Memorandum

Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Compliance and Biologics Quality
Division of Manufacturing and Product Quality

To: **STN 125473 Timothy Grass Pollen Allergen Extract**

From: Deborah Trout, BLA Committee Member, OCBQ/ DMPQ/MRB1 HFM-675

Through: Carolyn Renshaw, Branch Chief, MRB1, DMPQ, OCBQ, HFM-675

Subject: Review of BLA-amendment 125473/0.13 received November 11, 2013

Action Due: April 7, 2014

Recommended Action: Merck's response to item 4 appears acceptable. Merck has adequately responded to all review issues identified. Outstanding inspectional issues will be addressed in a separate review memo. Once all inspectional items have been resolved I will recommend approval.

Review Narrative

FDA Comment 4:
Concerning your response dated May 3, 2013 to our request for information dated April 23, 2013. You did not provide validation data for the (b)(4) assay (IR comment 7) as requested. Please provide method validation to support the use of this assay. Your response should address the following:

- Does your package have adequate (b) (4) characteristics to test using the (b)(4) method?
- Is the (b)(4) standardized? Is (b)(4) added to the mixture? If so, to what concentration.
- What amount of (b)(4) is an operator able to visually see?
- Are you using a positive control (b)(4)) and have you challenged the procedure to determine what (b)(4) operators can detect?
- Do you challenge the method regularly to confirm its ability to detect defects?

Merck Response:

The (b)(4) Test ((b)(4)) is used as an in-process manufacturing control test to confirm the performance of the (b)(4) operation. This method is used (b)(4) test which is used for testing (b)(4) The questions posed by CBER for the (b)(4) method are consistent with the approach suggested in the article (b)(4) . The applicant has calculated and evaluated the (b) (4) characteristics of MK-7243 Timothy Grass Pollen Allergen Extract tablet blister package as described below. The results provide a high level of confidence that the (b)(4) method is effective at detecting defects.

The applicant will perform additional testing in order to further confirm and characterize the ability of the (b)(4) method to detect defects. The applicant proposes to provide this information to CBER post-licensure in the annual report.

Merck was sent the following information via email on March 31, 2014:

Please **do not** submit the additional characterization and testing information for the (b)(4) Test post licensure in the annual report. This information will be reviewed and verified during Catalent's next routine inspection.

1. Does your package have adequate (b) (4) characteristics to test using the (b)(4) method?

(b)(4)

(b)(4)

[redacted]

2. Is the (b)(4) standardized? Is (b)(4) added to the mixture? If so, to what concentration.

(b)(4)

[redacted]

(b)(4)

3. What amount of (b)(4) is an operator able to visually see?

(b)(4)

(b)(4)

4. Are you using a positive control ((b)(4)) and have you challenged the procedure to determine what (b)(4) can detect?

The applicant has not conducted studies using a positive control. This will be the subject of future studies and the applicant proposes to inform CBER of the completion of these studies

post-licensure. The applicant would like to note that (b)(4)

5. Do you challenge the method regularly to confirm its ability to detect defects?

The applicant currently does not challenge the (b)(4) method on a regular basis to confirm its ability to detect defects. Future studies to challenge the (b)(4) procedure will be conducted in order to evaluate and establish a suitable challenge method that can be applied. The applicant would like to note that the equipment ((b)(4)) used by the (b)(4) method is calibrated on a regular basis according to Catalent's (drug product manufacturer) governing procedures.

In summary, the applicant concludes that the (b) (4) characteristics of the MK-7243 Timothy Grass Pollen Allergen Extract tablet blister package provide a high level of confidence that the (b)(4) method is effective at detecting defects. The applicant will perform additional testing in order to further confirm and characterize the ability of the (b)(4) method to detect defects. The applicant proposes to provide this information to CBER post-licensure in the annual report.

Merck was sent the following information via email on March 31, 2014:

(b)(5)

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