



CBER REGULATORY REVIEW MEMORANDUM

Date 25 January, 2017

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Division of Biological Standards and Quality Control (DBSQC)
Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

To Biologics License Application Submission Tracking Number # 125592/0

Subject BLA: Review of Microbial Enumeration Test and Absence of Specified Microorganisms Method Qualifications for MK-8237 sublingual tablet (House Dust Mites Allergen Extract)

Through James L. Kenney, D. Sc. Chief, LMIVTS
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Applicant Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. (Merck)

Product MK-8237 sublingual tablets (House Dust Mites [HDM] Allergen Extract)

Submission Received by CBER 9 February, 2016

Review Completed 25 January, 2017

Material Reviewed

Method qualifications for: 1) microbial enumeration and 2) absence of specified microorganisms performed on the (b) (4) drug product (DP): Merck's responses to CBER's Information Request (IR) received on 14 September, 22 December of 2016, and 13 January of 2017.

Executive Summary

After a thorough review of this BLA, and the responses to CBER's IR (amendments 125592/0/21, 125592/0/43 and 125592/0/51), this reviewer finds Merck's microbial enumeration and absence of specified microorganisms tests were qualified in accordance with (b) (4) respectively.

Background

On 9 February, 2016, Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., (Merck) submitted this BLA for a house dust mites (HDM) allergen extract formulated as a sublingual immunotherapy tablets (MK-8237) indicated as immunotherapy for the treatment of HDM-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive skin test or *in-vitro* testing for *Dermatophagoides farina* (*Der far*) or *Dermatophagoides pteronyssinus* (*Der pte*) immunoglobulin-E (IgE) antibodies. The MK-8237 tablet is indicated for use in adults 18 years through 65 years of age.

The MK-8237 DP is manufactured from two separate DSs, each of which consists of a (b) (4) two cultivated HDM species *Der far* and *Der pte*. The HDM tablet is a non-sterile sublingual orally disintegrating tablet, lyophilized, white to off-white, and debossed. Each MK-8237 tablet consists of 12 SQ-HDM units (potency/strength). (b) (4)

The manufacture and testing of the DSs are performed by (b) (4), a contract manufacturer. The MK-8237 sublingual tablet is manufactured for Merck by Catalent Pharma Solutions Limited (Catalent), located in Blagrove, Swindon, United Kingdom. Catalent formulates/manufactures the DP, performs microbiological examination release testing and packages the tablets in final container blister packs (each containing 10 tablets), before they are shipped to Merck for secondary packaging.

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 release specifications for microbial and endotoxin testing to ensure they 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 biological products 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 test for specified microorganisms to ensure the MK-8237 product matrix is suitable for these intended test methods.

Review

The microbial enumeration and absence of specified microorganisms test method qualifications were performed using (b) (4), which has same formulation and manufacturing process as the MK-8237 product (Amendment: 125592/0/51).

Microbial Enumeration Test

Catalent performs the microbial enumeration test using (b) (4)

This reviewer finds their proposed acceptance criterion acceptable.

Microbial Enumeration Test Qualification for (b) (4) DP

The microbial enumeration test method qualification for (b) (4)

(b) (4)

The qualification test involved (b) (4)

[Redacted]

The microbial enumeration results performed on (b) (4)

. This reviewer finds their proposed acceptance criterion acceptable.

In addition, a few testing deviations were noted in the (b) (4) test results, there were reviewed and found to have no impact on their (b) (4) microbial enumeration qualification results.

Microbiological Examination: Absence of Specified Microorganisms

Catalent qualified their microbiological quality tests for (b) (4)

[Redacted]

(b) (4)

[Redacted text block]

Conclusion

After a thorough review of the information submitted in this BLA, this reviewer finds the Merck’s MK-8237 (b) (4) (b) (4) DP matrixes are suitable for testing using their microbial enumeration test method and their DP matrix is suitable for testing using their absence of specified microorganisms test method, as these tests were qualified and performed in accordance with (b) (4) [Redacted] respectively. Therefore, this reviewer finds these methods acceptable for their intended purpose.