

MEMORANDUM

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

DATE January 12, 2017

FROM Colonious King, Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality
Telephone: 240-402-8759 Fax: 301-595-1304

THROUGH Patricia Holobaugh, Chief, Bioresearch Monitoring Branch

THROUGH Carrie Mampilly, Director, Division of Inspections and Surveillance

TO Colleen Sweeney Chair, Review Committee
Kathleen Hise Clinical Reviewer
Matthew Steele RPM
Taruna Khurana RPM

SUBJECT Bioresearch Monitoring Discipline Review Memo
BLA/STN: 125592/0
IND: 15015
Sponsor: Merck, Sharp and Dohme Corporation
Product: House dust mites allergen extract (MK-8237)

FINAL SUMMARY STATEMENT:

The Bioresearch Monitoring (BIMO) inspections were completed at one domestic, and one foreign clinical study sites conducting study P05607/001-00 in 151 subjects. The study was conducted under IND 15015. A review of the Establishment Inspection Reports (EIRs) did not reveal problems that impact the data submitted in this Biologics Licensing Application (BLA).

BACKGROUND

Two clinical investigators were inspected in support of the BLA and the inspections were conducted in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators. The inspection assignments were issued for protocol P05607/001-00. The conduct of this protocol was reviewed during the BIMO inspections. The two clinical sites were selected based on subject enrollment for each protocol, previous inspectional history, and geographic location.

The inspection assignment included specific questions related to the study protocols and verification of the study data on safety and efficacy endpoints submitted by the sponsor in the BLA. Protocol P05607/001-00 was conducted at 182 sites worldwide. 4497 subjects were screened for the study and 1482 subjects were randomized in the study. The two inspected sites randomized 151 subjects which is 10% of the total subjects randomized for the study. The information submitted in the BLA was compared to source documents at the inspection sites.

PROTOCOLS AUDITED

A one-year placebo-controlled study evaluating the efficacy and safety of the house dust mite sublingual allergen immunotherapy tablet (SCH 900237/MK 8237) in children and adult subjects with house dust mite-induced allergic rhinitis/rhinoconjunctivitis with or without asthma. (Protocol No. P05607/001-00)

The table below summarizes the inspection results:

| Site Numbers | Study Site | Location | Enrolled Subjects | 483 Issued | Classification |
|--------------|---|---------------------------|-------------------|------------|----------------|
| 217 | Inflamax Research Inc. | Ontario, Canada | 132 | No | NAI |
| 89 | Timber Lane Allergy & Asthma Research, LLC. | South Burlington, Vermont | 19 | Yes | VAI |

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 s/he disclosed information about her/his financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children including if and when the information was updated. The inspected study sites had a copy of the financial disclosure forms on hand for the clinical investigator and sub-investigators.

INSPECTIONAL FINDINGS

Sponsor/Monitor Issues

There were no sponsor/monitor issues identified at the study sites audited.

Clinical Investigator (CI) Study Site Issues

Study Site 217: A Form FDA 483 was not issued at close of this inspection and the inspection was classified as NAI. A review was conducted of testing records, regulatory binders, study specific standard operating procedures, and general study conduct. In addition, source documents were reviewed and the information was compared to the data tables submitted by the sponsor in the application. No discrepancy was found between source documents at the site and the data submitted by the sponsor in the application.

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Study Site 89: The FDA investigator noted a few minor problems during the inspection. A review was conducted of testing records, regulatory binders, study specific standard operating procedures, and general study conduct. Informed consent was not properly documented in that the written informed consent used in the study was obsolete, having been replaced by an updated version, for three subjects. Not all research activities were approved by an Institutional Review Board prior to implementation. A Form FDA 483 was issued at close of this inspection and the inspection was classified as VAI.

BIMO ADMINISTRATIVE FOLLOW-UP

Information letters will be issued for the study sites inspected.

Please contact me should you have any questions about this memo or any aspect of Bioresearch Monitoring.

Colonious King
Consumer Safety Officer

Distribution

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|-----------------|-------------------|
| EDR | STN 125592/0 |
| Colleen Sweeney | Chair |
| Kathleen Hise | Clinical Reviewer |
| Matthew Steele | RPM |
| Taruna Khurana | RPM |
| Tawny Colling | FDA Investigator |
| Darin Wiegiers | FDA Investigator |

Draft: King: January 10, 2017

Reviewed: Holobaugh: January 12, 2017