DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Biological Standards & Quality Control, Office of Compliance & Biologics Quality,
Center for Biologics Evaluation & Research, Food & Drug Administration, 1401 Rockville Pike, Rockville, MD 20852

MEMORANDUM 11 July, 2013

To To the File for STN 125478/0

From Dr. Claire H. Wernly,

Through Dr. James L. Kenney, Lab Chief (acting)
Laboratory of Microbiology, *In-vivo* Testing and Standards

Dr. William M. McCormick, Director
DBSQC/OCBQ/CBER/FDA

Subject BLA: Review of Microbiological Test Validations for MK-3641 (Standardized Allergenic Extract, Short Ragweed *[Ambrosia artemisiifolia]*).

Conclusion

After a thorough review of this Biological License Application (BLA), this reviewer finds the microbial enumeration test and tests for specified microorganisms were qualified in accordance with (b) (4) (respectively) by demonstrating that the product matrix for MK-3641 is suitable for these intended test methods. Therefore, based on the review of the BLA and the response to CBER's Information Request, I recommend approval of this BLA.

Background

MK-3641 (proposed proprietary name: RAGWITEK (Standardized Allergenic Extract, Short Ragweed *[Ambrosia artemisiifolia]*)) sublingual tablets are manufactured for Merck Sharp and Dohme Corp. (Merck) in (b) (4) by Catalent UK Swindon (b) (4) . (Catalent), in Wiltshire, United Kingdom. MK-3641 is indicated as immunotherapy for diagnosed ragweed pollen induced allergic rhinitis, with or without conjunctivitis, in adults 18 years of age and older. Each tablet of MK-3641 contains 12 Amb a 1-U (*Ambrosia artemisiifolia* major antigen no.1) of ragweed pollen extract and is designed to rapidly disintegrate under the tongue. Catalent manufactures the drug product, performs microbiological examination release testing, packages the tablets in final container blister packs (each containing 10 tablets) before they are (b) (4) , (b) (4) . Other ingredients include gelatin and mannitol as (b) (4) for (b) (4) , sodium hydroxide used to (b) (4) and purified water (which is (b) (4)).

The Division of Biological Standards and Quality Control (DBSQC) reviews BLAs and their supplements to ensure product methods are appropriately validated, product matrix is suitable for the intended test method, and release specifications reflect process capability and meet regulatory compliance. These review activities support DBSQC's lot-release mission, which is the confirmatory testing of submitted product samples and review of manufacturers' lot-release protocols to ensure they are released according to licensed test methods and product specifications. Therefore, this review will focus on reviewing the qualification reports for their microbial enumeration test and tests for specified microorganisms to determine if the MK-3641 drug product matrix is suitable for these intended tests methods.

Review

The microbial enumeration and microbiological examination test method validations were performed using 12 Amb a 1-U of drug product, Merck's currently highest strength of manufactured drug product. Test method validations were performed using (b) (4) batches of finished product (batch numbers: (b) (4)).

(b) (4)

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(b) (4)

(b) (4)

Microbial Examination: Absence of Specified Microorganisms

MK-3641 is defined as an oromucosal product, as the recipient is instructed not to swallow the tablet; therefore, (b) (4) provides guidance on specified microorganism acceptance criteria,

for which the acceptance criteria for this test were set. The acceptance criterion is the absence of (b) (4).

Microbial Examination Test Qualification

(b) (4)

(b) (4)

No protocol deviations occurred during the execution of this validation protocol. Enumeration of the inoculum CFU counts for all microorganisms were between the required (b) (4) range. The uninoculated sample control plates showed no growth as well as the media control plates. This test was performed and compliant with (b) (4) and the recovery of each challenge microorganism indicated there was no product inhibition of microbial growth. Therefore, this test method is suitable for its intended purpose.

Summary

After a thorough review, this reviewer concludes that Catalent's microbial enumeration test and microbiological examination test for the absence of specified microorganisms were performed and qualified in accordance with (b) (4) respectively. These qualification studies indicate the product matrix for MK-3641 does not inhibit the growth of the indicator microorganisms; therefore, the product matrix is suitable for these intended test methods.