verification Protocol for the Appearance Adenovector Test Method (executed)
- Document VSR456004 Verification Summary Report: Determination of the Extractable Volume of Parenteral Preparations According to (b) (4) methods
- Document VPPO0277: Validation Summary for Determination of (b) (4)
- Document TR499000 (b) (4) Summary Transfer Report – Particulate Contamination: (b) (4)

Amendment 35, dated May 23, 2025

- Response to IR #19, Question 3a and 3b
- Updated SOP QV-TM-00002: (b) (4) for Adenovector (Version: 3.0)

Amendment 41, dated June 10, 2025

- Response to 28May2025 IR (IR32, DBSQC IR)
- Updated SOP QV-TM-00012: Purity by (b) (4) for PRGN-2012 (Version: 5.0)
- Updated SOP QV-TM-00014: Quantitative Analysis of (b) (4) (Version: 4.0)
- Document QV-RPT-00421 of Precigen: Volume in Container Test Method Verification Report
- Document QV-RPT-00421 of Precigen: (b) (4) Test Method Verification Report

Amendment 43, dated June 23, 2025

- Response to IR #19, Question 1b
- Response to IR #32, Question 3b
- Supplement validation report: (b) (4) Test Method – QV-RPT-000431
- Supplement validation report: Purity by (b) (4) for PRGN-2012 – QV-RPT-000427

Amendment 44 dated June 24, 2025

- Response to IR #32, Question 2b
- Supplement validation report: (b) (4) – QV-RPT-00433

Background

PAPZIMEOS (zopapogene imadenovec, also referred as PRGN-2012) is a gene therapy, a non-human primate adenoviral vector (GC46) that codes for a human papillomavirus (HPV) antigen, and whose expression is under control of a constitutive cytomegalovirus (CMV) promoter. It is designed to generate T cell responses directed against papilloma cells infected with HPV 6 or HPV 11. It is administered by subcutaneous injection for the treatment of recurrent respiratory papillomatosis (RRP) in adults.

PAPZIMEOS DS is formulated in (b) (4)

(b) (4) with the target PRGN-2012 concentration of (b) (4) particles units (PU)/mL. The DS is stored at (b) (4). PAPZIMEOS DP is formulated in (b) (4) buffer (b) (4) with the target PRGN-2012 concentration of 5.0×10^{11} PU/mL. The DP is presented in a 2 mL vial for a minimum extractable volume of 1.0 mL. DP is (b) (4) stored at $\leq -60^\circ\text{C}$.

In this memo, lot release tests for the (b) (4) DP and their associated qualifications and validations were reviewed.

1. Purity by (b) (4)

DP)



The specification of purity is (b) (4) for (b) (4) DP.

Method

(b) (4)

12 Pages have been determined to be not releasable: (b)(4)

(b) (4)




6. pH (b) (4) DP)

The pH specifications are (b) (4) for DP.


Method

The analytical procedure of the pH determination for DP is provided in QV-TM-00023, which is according to (b) (4)



Method Verification

(b) (4)



Their pH results from Precigen lab were all in compliance with the proposed specifications.

Conclusion

Based on the information provided in the initial submission, this simple (b) (4) method was verified by the adequate supporting data in batch analyses for its intended purpose.


7. Appearance (DP)

The appearance specification is slightly opalescent to opalescent colorless liquid, and free of visible particulates for DP.

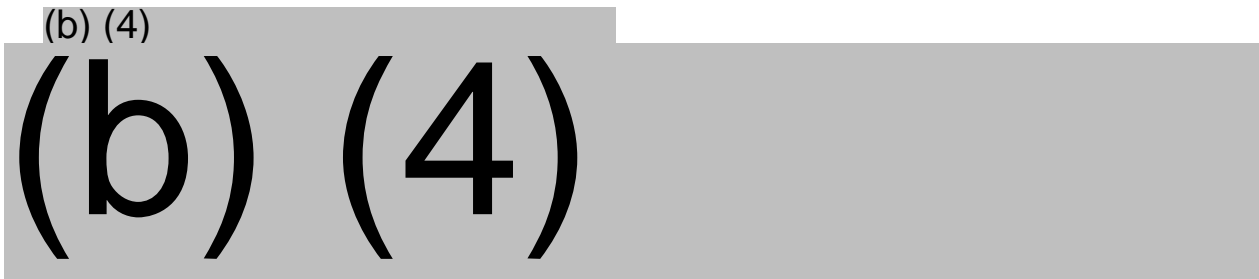
Method

The analytical procedure for appearance test was provided in QV-TM-00033. The method summary was also provided in 3.2.P.5 Control of Drug Product – 2. Analytical Procedures – Appearance.

(b) (4)



(b) (4)



An IR (IR #19) was sent to the firm to confirm that the proposed appearance specification of “Slightly Opalescent to Opalescent Colorless Liquid” includes a DP sample with the opalescence result from (b) (4). The firm stated that it is true based on development data using DP sample at the targeted concentration of 5×10^{11} PU/mL in amendment 26. The response is satisfactory.

Method Verification

Method verification report QCP-036 was submitted in Amendment 26 from Precigen lab upon this reviewer’s request. (b) (4) DP (b) (4) were used for the method verification. Precision and robustness were evaluated. (b) (4) analysts found that the (b) (4) samples were clear colorless liquid, and free of visible particles (b) (4) and DP samples were slightly opalescent to opalescent colorless liquid (b) (4) free of visible particles by using (b) (4) determinations of each sample. The firm

also stated that analysts were trained and qualified for visual acuity and color perception to ensure result consistency and reliability in Amendment 26. (b) (4) values were provided in Amendment 41 upon this reviewer's request. The responses are acceptable.

In 3.2.P.5.4 Batch Analyses, there are (b) (4) clinical process DP lots (b) (4) engineering and pre-PPQ DP lots, and (b) (4) PPQ DP lot. The appearance results were all in compliance with the proposed specification.

Conclusion

Based on the information provided in the initial submission and Amendments 26 and 41, appearance test was adequately verified for its intended purpose.

8. Volume in container (DP)

The specification of volume in container is (b) (4) 1 mL for DP.

Method

Volume in container is determined in accordance with (b) (4) for DP and the method used by Precigen lab is described in QV-TM-00051. (b) (4)

The SOP TS456004GMP used by (b) (4) is equivalent to that described above.

Method Verification

Method verification report VSR456004 from (b) (4) was submitted in Amendment 26 upon this reviewer's request. (b) (4)

(b) (4) which met the proposed specification of volume in container (b) (4) 1 mL. In 3.2.P.5.4 Batch Analyses, there are (b) (4) clinical process DP lots, (b) (4) engineering and pre-PPQ DP lots, and (b) (4) PPQ DP lot. The volume in container results obtained by (b) (4), which are all in compliance with the proposed specification.

Method verification report QV-RPT-00421 from Precigen lab was submitted in Amendment 41 upon this reviewer's request. The extractable volume was measured by (b) (4)

(b) (4) which met the proposed specification of (b) (4) 1 mL.

Conclusion

Based on the information provided in the initial submission and Amendments 26 and 41, this simple (b) (4) method is verified for its intended use by both Precigen lab (b) (4).

(b) (4)

[REDACTED]

[REDACTED]



[REDACTED]

[REDACTED]

[REDACTED]


[REDACTED]

(b) (4)




10. Particulates (DP)

(b) (4)



Method



(b) (4)



. The system suitability standard and acceptance criteria were provided in Amendment 26 upon this reviewer's request. Section 3.2.P.5.2 Control of Drug Product, Analytical Procedures was updated to include this critical information.

Method Verification

(b) (4)



(b) (4)

, which are all in compliance with the proposed specifications.

Conclusion

Based on the information provided in the initial submission and Amendment 26, this

(b) (4) method is verified for its intended use.