



MEMORANDUM

To: Administrative file for STN 125722

From: Noel Baichoo, Ph.D.
Laboratory of Biochemistry, Virology, and Immunochemistry (LBVI)
Division of Biological Standards and Quality Control (DBSQC)
Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

Through: Muhammad Shahabuddin, Ph.D.
Chief, LBVI/DBSQC/OCBQ/CBER/FDA

Kori Francis (Acting Division Director) for Maryna Eichelberger PhD.
Division Director, DBSQC/OCBQ/CBER/FDA

Applicant: PTC Therapeutics

Subject: Review of Analytical Methods used for determining (b) (4) purity for Eladocagene exuparvovec

Recommendation: Based on the data reviewed in this submission, the analytical methods and their validations are acceptable.

Summary:

This document constitutes the Primary Review Memo from DBSQC for the following analytical methods and their validation, as used for lot release.

1. Purity of (b) (4) Drug Product by (b) (4)
2. (b) (4) Drug Product by (b) (4)

Background:

On March 15, 2024, PTC Therapeutics Inc submitted a BLA (STN 125722) for Eladocagene exuparvovec for the treatment of patients with aromatic L-amino acid decarboxylase (AADC) deficiency.

The Drug Product (DP) is a recombinant adeno-associated virus serotype 2 (AAV2) capsid-based gene therapy vector. The vector is non replicating and contains a complementary DNA (cDNA) for the human dopa decarboxylase (hDDC) gene. When a cell is infected with the vector, transgene expression produces human L-amino acid

decarboxylase (hAADC) protein. This enzyme converts L-3,4-dihydroxyphenylalanine to dopamine. The DP is indicated for treatment of patients with AADC deficiency. The DP is administered by surgical infusion into the putamen of the brain. Patients receive a total dose of 1.8×10^{11} viral genomes (vg) delivered as four 80 μ L (0.45×10^{11} vg) infusions (2 per putamen).

(b) (4)

Documents Reviewed:

This is an electronic submission. Information submitted and reviewed includes:

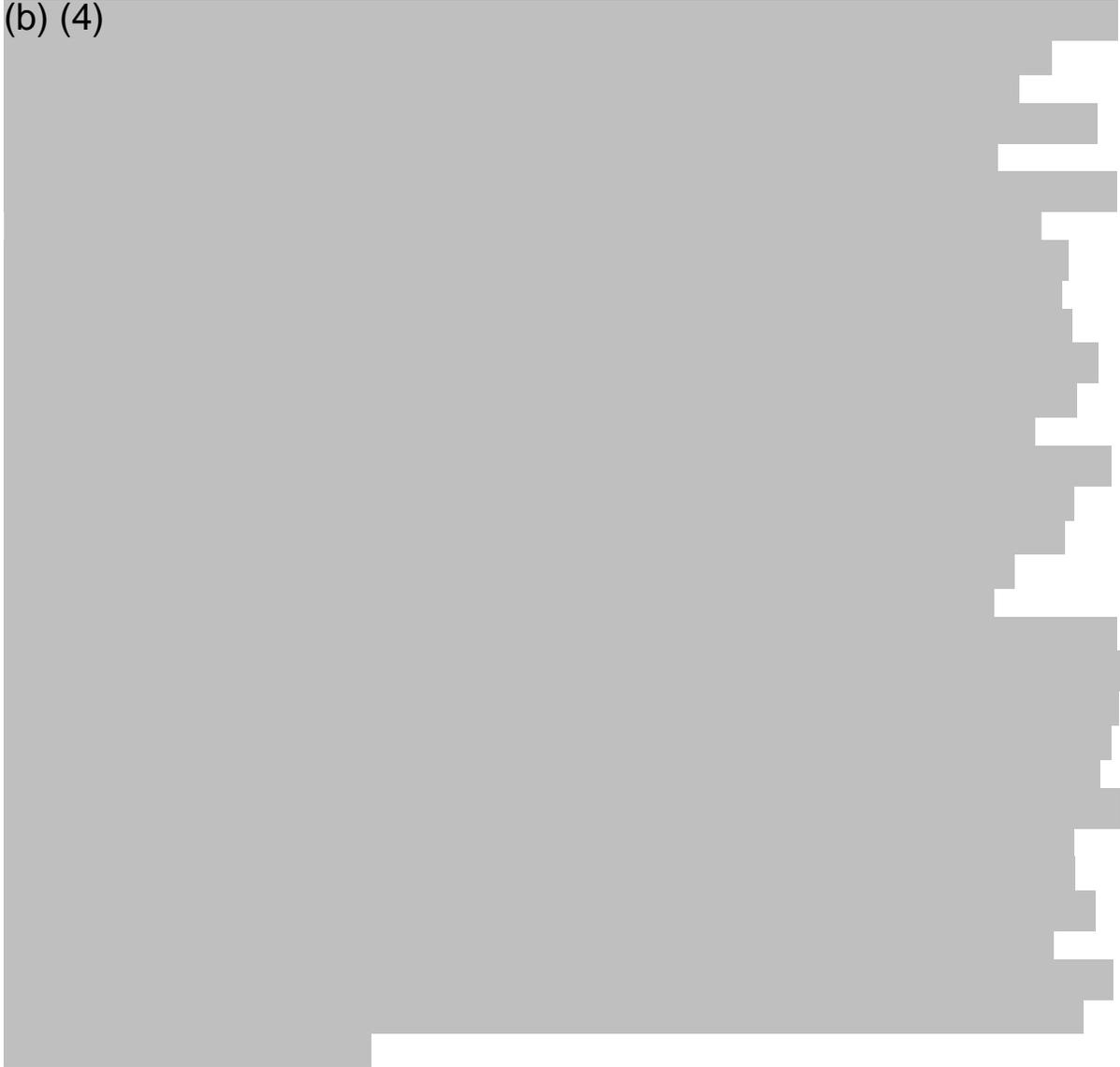
- 125722 - 3.2.R - R-2020-101: (b) (4) Pre-Validation Report
- 125722 - 3.2.R - 27QC066: Detection of (b) (4)
- 125722 - 3.2.R - (b) (4) : Analytical Method Validation Protocol for 27QC066: Detection of (b) (4)
- 125722 - 3.2.R - R-2019-140: Analytical Method Validation Report for 27QC066: Detection of (b) (4)
- 125722 - 3.2.S.4.2 - Analytical Procedures - Purity (b) (4)
- 125722 - 3.2.S.4.3 - Validation of Analytical Procedures - Purity (b) (4)
- 125722 - 3.2.R - 27QC067: Determination of (b) (4)
- 125722 - 3.2.S.4.2 - Analytical Procedures – (b) (4)
- 125722 - 3.2.S.4.3 - Validation of Analytical Procedures - (b) (4)
- 125722 - 3.2.R - (b) (4) : Validation Protocol for 27QC067: Determination of (b) (4)

- 125722 - 3.2.R - R-2019-133: Analytical Test Method Validation Report:
Determination of (b) (4)
- 125722 - 3.2.P.5.1 Specification(s)
- 125722 - 3.2.S.4.1 Specification(s)
- 125722 - 2.3.S.5 Reference Standards or Materials

1. Purity by (b) (4)

Method

(b) (4)



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

(b) (4)

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

3. Qualification of Reference Standards

Qualification of new reference standards is described in Section 3.2.S.5 Reference Standards or Materials. Qualification of the first reference standard, (b) (4) and the current reference standard, (b) (4) is also described. Qualification of (b) (4) was performed using acceptance criteria for DP (b) (4) release tests in addition to characterization tests not used for release. These tests included assays for (b) (4)

Qualification of future reference standards was described in Section 3.2.S.5. Future standards will be prepared from commercially manufactured batches. All tests of the new reference must meet release specifications at the time of testing. Additional characterization tests will be performed are for (b) (4)

Reference standards will be reevaluated (b) (4) for continued use. (b) (4) reevaluation consists of tests for (b) (4)

(b) (4) components of the qualification are acceptable, however the reviewer defers to the Product Office and statistician on requirements for other assays used in the requalification and reevaluation of the reference standards.

Conclusion: The assays for purity, and (b) (4) were adequately validated and are suitable for use in release testing.