DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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

MEMORANDUM 25 May, 2013

To The Administrative file for STN 125473/0

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

Cc Dr. William M. McCormick, Director
Division of Biological Standards and Quality Control (DBSQC)

Subject BLA: Review of Microbiological Test Validations for GRASTEK®

Conclusion

After a through 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) by showing the GRASTEK® product matrix is suitable for these intended test methods. Therefore based on the scope of this review, I recommend approval of this BLA.

Background

GRASTEK® (Standardized Allergenic Extract, Timothy Grass [Phleum pratense]) sublingual tablets are manufactured for Merck Sharp and Dohme Corp. (Merck) in (b)(4), by Catalent UK Swindon Zydis Ltd. (Catalent), in Willshire United Kingdom. GRASTEK is indicated as an allergy treatment to assist the immune system in treating the underlying causes of grass allergy. The GRASTEK® tablet is designed to rapidly disintegrate under the tongue, thereby releasing 2800 bioequivalent allergy units of standardized Phleum pretense grass pollen extract. 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 shipped to Merck in (b)(4), for secondary packaging. Other ingredients include gelatin and mannitol as (b)(4) sodium hydroxide used to (b)(4), and purified water (which is (b)(4).

The DBSQC reviews BLAs and their supplements to insure 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 insure biological products are released according to their 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 GRASTEK® drug product matrix is suitable for these intended test methods.

Review

The microbial enumeration and microbiological examination test method validations were performed using GRAZAX® (75,000 SQ-T), Merck's highest strength currently manufactured drug product, which is the European tread name for the same GRASTEK® drug product. Test method validations were performed using three batches of GRAZAX® (batch numbers: (b)(4) . Complete testing was performed on each batch, so each test method validation report had three sets of resultant data.

Microbial Enumeration Test

Catalent performs the microbial enumeration test using (b) (4) This reviewer finds their proposed acceptance criterion acceptable.

Microbial Enumeration Test Qualification

Catalent performed their microbial enumeration test method validation using three batches of GRAZAX® to demonstrate their GRASTEK® product matrix does not inhibit bacterial and fungal growth under aerobic conditions.

(b) (4)

Two protocol deviations occurred during the execution of this validation protocol; (b)(4)

. Therefore, this test method is suitable for its intended purpose.

Microbiological Examination: Absence of Specified Microorganisms

The GRASTEK® drug product is defined as an oromucosal product, as the recipient is instructed not to swallow the tablet; therefore, (b)(4)

Microbiological Examination Test Qualification

(b)(4)

(b)(4)

There was one protocol deviation, (b)(4) and the test was repeated correctly; and the results were satisfactory.

(b)(4) . Therefore, this test method is suitable for its intended purpose.

Conformance Batch Test Results

A total of (b)(4) conformance batches (i.e., (b)(4)) were manufactured and tested at Catalent. All conformance batch test results met their specifications, with their microbial enumeration (b)(4) results all being (b)(4) , and their microbiological safety test results showing an absence of specified microorganisms (i.e. (b)(4)).

Summary

After a through review, the 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) . These qualification studies indicate the GRASTEK® drug product does not inhibit growth of the indicator microorganisms required to demonstrate the product matrix is suitable for its intended purpose.