



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To The file: STN 125820

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Applicant Bavarian Nordic A/S (Bavarian)

Subject Review of Sterility and Endotoxin Analytical Methods for
Chikungunya Vaccine, Recombinant (VIMKUNYA)

Recommendation: Approval

Executive Summary:

The sterility and endotoxin analytical methods used for testing and release of VIMKUNYA and the associated analytic method qualifications or validations, were reviewed. The assays were adequately described and shown to be suitable for their intended purpose.

Conclusion: The analytical methods and their qualifications or validations reviewed for VIMKUNYA (b) (4) drug product were found to be adequate for their intended use.

Documents Reviewed

Information in sections of the original submission that describe control of (b) (4) (b) (4) Drug Product (DP) (3.2.S.4 and 3.2.P.5, respectively), including descriptions of (b) (4) DP specifications, their analytical procedures, and their method qualifications or validation were reviewed. In addition, responses to CBER's Information Requests (IRs) received on September 11, 2024 (Amendment #17), November 18, 2024 (Amendment #41), and December 13, 2024 (Amendment #49) were also reviewed as mentioned below.

1. Sterility Method (b) (4) DP)

Introduction

Sterility testing for (b) (4) DP is performed at contracting laboratories: (b) (4)
 (b) (4) DP at (b) (4)
 (b) (4) Acceptance criterion of 'No Growth'
 must be met for the release of (b) (4) DP.

Method

(b) (4)

The submission lacked sufficient information to complete review of sterility test, therefore, an IR was sent requesting missing information, and a response was received on September 11, 2024 (Amendment #17), which was found acceptable and explained below.

Sterility Test Qualification

(b) (4) and (b) (4) qualified their (b) (4) method for testing
 (b) (4) DP by performing bacteriostatic and fungistatic qualification studies
 using (b) (4) indicator microorganisms (i.e., (b) (4))
 on (b) (4) lots of:

- (b) (4) at (b) (4)
- (b) (4) at (b) (4) and
- DP (b) (4) at (b) (4)

Bavarian stated that their representative environmental isolates (b) (4)
 (b) (4) from their manufacturing sites:
 Bavarian Nordic (b) (4) in (b) (4) and/or (b) (4)
 in (b) (4) were not tested during the method qualification study, as
 their morphology and characteristics are similar to the (b) (4) indicator microorganisms
 and CBER found this acceptable.

The test for each microorganism was performed using (b) (4) of lots mentioned above
 and (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 inhibition of microorganism growth, thus indicating the (b) (4) sterility test method is appropriate under the actual conditions of use.

2. Endotoxin Methods

Introduction

Endotoxin testing for (b) (4) on DP is performed at (b) (4). A specification of (b) (4) must be met for release of (b) (4) DP.

Methods

The (b) (4) BET is a (b) (4) assay where (b) (4)
(b) (4)

The (b) (4) BET is a (b) (4) assay that is based on the (b) (4)

The method is described in more detail below together with the tests performed to determine the suitability of the test method for its intended use.

The endotoxin tests lacked sufficient information to complete review of the method qualification. In addition, endotoxin specification of (b) (4) for VIMKUNYA (b) (4)

(b) (4) DP was determined to be high when results of different batches tested as (b) (4) for DP. Therefore, IRs were sent requesting missing information and to either update their endotoxin specifications to better reflect their production process capabilities or to set alert limits so their production process can be better tracked and trended. Bavarian provided the requested information on September 11, 2024 (Amendment #17), November 18, 2024 (Amendment #41), and December 13, 2024 (Amendment #49), which were reviewed as part of the endotoxin tests below and Bavarian set Alert limits of (b) (4) (b) (4) for (b) (4) DP, (b) (4)

(b) (4)

(b) (4) -BET Qualification for DP

(b) (4) qualified their (b) (4) -BET method for DP using (b) (4) lots (b) (4) (b) (4) The (b) (4) of DP was calculated to be (b) (4) by (b) (4)

The test for (b) (4) was performed on (b) (4) lots of DP mentioned above at (b) (4) The positive product control (b) (4) recoveries were (b) (4) (acceptance criterion is (b) (4) The (b) (4) concentration results for all DP samples during the method qualification testing were all within the release specification of (b) (4) and were found acceptable.

Conclusion

The method suitability tests for DP were performed and compliant with (b) (4) and all test results indicate there is no product interference from (b) (4) DP

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test samples, thus indicating the BET endotoxin test methods are appropriate under the actual conditions of use.