



BLA STN Number: 125827.0 (Class I Resubmission) Serial No. 0127

Applicant: Replimune Inc.

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Through: Brian Stultz, Chief GTB3/DGT1/OGT/OTP/CBER
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Submission date: June 2, 2026

Action Due Date: August 2, 2026

Review Date: July 15, 2026

Executive Summary:

The resubmission addresses the clinical deficiency communicated in the CR letter FDA issued to the Applicant on April 10, 2026. A Cell Tissue & Gene Therapy Advisory Committee meeting is being scheduled for July 30, 2026. This review is to draft language for the PMC items to be included in the approval letter, should the BLA be approved.

Review of Information included in the Resubmission:

The resubmission contains no new CMC information. Minor changes were made to the USPI, but these do not affect CMC review or product quality.

The following PMC items were listed in Section 3 of 2.5 Clinical Overview Addendum 2 in the resubmission and extracted in its entirety below:

FDA PMC Request 1

Replimune commits to re-evaluate the [REDACTED] acceptance criterion for release testing of TUDRIQEV [REDACTED] based on manufacturing experience when data from [REDACTED] total PPQ and post-PPQ batches are available and revise the acceptance criterion if appropriate. The final re-evaluation report will be submitted as a "Postmarketing Study Commitment - [REDACTED] Acceptance Criterion Final Study Report." within 60 days

after release of the (b) (4) batch.

- Final study report submission date: July 31, 2028.

Replimune PMC Response 1

Replimune agrees with PMC #1 to re-evaluate the (b) (4) acceptance criterion and submit the final study report by 31 July 2028.

FDA PMC Request 2

Replimune commits to re-assess the (b) (4) based on data from (b) (4)

(b) (4) according to study protocol 1131-0157 Rev.01.

Replimune will submit the final study report as a “Postmarketing Study Commitment – (b) (4) Final Study Report”.

- Final study report submission date: December 31, 2026 (revised from July 31, 2026)

Replimune PMC Response 2

Replimune agrees with PMC #2 to re-assess the (b) (4) and submit the final study report by 31 December 2026.

FDA PMC Request 3

Replimune commits to conduct an in-use stability study to support a maximum hold duration in syringe for 2 hours after storage of thawed TUDRIQEV drug product under the worst case conditions according to Section 16.2 Table 6 of the approved USPI. Replimune will submit the final study report as a “Postmarketing Study Commitment – In-use Stability Final Study Report” and revise the hold duration in the syringe in the USPI as supported by the in-use stability data.

- Final study report submission date: December 31, 2026 (revised from July 31, 2026).

Replimune PMC Response 3

Replimune agrees with PMC #3 to conduct in-use stability study to support a maximum hold duration and to submit the final study report by 31 December 2026.

FDA PMC Request 4

Replimune commits to provide the leachables analytical data and associated toxicological assessment (for (b) (4) compounds) from an ongoing leachable assessment study with drug product stability lot(s) at 36-, 48- and (b) (4)-month timepoints.

- Final report of 36-month data submission date: 10 October 2026
- Final report of 48-month data submission date: 10 October 2027
- Final report of (b) (4)-month data submission date: 10 October 2028

Replimune PMC Response 4

Replimune agrees with PMC #4 to submit the final reports for 36-, 48-, and (b) (4)-month timepoints for both the nominal doses, 10^6 PFU/mL and 10^7 PFU/mL, on an annual basis, submitting the final report by 10 October 2028.

Reviewer's comments: The first three PMC items are the same as those listed in the original BLA submission with PMC #4 on leachables analytical data. New due dates are being proposed in line with the resubmission.

The following paragraphs are drafted for PMC items to be included in the approval letter if BLA is approved:

We acknowledge your written commitments as described in your letter of June 2, 2026 as outlined below:

PMC #1:

Replimune commits to re-evaluate the (b) (4) acceptance criterion for lot release testing of the TUDRIQEV (b) (4) based on manufacturing experience when data from (b) (4) total PPQ and post-PPQ batches are available and revise the acceptance criterion if appropriate. The final re-evaluation report will be submitted as a "Postmarketing Study Commitment – (b) (4) Acceptance Criterion Final Study Report" within 60 days after release of the (b) (4) batch.

Final study report submission date: July 31, 2028.

PMC #2:

Replimune commits to re-assess the (b) (4) based on data from (b) (4) according to study protocol 1131-0157 Rev.01. Replimune will submit the final study report as a "Postmarketing Study Commitment – (b) (4) Final Study Report" by December 31, 2026.

Final study report submission date: December 31, 2026

PMC #3:

Replimune commits to conduct an in-use stability study to support a maximum hold duration in the syringe for 2 hours after storage of thawed TUDRIQEV drug product under the worst-case conditions according to Section 16.2 Table 6 of the approved USPI. Replimune will submit the final study report as a "Postmarketing Study Commitment – In-use Stability Final Study Report" and revise the hold duration in the syringe in the USPI as supported by the in-use stability data.

Final study report submission date: December 31, 2026.

PMC #4:

Replimune commits to submitting the leachables analytical data and associated toxicological assessment (for (b) (4) compounds) from the ongoing leachable assessment

study with drug product stability lots at 36-, 48-, and (b) (4)-month timepoints. A final study report with data from all timepoints will be submitted in a “Postmarketing Study Commitment – Final Study Report” by October 10, 2028. However, if the leachable level at any timepoint is over the safety concern threshold, Replimune commits to submitting an interim report in a Product Correspondence as a “Postmarketing Study Commitment – Status Update” within three months.

Final study report submission date: October 10, 2028.

An updated PMR/PMC list was submitted on August 5, 2026 in Amendment 125 with revised timelines. The report dates for PMC #4 were changed to Oct 31, 2026, 2027, 2028 from Oct 10, 2026, 2027, and 2028. The revised PMC #4 sent by the Applicant is shown below:

Replimune commits to provide the leachables analytical data and associated toxicological assessment (for both [REDACTED] compounds) from ongoing leachable assessment study with drug product stability lot(s) at 24-, 36-, 48- and (b) (4)-month timepoints.

- Final report of 36-month data submission date: October 31 ,2026 (revised from October 10, 2026)
- Final report of 48-month data submission date: October 31 ,2026 (revised from October 10, 2026)
- Final report of (b) (4)-month data submission date: October 31 ,2026 (revised from October 10, 2026)

Reviewer's Comments: The sponsor removed the original request of submitting interim report if a test result is over the safety concern threshold. Since they plan to submit annual report for three consecutive years, removal of the requirement of interim report is acceptable. The change of report submission time from Oct 10 to Oct 31 for each reporting year is acceptable.

A change of “Table 6” to “Table 4” was made in PMC #3.