RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125473/0 Office: OVRR

Product: Timothy Grass Pollen Allergen Extract

Applicant: Merck Sharp & Dohme Corp.

Telecon Date/Time: 06-Feb-2014 11:25 AM Initiated by FDA? Yes

Telephone Number:

Communication Categorie(s): 1. Advice; 2. Information Request

Author: RANA CHATTOPADHYAY

Telecon Summary: Advice on submission of the revised stability data and information request for including CAPA reports along with that stability data

FDA Participants: Rana Chattopadhyay

Non-FDA Participants: Scott Greenfeder

Trans-BLA Group: No; Related STNs: None; Related PMCs: None

Telecon Body:
From: Chattopadhyay, Rana
Sent: Thursday, February 06, 2014 11:25 AM
To: 'Greenfeder, Scott'
Cc: Lacayo, Juan; Daugherty, Jon
Subject: RE: CMC information regarding BLA 125473

Scott:
Thanks for the information. Please include the CAPA reports along with the revised stability data in the proposed amendment.

Regards.

Rana

From: Greenfeder, Scott [mailto:scott.greenfeder@merck.com]
Sent: Wednesday, February 05, 2014 2:07 PM
To: Chattopadhyay, Rana; Lacayo, Juan
Subject: CMC information regarding BLA 125473

Dear Juan/Rana,

On 22 October 2013, the applicant submitted 36 months long term stability data for the Grastek drug product Process Validation (PV) batches (b)(4) stored at real time conditions of 25°C (b)(4) °C (b)(4) in the response to comment 42 (Attachment 1: Table 1 through 6) received in CBER's Information Request of September 16, 2013.

Following this submission, the 36 months results for the FDA competition ELISA were re-examined and invalidated due to the conclusions reached during an investigation of potential OOS results of two Grastek batches that were below the acceptance criteria.

All results generated with the FDA competition ELISA showed a downward shift in potency since April 2013 resulting in consistently low potency results close to the lower acceptance limit for release (b)(4). This downward shift in potency was not observed in the (b)(4) assays: (b)(4) . The investigation showed that the root cause of this systematic error was caused by a specific lot of detection antibody ((b)(4)). Therefore, all test results that were generated, during the period of April 2013 to October 2013, with this specific detection antibody lot were invalidated. Another qualified detection antibody lot was used to perform the retesting, resulting in potency values of the drug product lots close to (b)(4) (n=3).

Because the PV, 36 month stability time points cannot be recreated, samples were tested at (b)(4) by the FDA competition ELISA and valid test results were obtained using a previously qualified detection antibody. These data are provided in the Attachment provided (Table 1 through Table 6). The (b)(4) potency results are in alignment with the previous time points and are in agreement with the (b)(4) stability results. The additional data points demonstrate that there are no stability trends showing that there is no impact on the conclusions of the drug product stability studies and continue to support that the Grastek drug product is stable at 36 months when stored at 25°C (b)(4) °C/(b)(4)

Two corrective and preventive actions (CAPAs) were initiated to prevent recurrence. One CAPA was initiated to establish a supply of detection antibody that gives acceptable performance. The other CAPA was initiated to improve the control procedures applied before introduction of new batches of the detection antibody for use in the FDA competition ELISA.

We wanted to give you advanced notice of this issue. We will submit the revised stability data as an amendment to the BLA.

Regards,
Scott