



**To:** Administrative File BLA 125706/0

**From:** Christine Harman, Lead CSO, CMC/Facilities, CBER/OCBQ/DMPQ/MRB2

**Through:** Anthony Lorenzo, Branch Chief, CBER/OCBQ/DMPQ/MRB2

**CC:** Matthew Klinker, Product Reviewer (Chair), CBER/OTP/OCTHT/DCT1  
Adriane Fisher, RPM, CBER/OTP/ORMRR/DRMRR1

**Applicant:** Mesoblast Inc. (Lic #2140)

**Product:** remestemcel-L (cryopreserved suspension of ceMSC)  
Route of Administration- intravenous

**Indication:** Treatment of Steroid Refractory acute Graft versus Host Disease (SR-aGvHD) in pediatric patients.

**Subject:** Complete Response (CR) Review: Review of the response to the CR letter item, pertaining to DMPQ issues.

**ADD:** August 2, 2023

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**Recommendation:**

Based on the information obtained during the pre-license inspection (PLI) of Lonza Bioscience performed May 11-19, 2023 to address the complete response item regarding conducting an inspection of the drug substance and drug product facility, approval is recommended provided that all Office of Therapeutic Products (OTP) issues have been resolved.

**Executive Summary**

Mesoblast, Inc. submitted a response received by CBER January 21, 2023 (eCTD 0065) to the complete response letter issued September 30, 2020 regarding BLA 125706/0 for the product remestemcel-L. Several CR issues were noted in the letter including an issue regarding not conducting a PLI of the facility due to deficiencies of data submitted to the submission. During the review of the CR response, a PLI of the facility, Lonza Bioscience Singapore Pte Ltd (FEI: 3009725845), located in Singapore, was conducted May 11-19, 2023. No major issues were identified, and no Form FDA 483 was issued. Based on the results of the PLI, performed to resolve one of the complete response issues regarding conducting an inspection, approval is recommended, provided that all OTP issues have been resolved.

**CR response Review Narrative**

This review specifically covers the Chemistry, Manufacturing and Controls CR item #2 noted as follows:

**2. Due to the inadequacy of the data submitted to support approval, the agency did not conduct a pre-license inspection of your manufacturing facility. This inspection will need to be performed after the agency receives a complete response with adequate data to address the deficiencies identified in this letter (21 CFR 601.3(a)(2)).**

Response for CR item #2: A PLI of the Lonza Bioscience facility located in Singapore was conducted May 11-19, 2023. The inspection coverage included evaluation of the facilities, equipment, utilities and processes associated with the DS and DP manufacturing. The inspection team reviewed the documents related to facility and equipment qualification, process validation, environmental monitoring, quality systems, laboratory controls, production, computer systems, inventory system, control of materials, components and starting materials, management of workflow, training of operators, etc. In addition, the inspection team observed critical activities related to the production of remestemcel-L including passages, harvest, filling, cryopreservation, packaging, storage and QC testing.

At the conclusion of the inspection, there were several items of concern discussed with the firm; however, no major issues were noted and no Form FDA 483 was issued. For details of the inspection and coverage, please refer to the Establishment Inspection Report (EIR). The classification of the inspection is currently pending; however, since no Form FDA 483 was issued, the inspection will be classified as No Action Indicated (NAI).

**Reviewer Comment:** *As the inspection did not uncover any significant issues in manufacturing the remestemcel-L product; the Lonza Bioscience facility located in Singapore appears acceptable to support approval of BLA 125706/0.*