

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Food and Drug Administration  
Center for Biologics Evaluation and Research

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DATE November 21, 2013

FROM Lillian Ortega, Bioresearch Monitoring, HFM-664  
Division of Inspections and Surveillance  
Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Bioresearch Monitoring Branch Chief, HFM-664

TO Jon Daugherty, HFM-481, Chairperson  
Ronald Rabin, HFM-422, Clinical Reviewer  
Rana Chattopadhyay, HFN-481, RPM  
Juan Lacayo, HFM- 481, RPM

SUBJECT Bioresearch Monitoring Final Review Memo  
BLA/STN: 125473/0  
Sponsor: Merck Sharp & Dohme Corp  
Product: GRASTEK [Standardized Allergenic Extract, Timothy Grass (Phleum pratense) extract]

SUMMARY STATEMENT

The results of Bioresearch Monitoring inspections of protocol P08067 at six (6) clinical investigator sites did not reveal problems that impact the data submitted in the application.

PROTOCOL AUDITED

*P08067: Phase III A Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study Evaluating the Efficacy and Safety of Grass (Phleum pratense) Sublingual Tablet (MK-7243/SCH 697243) in Subjects Between 5 and 65 Years of Age, with a History of Grass Pollen-Induced Rhinoconjunctivitis, With or Without Asthma.*

BACKGROUND

There were five domestic and one foreign clinical investigator (CI) inspections performed in support of the Biologics License Application (BLA) 125473/0 and were conducted in accordance with FDA's Compliance Program Guidance manual 7348.811, Inspection Program for Clinical Investigators. The inspections represented **11%** of the total subjects enrolled in **P08067**. The inspection assignment included specific questions in reference to the study protocol and verification of the study data on safety and efficacy endpoints submitted by the sponsor in the BLA. The following table identifies the inspection results:

### INSPECTION OF CLINICAL SITES AND OUTCOMES

<b>Site</b>	<b>Location</b>	<b>Subjects Enrolled</b>	<b>FDA Form 483 Issued</b>	<b>Inspection Final Classification</b>
11	Rochester, New York	19	No	NAI
18	Upland, Pennsylvania	23	No	NAI
55	Ypsilanti, Michigan	18	No	NAI
116	Medford, Oregon	32	No	NAI
127	High Point, North Carolina	24	No	NAI
308	Quebec, Canada	45	No	VAI

Classification: NAI – No Action Indicated;VAI- Voluntary Action Indicated

### FINANCIAL DISCLOSURE

The Clinical Investigator Compliance Program directs the FDA investigator to ask the clinical investigator if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any subinvestigators, spouse(s) and dependent children, and if and when the information was updated. The inspections were conducted in accordance with the compliance program.

### INSPECTIONAL FINDINGS

#### Sponsor/Monitor Issues

A review of the Establishment Inspection reports (EIR) of the six clinical investigator study sites did not reveal any sponsor or monitoring issues.

#### Clinical Investigator Study Site Issues

Site 11: The inspection revealed no deviations from applicable regulations.

Site 18: The inspection revealed no deviations from applicable regulations.

Site 55: The inspection revealed no deviations from applicable regulations

Site116: The inspection revealed no deviations from applicable regulations

Site127: The inspection revealed no deviations from applicable regulations

Site308: The inspection revealed three subjects had Early Termination (ET) visits that included physical exams (PE) performed by the study coordinator. This procedure was to be performed by the Clinical Investigator or Sub Investigator only and not delegated to the study coordinator.

### BIMO ADMINISTRATIVE FOLLOW-UP

Letters were issued to the clinical investigators after complete review of the EIRs. Should you have any questions or concerns about the content of this memo or any aspect of Bioresearch Monitoring, please contact me at 301-827-6335.

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Lillian Ortega  
Consumer Safety Officer

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HFM-481	Rana Chattopadhyay, RPM
HFM-481	Juan Lacayo, RPM
HFM-650	Gilliam Conley

Draft : Ortega 11/20/2013

Review : Holobaugh