U.S. FOOD & DRUG ADMINISTRATION

Research

Center for Biologics Evaluation and

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DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file: STN 125738/0

From:

Reviewer	Role	Date finalized	Stamp	Supervisor	Stamp
Salil K Ghosh, Ph. D	Lead Reviewer			Tao Pan, Ph. D.	
Simleen Kaur, M.S.	Reviewer			James L, Kenney, D.Sc.	

Through Maryna Eichelberger, Ph.D.
Division Director, DBSQC/OCBQ

Applicant: Gamida Cell Ltd. (Gamida)

Subject: Lot-release test methods and their validations for the (b) (4) (omidubicel) drug product (DP)

Recommendation: Approval

Executive Summary:
The following analytical methods used for release of cultured fraction (CF), non-cultured fraction (NF) and infusion solution (IS) for (b) (4) and the associated analytic method validations or qualifications, were reviewed:

1. Sterility (CF, NF and IS) (Simleen Kaur)
2. Bacterial Endotoxin Test (CF, NF and IS) (Simleen Kaur)
3. Rapid Contamination Test (CF only) (Simleen Kaur)
4. Mycoplasma (CF only) (Simleen Kaur)
5. Appearance (CF, IS and NF) (Salil Ghosh)
6. Percent human serum albumin (HSA) and related substances (IS) (Salil Ghosh)
7. Identity of HSA (IS) (Salil Ghosh)

8. Identity of Dextran (IS) (Salil Ghosh)
9. Determination of (b) (4) (IS) (Salil Ghosh)
10. Determination of (b) (4) (IS) (Salil Ghosh)
11. Determination of (b) (4) (IS) (Salil Ghosh)

Conclusion: The analytical methods and their qualifications reviewed for (b) (4) CF, NF and IS were found to be adequate for their intended use.

Documents Reviewed
Information in sections of the original submission that describe control of Drug Substance (DS) (3.2.S.4) and Drug Product (DP) (3.2.P.5), including descriptions of DS and DP specifications, analytical procedures of DS and DP and qualifications of these analytical procedures were reviewed.

Background:
A new BLA (125738/0) was received on 31 May 2022 for Omidubicel; it is an allogeneic advanced cellular therapy for the treatment of patients with hematologic malignancies in need of a hematopoietic stem cell transplant. Omidubicel consists of expanded hematopoietic stem cells (Cultured Fraction, CF) and differentiated immune cells (Non-cultured Fraction, NF); both fractions derived from the same umbilical cord blood unit are cryopreserved at the end of their manufacturing process. Omidubicel DP is thawed and diluted before infusion using the Infusion Solution (IS), the Infusion solution contains 8% w/v HSA and 6.8% dextran-40, and is diluted with diluent and placebo solution to adjust the concentration.

1. **Sterility Method**

(b) (4)

Sterility Test Qualification

(b) (4)

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(b) (4)

Conclusion

The method suitability tests were performed and compliant with (b) (4) and the test results indicate there is no product inhibition on microorganism growth, thus indicating the (b) (4) method for CF and NF and (b) (4) method for IS are appropriate under the actual conditions of use.

2 Bacterial Endotoxin Testing (BET) Method

(b) (4)

Bacterial Endotoxin Test Qualification

(b) (4)

(b) (4)

Conclusion

The method suitability tests were performed and compliant with (b) (4) and the test results indicate there is no product interference from CF, NF and IS test samples, thus indicating the (b) (4) test method is appropriate under the actual conditions of use.

3 Rapid Contamination Test Method

(b) (4)

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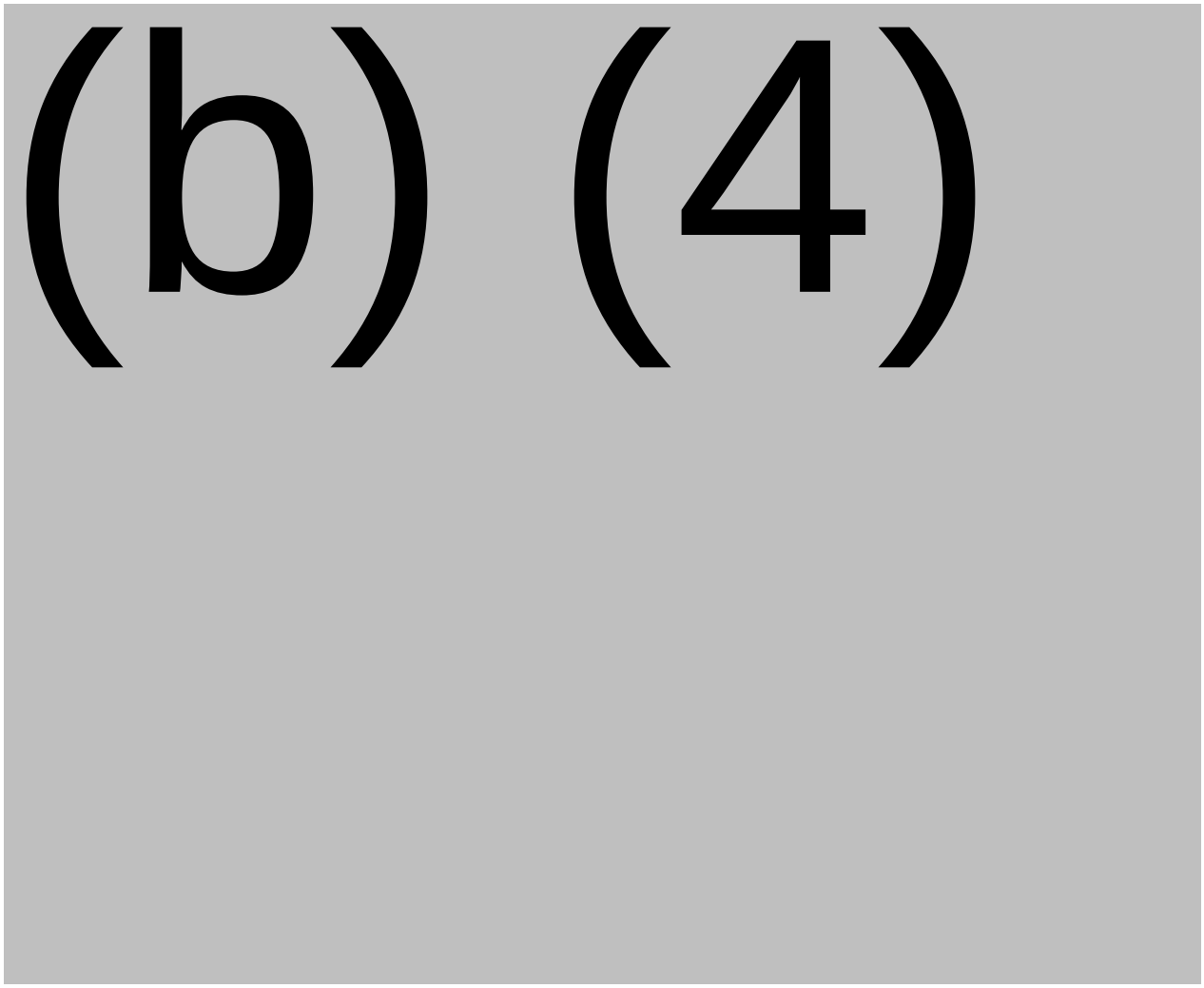
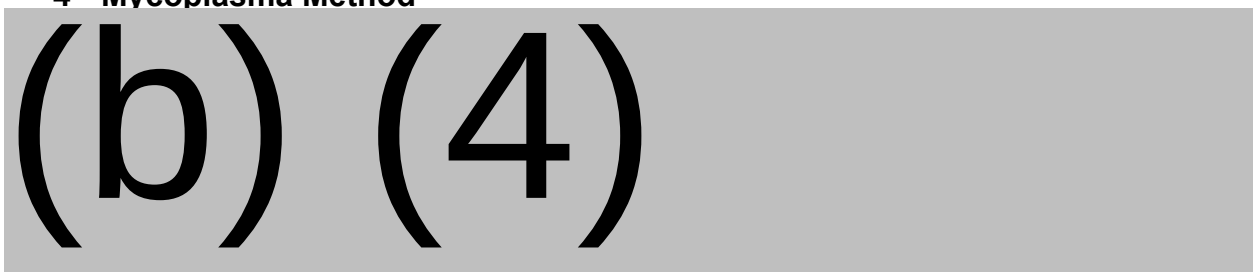


Conclusion

The LOD sensitivity did not meet (b) (4) requirement for most of the microorganism tested. It was discussed with the product office and found acceptable because rapid contamination test is used as a screening test prior to product infusion and a compendial sterility is performed on the product as part of the final release. The rapid contamination test performed on CF samples was validated in accordance with (b) (4) by demonstrating the tested product is suitable for the intended test method.

4 Mycoplasma Method



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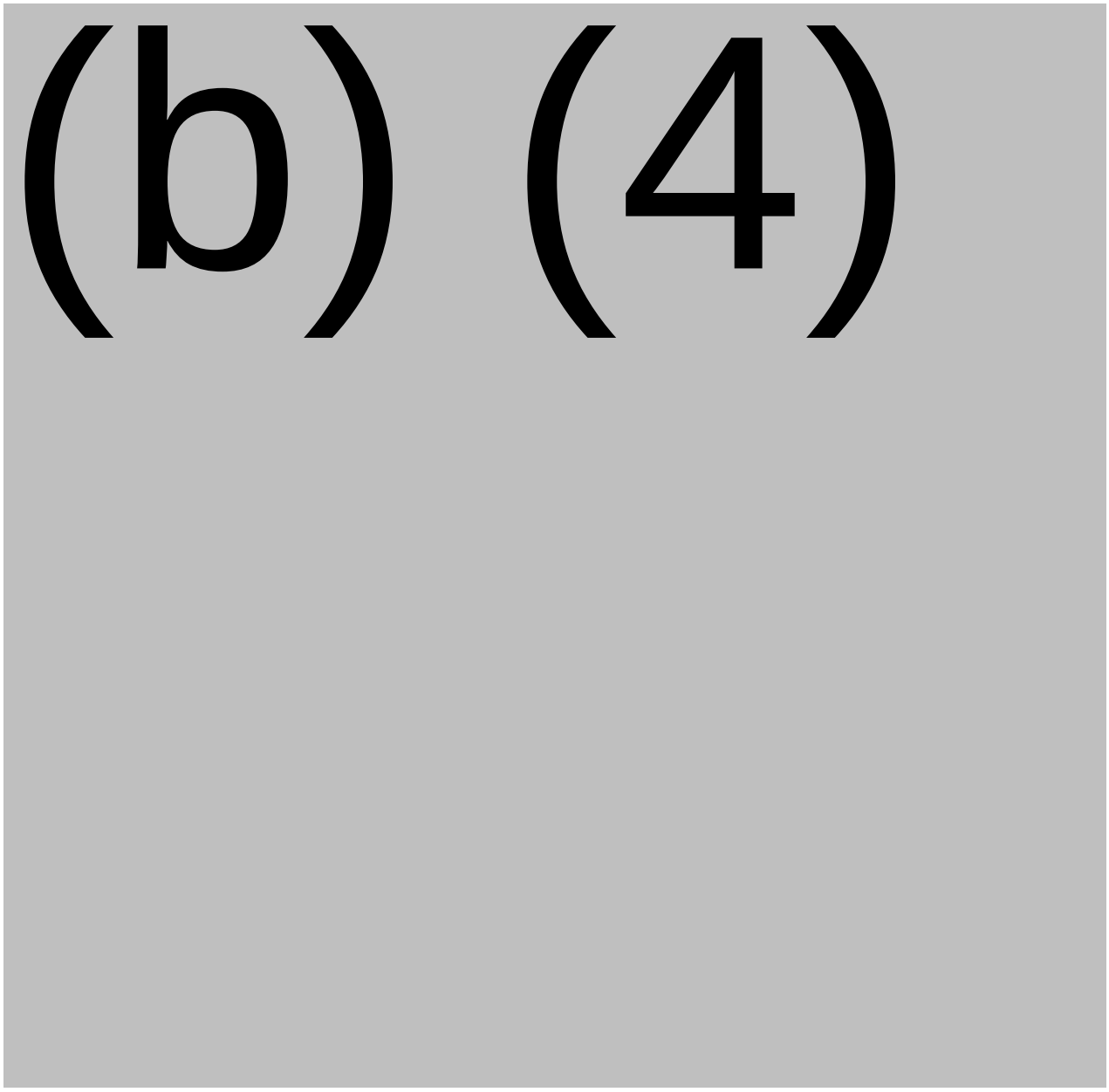

Conclusion

The (b) (4) based mycoplasma test method performed on (b) (4) harvest was validated in accordance with (b) (4) by demonstrating the tested product is suitable for the intended test method. Gamida demonstrated the test method provides assurance of tested matrix safety and purity that is equal to, or better than, the assurance of the current compendial method.

5 Appearance (CF, IS and NF)

The appearance test of CF, IS and NF is conducted by visual inspection through a liquid inspection viewer. The specification for CF is yellowish suspension, essentially free of visible white clumps and foreign particulates; for (b) (4)

solution, essentially free of visible particulates; and for NF is reddish suspension, essentially free of visible white clumps and foreign particulates. This test was performed at Gamida Cell's manufacturing facility in Jerusalem (GSI) concomitantly to (b) (4) manufacturing facility located in (b) (4) The validation was performed at the (b) (4) Gamida Cell manufacturing facility built in Kiryat Gat, Israel (KGI).

Method:

(b) (4)

Method validation:

(b) (4)

Conclusion:
The appearance assay is suitable for CF, IS and NF lot release testing.

6 Percent HSA and related substances (IS)

(b) (4)

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(b) (4)

Conclusion

The validation data show that the (b) (4) method is suitable for determining percent HSA and HSA related substances.

7 Identity of HSA (IS)

The identity of HSA is determined by (b) (4) This test was performed at GSI concomitantly to (b) (4) The validation was performed at (b) (4) Gamida Cell manufacturing facility at KGI.

(b) (4)

(b) (4)

Conclusion

The validation data show that (b) (4) are suitable for determining identity of HSA in IS.

8 **Identity of Dextran (IS)**

The specification of dextran identity by (b) (4) method is that (b) (4) (b) (4) should correspond to that of a standard solution of dextran-40. This test was performed at GSI concomitantly to (b) (4) The validation was performed at (b) (4) Gamida Cell manufacturing facility at KGI.

Method

(b) (4)

Method validation

(b) (4)

Conclusion

The method is suitable for identification of dextran-40 in IS.

(b) (4)

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