DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

CBER REGULATORY REVIEW MEMORANDUM

Date 10 March, 2020

From Simleen Kaur, M.S.
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Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

To Biological License application (BLA) Submission Tracking Number 125703/0

Subject BLA: Review of Sterility, Mycoplasma, and Endotoxin Test Method Qualifications; and (b) (4) Sterility and (b) (4) Mycoplasma Test Method Validations for KTE-X19

Through James L. Kenney, D.Sc., Chief, LMIVTS
Maryna Eichelberger, Ph.D., Director, DBSQC

Applicant Kite Pharma (Kite)

Product KTE-X19

Biological License Application Submission Tracking Number (STN) 125703/0

Submission Received by CBER 11 December, 2019

Review Completed 10 March, 2020

Material Reviewed
Method qualifications for 1) sterility; 2) mycoplasma; and 3) bacterial endotoxin test (BET); and method validations for 1) (b) (4) sterility test and 2) (b) (4) for the detection of mycoplasma. In addition, information request response received 30 January, 2020 was also reviewed.

Executive Summary

After a thorough review of this BLA, this reviewer finds Kite's (b) (4) sterility test method and (b) (4) mycoplasma test method using (b) (4) performed on the KTE-X19 drug product (DP) were validated in accordance with (b) (4) , respectively, by demonstrating the methods are suitable under the actual conditions of use. Kite demonstrated these test methods provide assurance of tested matrix safety and purity that is equal to, or greater, than the assurance of the current compendial methods. Also, sterility and mycoplasma using (b) (4) method (b) (4) , and bacterial endotoxin (b) (4) DP) test methods were qualified in accordance with (b) (4) respectively, by demonstrating they are suitable under the actual conditions of use.

Background

On 11 December, 2019, Kite submitted this BLA for KTE-X19 for the treatment of adult patients with relapsed/refractory mantle cell lymphoma.

KTE-X19 consists of autologous T cells that have been genetically modified ex vivo to express a chimeric antigen receptor (CAR) to target CD19 on the cell surface of malignant B cells. The active substance of KTE-X19 is composed of a patient's T cells that has undergone ex vivo T cell activation, gene transfer by replication-deficient retroviral vector (b) (4) vector), and expansion. These transduced T cells are then formulated in a cryopreservation medium suitable for infusion. KTE-X19 is supplied cryopreserved at a temperature of ≤ -150°C in cryostorage bags. Each bag of KTE-X19 is filled to deliver a dose of (b) (4) anti-CD19 CAR T cells/kg of patient weight (maximum allowable dose: 2.0×10^8 anti-CD19 CAR T cells based on patient weight ≥ 100kg) in a nominal volume of 68 mL.

The (b) (4) vector is manufactured at (b) (4) and is tested for (b) (4) . The KTE-X19, final product is manufactured by Kite, CA, USA. The manufacturing process is (b) (4) The KTE-X19 DP is tested for sterility using (b) (4) system, mycoplasma using (b) (4) and bacterial endotoxin.

The DBSQC reviews BLAs and their supplements to ensure analytical methods are appropriate, properly validated and the product matrix is suitable for the intended test method. DBSQC also reviews endotoxin release specifications to ensure they reflect process capability and are regulatory compliant. These review activities support DBSQC's lot-release mission: the confirmatory testing of submitted product samples; review of manufacturers' lot-release protocols to ensure biological products are released according to licensed test methods and product specifications. In addition, DBSQC has subject matter expertise in mycoplasma method qualification, antimicrobial effectiveness and other test methods. Therefore, this review will focus on the validation of the (b) (4) system for sterility and (b) (4) for mycoplasma testing for DP, to determine if the methods are suitable under the actual conditions of use and if these methods provide assurance equal to or greater than the

compendial methods. In addition, the qualification of (b) (4) vector to indicate if the methods are suitable under the actual conditions of use.

(b) (4)

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(b) (4)

4 pages determined to be not releasable: (b)(4)

(b) (4)

(b) (4)

Conclusions

After a thorough review of the information submitted in this BLA, this reviewer finds Kite's (b) (4) sterility and the (b) (4) mycoplasma test method performed on DP were validated in accordance with (b) (4), respectively, and demonstrated that these methods are suitable under their actual conditions of use. Kite also demonstrated these test methods provide assurance of tested matrix safety and purity that is equal to, or greater, than the assurance of the current compendial methods. In addition, the sterility, mycoplasma using the (b) (4), and bacterial endotoxin (b) (4) DP) test methods were qualified in accordance with (b) (4) respectively, by demonstrating the methods are suitable under the actual conditions of use. Therefore, this reviewer finds these methods acceptable for their intended purpose and recommends their approval.