



DBSQ/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file STN 125868/0

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Sponsor: Orca Biotherapeutics Inc. (Orca Bio)

Subject: Review of Analytical Methods used for TREGZI ([REDACTED])

Recommendation: Approval

Executive Summary:

The analytical methods used for testing and release of TREGZI ([REDACTED]) DP and the Tcon diluent (dil) DP, were reviewed. All the methods were adequately described and shown to be suitable for their intended purpose.

1. (b) (4) of Tcon dil DP
2. (b) (4) of Tcon dil DP
3. Appearance of TREGZI DP and Tcon dil DP

Conclusion: The analytical methods and their validations and/or qualifications reviewed for the TREGZI ((b) (4) [REDACTED]) DP and Tcon dil DP were found to be adequate for their intended use.

Documents reviewed

Information in sections of the original submission that describe control of DS and DP (3.2.S.4 and 3.2.P.5, respectively), including descriptions of DS and DP specifications, analytical procedures of DS and DP and validation of these analytical procedures were reviewed. In addition, the responses to CBER's Information Requests (IRs) received on November 21, 2025 (Amendment #19), January 30, 2026 (Amendment #37), and February 26, 2026 (Amendment # 43), were also reviewed.

Background

On August 5, 2025, Orca Biotherapeutics submitted Biologics License Application (BLA) 125868 for TREGZI ([REDACTED]) an allogeneic stem cell and T-cell immunotherapy derived from an HLA-matched donor. The product is intended for adult patients with hematologic malignancies to enhance survival free from graft-versus-host disease (GVHD) when used alongside an appropriate conditioning regimen.

TREGZI DP consists of purified cellular components, including hematopoietic stem and progenitor cells (HSPCs), regulatory T cells (Tregs), conventional T cells (Tcons), and a Tcon dil DP. All cellular components are derived from apheresis starting material obtained from a human leukocyte antigen (HLA)–matched donor whose peripheral blood has been mobilized with granulocyte colony-stimulating factor (G-CSF). The Tcon dil DP is a sterile, (b) (4) solution composed of multiple electrolytes injection (MEI), Type I, (b) (4), and human serum albumin (HSA).

The HSPC DP and Treg DP are each formulated at an approximate volume of 100 mL and are shipped fresh for intravenous (IV) administration in their entirety on Day 0. The Tcon DP is formulated at an approximate volume of 15 mL and is cryopreserved for shipment. On Days +2 to +3, the Tcon DP is thawed, diluted with the Tcon dil DP, and prepared for infusion at the transplant center before being administered intravenously. This multi-component, staged administration approach reflects the complex nature of this personalized allogeneic immunotherapy designed to harness the therapeutic potential of multiple cell types in treating patients. TREGZI DP is a multicomponent DP

TREGZI DP	HSPC DP and Treg DP	Intravenous administration day 0
	Tcon DP diluted with Tcon diluent	Intravenous administration day 2 to 3

This review focuses on the qualification of the [REDACTED] and appearance tests as performed on TREGZI DP and Tcon dil, to indicate if the product matrix is suitable for testing using the intended test method.

Review Narrative

(b) (4)

(b) (4)



3. Appearance of TREGZI DP and Tcon dil DP

Introduction

Appearance testing for the TREGZI DP and the Tcon dil DP is performed by visual inspection using a liquid inspection viewer. All DP release specifications, as outlined in Section 3.2.P.5.1, are as follows:

1. Physical state: TREGZI DP and the Tcon dil DP are liquid.

2. Color: The Tcon dil DP is specified as colorless to yellow. TREGZI DP have variable color specifications, ranging from off-white and white to yellow, orange, or red.
3. Clarity: TREGZI DP may range from clear to opaque, while the Tcon dil DP must be clear.
4. Visible particulates: All three DPs and the Tcon dil DP must be free of visible foreign particulates.

Lot release testing for appearance is conducted at the Orca Bio facility in MP, CA.

Method:

Appearance testing for the TREGZI DP (Treg, HSPC, and Tcon) and the Tcon dil DP is conducted in accordance with (b) (4)

. A systematic approach was implemented to evaluate critical factors affecting visual inspection performance, including solution type, color, (b) (4), and container type. These factors were assessed by the qualified inspector under appropriate inspection conditions using (b) (4).

(b) (4)

Method Validation

Validation reports RPT-0422, RPT-0432, and RPT-0447 were generated for the appearance testing of TREGZI DP and the Tcon dil DP at the MP facility in CA, in accordance with validation protocols PRO-0094 and PRO-0103. The purpose of these protocols was to demonstrate that the manual visual inspection process can reliably and reproducibly detect predefined defects in TREGZI DP and the Tcon dil DP in a qualitative manner under controlled conditions during routine manufacturing operations. Detection of visible particles is inherently probabilistic and may be influenced by factors such as particle size, color, shape, and contrast with the solution and the container.

The acceptance criteria required a for defects, and each analyst was required to achieve an overall correct detection rate of (b) (4). (b) (4) analysts participated in the study over (b) (4) separate days, using multiple instruments and performing runs to assess repeatability and intermediate precision for physical state, color, clarity, and the presence of particulates.

One page has been determined to be not releasable: (b)(4)

(b) (4)

Conclusion:

The data provided adequately support validation of the appearance test for TREGZI DP and Tcon dil DP, at the Orca bio facility in MP, CA.